

# POSITIVE

FA 1403 - POSITIVE

Interindividual variation in response to consumption of plant food bioactives and determinants

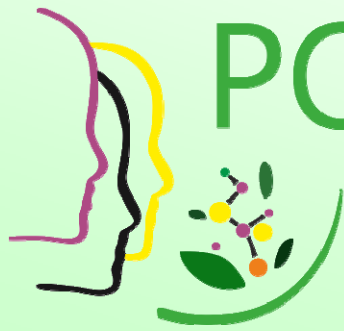
## NEWSLETTERS 2015-2018



EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY

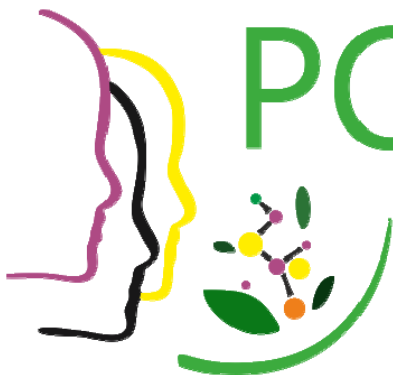


COST is supported by the EU Framework Programme Horizon 2020



# POSITIVE

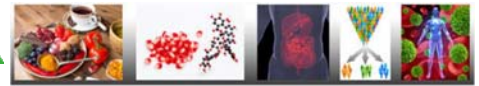
ISSUE 1



# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE 1, JUNE 2015

## WELCOME

On behalf of Iwona Kieda (Focus Group co-leader) and myself, we would like to welcome you to the first issue of POSITIVE e-newsletters. We also want to thank the rest of the FG members and all the partners for their help during the production of this document.

The aims of this publication are to keep you informed of all the events, outcomes, initiatives and updates concerning POSITIVE COST Action and to encourage the building of rapport and networking among us. We very much hope that you find the contents attractive, stimulating and a valuable resource for collecting information related to POSITIVE primary objectives and partners.

POSITIVE e-newsletters will be e-mailed twice yearly and will also be accessible through the website. Any member that might have not received this document and would like to, please, contact us and send your e-mail address so that we can update the list of subscribers. The success of this

e-newsletter depends, in part, on the support and contributions of the partners and thus, we welcome your suggestions and feedback.

Please send your comments and proposals via e-mail to Iwona Kieda ([i.kieda@pan.olsztyn.pl](mailto:i.kieda@pan.olsztyn.pl)) and/or to María-Teresa García-Conesa ([mtconesa@cebas.csic.es](mailto:mtconesa@cebas.csic.es)).

Yours sincerely  
María-Teresa García-Conesa, PhD  
FG leader



## NEWS FROM THE ACTION

### POSITIVE Inaugural Meeting 11<sup>th</sup> December 2014, Brussels, Belgium



The inaugural meeting of the COST Action FA1403 POSITIVE was held in Brussels the past 11<sup>th</sup> of December 2014. The meeting was attended by POSITIVE partners from 29 countries: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Luxemburg, Macedonia,

the Netherlands, Norway, Poland, Portugal, Romania, Serbia, Spain, Sweden, Switzerland, Turkey, and the United Kingdom. The participants were welcomed by the COST Office representatives - Ioanna Stavridou, Scientific Officer and Christophe Peeters, Administrative Officer. Ioanna gave a briefing on the COST mechanisms of action, presenting the general framework for this programme specifically created to promote scientific and technical cooperation in Europe. Next, Christophe Peeters informed the delegates about the principles and procedures related to the COST Actions and about the possibilities of getting activities funded by the COST budget.

Following COST officers presentations, the Management Committee elected Dr. Christine MORAND (FR) to the Chair of COST Action FA1403 and Dr. Francisco Tomas-Barberan (ES) to Vice-Chair, while INRA was approved as the **Grant Holder Institution**. Subsequently, the Action Chair presented POSITIVE to the attendees, highlighting its main aims:

(i) to create an open European scientific network to tackle the question of the interindividual variation in response to plant food bioactives consumption

(ii) to work with the industry and regulatory authorities to translate the findings into innovation and refinement of

## POSITIVE Inaugural Meeting cont.

dietary recommendations. The Action will be organized into a Management Committee (MC), a Steering Committee (SC), three main Working Groups (WGs) and a Focus Group (FG) which will devote their efforts to the development and achievement of the POSITIVE objectives.

**Working Group 1: Interindividual variation in bioavailability;** Leader: Tom Van de WIELE (University of Ghent, Belgium), Co-Leader: Rikard LANDBERG (Swedish University of Agricultural Science, Sweden)

**Working Group 2: Interindividual variation in the biological responsiveness regarding cardiometabolic endpoints;** Leader: Ana RODRIGUEZ-MATEOS (University of Dusseldorf, Germany), Co-Leader: Jaap KEIJER\* (University of Wageningen, the Netherlands)

**Working Group 3: From emerging science to applications;** Leader: Baukje De ROOS (Rowett Institute, Aberdeen, UK), Co-Leader: Marina HEINONEN (University of Helsinki, Finland)

**Focus Group: Communication and Dissemination of scientific information;** Leader: Maria-Teresa GARCIA CONESA (CEBAS-CSIC, Murcia, Spain), Co-Leader: Iwona KIEDA (Institute of Animal Reproduction and Food Research, Olsztyn, Poland)

The Working Groups and Focus Group have been invited by the MC to cooperate as closely as possible and to ensure the necessary flow of information. It was also agreed that Aleksandra KONIC-RISTIC (University of Belgrade, Serbia) would hold the responsibility for the Short Term Scientific Mission (STSM) coordination. All members of the MC have been invited to encourage young scientists to participate in this scheme. The applications for STSM should be sent to Aleksandra KONIC-RISTIC at the Institute for Medical Research, Centre of Research Excellence in Nutrition and

Metabolism, University of Belgrade, Serbia. For 2015, POSITIVE ost Action will fund 2 STSMs (only for 1<sup>st</sup> Call).

To facilitate communication between the members of the Action and to promote distribution of information on the research activities performed in the field of COST Action FA1403, the website of POSITIVE will be maintained and hosted by the Grant Holder Institution INRA. In addition, MC members have been invited to support the Action Chair in building up an informative website by providing adequate information material.



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\* Due to a greater workload at the University, Prof. Jaap KEIJER (Wageningen University, The Netherlands) who attended the opening meeting in Brussels as the WG2 co-leader has had later to renounce to this position. However Prof J. Keijer and his research group will remain active participants in the network. At present, Dr. Eileen Gibney (University College Dublin, Ireland) has been approached to become the new WG2 co-leader and her nomination will be submitted to the approval of the MC during its next MC meeting in Murcia (September 2015).

## SAVE THE DATE

**22 - 23 September, 2015**

**WORKING GROUPS 1,2 & 3 AND FOCUS GROUP MEETING  
MANAGEMENT COMMITTEE & STEERING COMMITTEE MEETINGS**

**Venue: Scientific Park, Campus de Espinardo, MURCIA (SPAIN)**

Organized by **Prof. Francisco Tomas Barberan** and **Dr. Maria-Teresa Garcia-Conesa** from the Spanish Research Institution **CEBAS-CSIC**.



## POSITIVE Opening Meeting, 24-26 March, 2015, Belgrade, Serbia

The **first working meeting of the COST Action POSITIVE** was successfully held at the Best Western Hotel M, in Belgrade the past 24<sup>th</sup> to 26<sup>th</sup> of March. From the FG and on behalf of all the POSITIVE participants, we would like to thank and congratulate Professor Maria Glibetic and her team for the warm welcoming to Belgrade and the excellent organization of the meeting. During this 1<sup>st</sup> meeting attendants had the opportunity to meet with each other and to start working on the various tasks of the Action while enjoying a very friendly and relaxed atmosphere.

Due to the importance of the activities within the WG1

and WG2 and a considerable number of participants in these WGs, the leaders proposed to involve second co-leaders to ensure a smooth running of the actions planned. The second co-leaders were chosen with reference to the complementarity of their expertise and their willingness to actively contribute to the management of the activities. Claudine Manach and Dragan Milenkovic were proposed by Tom Van de Wiele and Ana Rodriguez-Mateos as second co-leaders of WG1 and WG2, respectively. These propositions have been validated by the Steering Committee of the Action.

The main tasks proposed and objectives achieved by each WG during the meeting in Belgrade are summarized in this section.



*POSITIVE members attending the Opening Meeting in Belgrade, March 2015*

## 1<sup>st</sup> POSITIVE Scientific Workshop

The **1<sup>st</sup> Scientific Workshop** organized by POSITIVE will be held next **October 26-27, 2015 in Tours (FRANCE)** in satellite to the 7<sup>th</sup> International Conference in Polyphenols and Health (ICPH).

- ◆ The aim of this symposium is to raise awareness of the scientific community to the relevance of interindividual variability in the bioavailability and physiological responses to the consumption of plant food bioactives in relation to the prevention of cardiovascular and metabolic disorders.
- ◆ Invited scientists leaders in the area will review and present state-of-the-art information on the topic, as well as their views and perspectives in this emerging field.
- ◆ POSITIVE will contribute to the expenses of 50 to 60 partners attending the workshop by providing a fixed amount of 160 euros (covering 1 night at the hotel and 2 meals).
- ◆ Participation to this workshop is subjected to registration at <https://colloque.inra.fr/workshop-cost-positive-2015/Registration>.
- ◆ The detailed program is given on the website: <https://colloque.inra.fr/workshop-cost-positive-2015/Program>.



## RESEARCH HIGHLIGHTS

### Work Group 1



Prof. Tom Van de WIELE

WG1 Leader

POSITIVE's WG1 focuses on the creation of a database compiling existing knowledge on interindividual variation in the absorption, metabolism, distribution and excretion (ADME) of plant bioactives. This information

will be combined with the identification of candidate (human) genes that likely affect any of the ADME processes and thus provide an explanatory basis for between-subject differences. What's more, efforts are undertaken to grasp the interindividual differences that exist in gut microbiome composition and what impact this has on the metabolism and putative health effects of plant bioactives.



WG1 meetings in Belgrade, Serbia



An enthusiastic group of 35 scientists attended the meeting in Belgrade. The main organizational outcome was the creation of different subgroups (around 5 participants/group) focusing on either different plant bioactive families or methodological expertise. A leader was appointed for each of these subgroups who will oversee the activities and report to the WG1 (co-)leaders. A first task for the WG1 coordinators is the preparation of a template for literature extraction, which

can be conducted on the basis of suggested key words. WG1 coordinators will send out to WG1 participants a data entry template that takes into account the different ADME parameters and list of determinants. Working on the data input template, each compound subgroup will fix a set of key words which will serve as a basis for literature searches. Relevant papers will be filtered out and put in the database covering the different aspects on ADME or determinants affecting this (age, gender, etc.). In addition, metabolic pathways for 2 com-

pounds will be drawn and key metabolites, enzymes and genes will be identified. From the methodology subgroups (metabolomics/in silico, gene variants, microbiome variants) participants will work on a common database for metabolic pathways (gene variants group), identification of online resources where data from the POSITIVE network could be added (metabolomics/in silico group) and selection of one lead compound from 5 different chemical families (isoflavones, flavan-3-ols, lignans, ellagitannins and flavanones) for which variability in gut microbiome is known to lie at the basis of conversion efficiency. In addition, a questionnaire will be sent around to collect the interest of partners in following metabolomics training courses, while the different subgroups are also on the lookout for possible STSMs.

## RESEARCH HIGHLIGHTS

### Work Group 2



Dr. Ana RODRIGUEZ-MATEOS

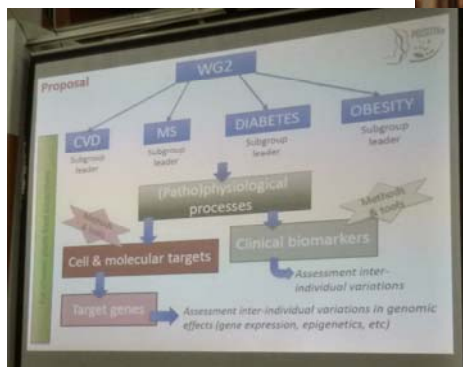
WG2 Leader

The first WG2 meeting of POSITIVE took off in Belgrade with the participation of 27 researchers. The aim of this WG is to assess the interindividual variation in selected clinical and molecular biomarkers of cardiometabolic risk in response to plant food bioactives consumption, and to investigate the main factors responsible for such variability.

The major goals for the 1<sup>st</sup> year are to decide the specific bioactives, clinical biomarkers and cell and molecular targets to evaluate and to initiate the search in the literature on the impact of plant food bioactives on those selected biomarkers and targets. The tools and methods to be used such as templates for data entry need also to be defined. The first point established was that the project would focus on cardiovascular diseases (CVD) and metabolic diseases (MD), i.e. metabolic syndrome, obesity and diabetes.

Next, the WG discussed: i) which bioactives and biomarkers would be considered and ii) which methodological approach would be used to best assess interindividual variability.

The work will be initiated by targeting only one group of bioactives and a few most relevant clinical biomarkers so that we could first test the feasibility of the methodological approach. Based on data availability and the WG2 expertise it was decided that 1) flavanols (from tea, cocoa and apples) and 2) the biomarkers blood pressure, flow-mediated dilation, blood lipids, platelet aggregation, exercise capacity, BMI, waist to hip ratio, HOMA-IR, insulin and glucose would be selected for the initial evaluation. The first step will be to begin the search in the literature to find relevant data that would be used later for the assessment of interindividual variability. The



WG2 was divided into various subgroups with specific tasks.

One subgroup will first produce a document with a list of standard rules for conducting systematic reviews as well as specific scientific criteria to be applied in the literature search. These criteria will be circulated to the WG2 partners so that they can start searching in the literature for the biomarkers and bioactives selected. The results obtained from all the participants will be merged in a common template for data entry that was also created during the meeting, and will be distributed to all WG2 members. A system for online data sharing (Google docs) was discussed and will be implemented so the literature search will be completed before the second Positive meeting this year. Further, it was proposed that animal and relevant cell studies looking at the impact of bioactives on cardiovascular and metabolic diseases will be reviewed with the aim of identifying other potential cell and



WG2 meeting in Belgrade, Serbia

molecular targets, which can then be used to create a list of candidate genes to investigate the available omics data from clinical studies.

A working subgroup will start preparing a proposal on how to address the search of cell and molecular targets and start looking for targets in the processes associated to the selected clinical biomarkers, using the bioactive flavanol as an example. It has been accepted that one of the criteria for the selection of papers for analysis must be experimental conditions: use of the right molecules (metabolites) at the right concentrations (physiologically relevant).

Further, a review on the existing knowledge regarding interindividual variation in biological responsiveness to plant food bioactives will also be conducted and published in a relevant journal this year.

## RESEARCH HIGHLIGHTS

### Work Group 3



**Prof. Marina HEINONEN**  
WG3 Co-Leader

**Dr. Baujke DE ROOS**  
WG3 Leader



A summary with the main activities to be developed by this group was presented at the meeting. The main tasks in WG3 are to: 1) Integrate key findings from WG1 & 2 and identify those with greatest interest for translation into applications, and 2) determine pertinent research priorities for Europe.

For the 1<sup>st</sup> year the most important activity is to identify and prioritise deliverables (from a long list of expected outcomes) that are most important for each of the different stakeholders and end-user groups.

- Identify various categories of stakeholder and end-user groups that are potentially interested in the topic and outcomes of POSITIVE
- ◆ *Initial inventory of important stakeholder groups*
- ◆ *Ask WG3 members to add further stakeholders and end-users, including contact details, to each of the groups*



*POSITIVE Opening Meeting in Belgrade, Serbia*

- Gather the views and expectations of the various stakeholder groups and end-user groups with respect to the importance of the various activities of the POSITIVE network
- ◆ *Development of a questionnaire to collect the views and expectations of various stakeholders and end-user groups*
- ◆ *Ranking of the deliverables of the Action that are of most importance to the stakeholders and end-users groups*



*Dinner during POSITIVE meeting in Belgrade, Serbia*

## SOCIAL NETWORKS

FIND US ON FACEBOOK:



<https://www.facebook.com/costpositive>





## RESEARCH HIGHLIGHTS

### Think Thank Group

The 1st Think-Tank Group meeting in Belgrade was an icebreaker meeting. The main aims of this first gathering were that Early Career Investigators (ECIs) involved in POSITIVE got to know each other and that all present ECIs voted and elected two members of the Think-Tank group to act as leaders and to represent them in the Steering Committee (SC). At the SC meetings the Think-Tank group leaders will have the



*POSITIVE Meeting in Belgrade, Serbia*

opportunity to regularly communicate the ideas & proposals produced by the ECIs.

In addition, they also defined a strategy to stay in contact and maintain work discussions between the two annual COST meetings. For this purpose, two propositions were made:

- 1) the implementation of an on-line forum system (asana.com or similar)
- 2) the organization of on-line meetings every two-three months by using the Going-to-meeting application.



*Laurent-Emmanuel Monfoulet and Mireia Urpi Sarda  
Think Thank Group Coordinators*

The Think-Tank group is currently engaged in the creation of a group within the LinkedIn Network designated as 'ECIs-POSITIVE' with the aim of putting all ECI's in contact so that they can get to know each other and start discussions of interest in relation to the main objectives of POSITIVE. LinkedIn allows for the free participation of a larger number of people than asana.com. They will initiate the process by individual presentations of the ECIs and the setting up of discussions on various different topics such as, for example, the formulation of new functional foods or drinks combining polyphenol rich products with deuterium depleted water which appears to enhance the absorption of bioactive compounds in cells. The first on-line meeting is planned to take place the last week of June.

## 7<sup>th</sup> International Conference on Polyphenols and Health



### Information:

<http://www.icph2015.com/>

### Registration and abstract submission:

<https://colloque.inra.fr/icph2015-registration/>  
Registration

## STSMs PROGRAM



**Dr. ALEKSANDRA  
KONIĆ-RISTIĆ**

*Institute for Medical  
Research,  
University of Belgrade,  
Serbia*

**Short-Term Scientific Missions (STSMs)** are exchange visits between researchers involved in POSITIVE aimed at supporting scientists to visit an institution or laboratory in another partner country, strengthening the existing networks, fostering collaborations and promoting the development/learning of new techniques/methods, etc. STSMs are selected on the basis of their contribution to POSITIVE objectives.

STSMs successfully implemented will provide knowledge to be used in future work & research within the Action. STSMs are intended especially for young researchers.

**Application Information and Rules** are available from the Action website <http://www6.inra.fr/cost-positive>.

**After completion of the STSMs**, successful applicants are invited to prepare a short report (preferably accompanied with photographs) to be placed at the Action website as well as in the newsletters.

**Contact:**

POSITIVE STSM Coordinator  
Dr. Aleksandra KONIĆ RISTIĆ  
Institute for Medical Research  
Centre of Research Excellence in Nutrition and Metabolism  
University of Belgrade, Serbia  
E-mail: [sandrakonic@gmail.com](mailto:sandrakonic@gmail.com)  
Tel: +381 11 4061747

## THEMATIC TRAINING COURSES

Multidisciplinary training courses in areas relevant to the primary objectives of POSITIVE. The courses will be directed, principally, to early stage researchers with the aims of:

- i) enhancing their knowledge on interindividual variation in response to the consumption of plant bioactives and factors involved
- ii) developing their leadership skills for future European research. Detailed information about the training courses will be announced *via* the POSITIVE website and the e-newsletters.



## SCHOOL TRAINING PROPOSALS

**1<sup>st</sup> announcement on  
NUTRIMETABOLOMICS TRAINING**

**Coordinator:** Rafael Llorach, PhD  
University of Barcelona

(further details will be communicated later on in the year and at the POSITIVE website)



*Rafael Llorach, PhD*

## SCIENTIFIC EXPERT'S OPINION

### *POSITIVELY looking at the Future of Personalized Nutrition*

Ecological, case-control and cohort studies have reported associations between specific dietary patterns and risk of chronic diseases<sup>1</sup>. However, these investigations are observational in nature and do not provide the required level of scientific evidence typical of interventional studies based on controlled trials. This has resulted in recommendations and guidelines lacking solid scientific support and mechanistic evidence of causality. More recently, intervention studies have provided some support about the benefits of a Mediterranean dietary pattern<sup>2</sup>, or lack of support for a low fat diet<sup>3</sup>. Nevertheless, these global results and conclusions still lack mechanistic evidence and, most important, mask an important fact for the individual: each one of us is different, behave different and respond different to any type of intervention, whether this is pharmacological or nutritional.

The variability in response to therapies has a well-known fact in clinical practice and scientific literature. For example, reports from about a century ago go back and forth about the required doses of calcium for healthy bones and highlight the dramatic interindividuality in response observed among the study participants<sup>4</sup>. The reasons for this variability were mostly unknown, as these investigators lacked the technology and the knowledge that were going to be generated during the ensuing decades thanks to the advances in genetics. Today, three decades after we could start perusing into our genome in search of variants and one decade after the completion of the human genome project, we have much more advanced technology, some knowledge and above all, tremendous curiosity to gain more in depth understanding about the mechanistic bases of dietary response that should take us into an era of more solid, personalized and successful dietary guidelines aimed to prevent the common chronic diseases that represent such a high toll to our society.

Since the mid-eighties we have been making humble progress towards a better understanding of the genetic basis of variability in response. However, we had serious technological and experimental constraints, with studies that were generally woefully underpowered and therefore with very low level of replication and validation. More recently, with the creation of international consortia and combined populations amounting to hundreds of thousands of individuals, we are starting to get a more complete and reliable picture of the genetic basis of response. Thus, we have shown how certain genes modulate the relation between intake of Zinc and diabetes, uncovering a segment of the population for whom dietary intake may not be enough to reach the necessary protection<sup>5</sup>. Regarding the Mediterranean diet, we have seen how certain carriers of certain genotype of the TCF7L2 gene are

**Dr. JOSE M<sup>a</sup>  
ORDOVAS**

*Director  
of the Nutrition and  
Genetics Laboratory,  
Boston University, USA*

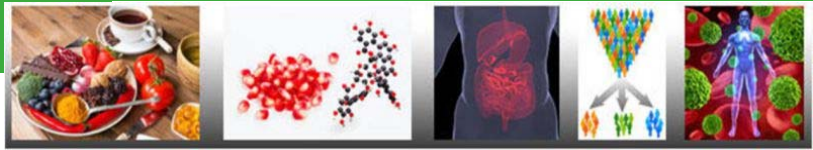


specially benefited by this dietary pattern in terms of stroke protection<sup>6</sup>. However, most of the studies have focused on macronutrients (i.e., dietary fat), leaving a huge gap of knowledge regarding other micronutrients and non-nutrients components of our food. This is especially true for the bioactive components of plants, which seem to be behind many of the health effects attributed to fruits and vegetables. This is obviously a much larger endeavor than the ones that we had tackled in the past. First, unlike for macronutrients, there are thousands of these bioactives and they are not well characterized or measured in the food databases. Second, there is a large variability in their concentrations across geography and time. Therefore, given the importance of these compounds in the health benefits of our diets, it is essential that we create consortia of investigators from multiple disciplines to tackle successfully this highly relevant but difficult challenge. POSITIVE has all the necessary "ingredients" to make this possible, combining expertise from all the fields from bioactive isolation to human genetics. The integrated activities of these investigators will, no doubt, provide the solid foundation for the development of this specific area of knowledge that will result in most relevant advances in the areas of nutrigenomics and nutrigenetics, ultimately leading to sound and successful personalized nutrition.

#### References:

- <sup>1</sup>Grosso G, Mistretta A, Frigiola A, Gruttadauria S, et al. 2014. Mediterranean diet and cardiovascular risk factors: a systematic review. *Crit Rev Food Sci Nutr* 54: 593–610.
- <sup>2</sup>Estruch R, Ros E, Salas-Salvadó J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med*. 2013 Apr 4;368(14):1279-90.
- <sup>3</sup>Howard BV, Van Horn L, Hsia J, et al. Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA*. 2006 Feb 8;295(6):655-66.
- <sup>4</sup>Outhouse J, Kinsman G, Sheldon D. The Calcium requirements of 5 preschool girls. *J Nutr*. 1939; 17:199-211.
- <sup>5</sup>Kanoni S, Nettleton JA, Hivert MF et al. Total zinc intake may modify the glucose-raising effect of a zinc transporter (SLC30A8) variant: a 14-cohort meta-analysis. *Diabetes*. 2011 Sep;60(9):2407-16.
- <sup>6</sup>Corella D, Carrasco P, Sorlí JV, et al. Mediterranean diet reduces the adverse effect of the TCF7L2-rs7903146 polymorphism on cardiovascular risk factors and stroke incidence: a randomized controlled trial in a high-cardiovascular-risk population. *Diabetes Care*. 2013 Nov;36(11):3803-11.

## RESEARCH DISSEMINATION



The aim of this section is to regularly present to all partners and subscribers of this e-newsletter the specific research carried out and published by POSITIVE partners that is relevant to the ACTION objectives and expected outcomes.

The work will be shown as a brief summary of the publication, highlighting the key points related to variability in human bioavailability and responsiveness to plant bioactives.

The full reference and pictures of author(s) will also be included.

This section will also include other communications and presentations of POSITIVE contributing to the dissemination of this COST Action or of the results generated by the research carried out under the frame of POSITIVE .

## COST ACKNOWLEDGEMENTS

The COST office recommends the following sentences to acknowledge the COST Action FA1403 in all publications & communications in the research area of POSITIVE. The partners may select the most appropriate ones:

**1. For works at least partially inspired by exchanges fostered by an Action or benefiting from the coordination provided by an Action, regardless of the number or the status of authors, following text shall be used:**

The author(s) would like to acknowledge the contribution of the COST Action FA 1403 POSITIVE (Interindividual variation in response to consumption of plant food bioactives and determinants involved).

OR

The authors are participating to the COST Action FA 1403 POSITIVE (Interindividual variation in response to consumption of plant food bioactives and determinants involved).

**2. For works co-authored by at least two WG/MC members from at least two different countries participating to the Action:**

The author(s) would like to acknowledge networking support by the COST Action FA 1403 POSITIVE (Interindividual variation in response to consumption of plant food bioactives and determinants involved).

**3. For outputs of Short-Term Scientific Missions:**

This work was supported by a STSM Grant from COST Action FA 1403 POSITIVE (Interindividual variation in response to consumption of plant food bioactives and determinants involved).



## FIND POSITIVE on EUFIC

EUFIC is a non-profit organisation established to communicate science-based information on nutrition and health, food safety and quality, to help consumers to be better informed when choosing a well-balanced, safe and healthy diet.



RESEARCH DISSEMINATION

Publications & Communications

Claudia N. Santos, *Instituto de Biologia, Portugal*

Gary Williamson, *School of Food Science and Nutrition, UK*



doi:10.1017/S0007114514003511

*British Journal of Nutrition* (2015), 113, 454–463  
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**Phenolic sulfates as new and highly abundant metabolites in human plasma after ingestion of a mixed berry fruit purée**

Rui C. Pimpão<sup>1,2</sup>, M. Rita Ventura<sup>1</sup>, Ricardo B. Ferreira<sup>1,3</sup>, Gary Williamson<sup>4</sup> and Claudia N. Santos<sup>1,2\*</sup>

<sup>1</sup>*Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Avenida da República, EAN, 2781-901 Oeiras, Portugal*

<sup>2</sup>*Instituto de Biologia Experimental e Tecnológica, Apartado 12, 2781-901 Oeiras, Portugal*

<sup>3</sup>*Instituto Superior de Agronomia, Universidade de Lisboa, Tapada da Ajuda, 1349-017 Lisboa, Portugal*

<sup>4</sup>*School of Food Science and Nutrition, University of Leeds, Leeds LS2 9JT, UK*

(Submitted 30 May 2014 – Final revision received 23 September 2014 – Accepted 3 October 2014 – First published online 9 January 2015)

This recent article by Pimpão et al. (*Br. J. Nutr.*, 2015) is a joint publication between POSITIVE partners: Universidade Nova de Lisboa, Instituto de Tecnologia Química e Biológica (Portugal) and, the University of Leeds, School of Food Science and Nutrition (UK). Using a combination of HPLC–MS/MS and chemically synthesized compounds the researchers have identified and quantified a number of plasma circulating metabolites following the ingestion of mixed berry fruits rich in polyphenols. The study focuses on colonic metabolites, especially those conjugated with sulfate groups. With regard to POSITIVE primary objectives, this article fits within the objectives of WG1 and highlights two important points:

1.- The need to identify **colonic metabolites and determine their kinetics of appearance** in plasma. These metabolites might have been so far underestimated and may well be involved in the benefits of polyphenols against cardiovascular diseases.

2.- The kinetic results presented in the article constitute a valuable example of the **large variability in absorption and metabolism data**. Indeed, the authors claim in several occasions that data: ...'have been averaged only when present in six or more volunteers'..., ...'quantified only in four volunteers'..., ...'were found in several volunteers'..., ... 'variability was high for all the quantified metabolites'...

Human studies like the one presented here are still much needed in order to improve our understanding of the bioavailability of polyphenols. However, and as for many other studies of the sort, the number of participants is still very low and does not yet allow for significant stratification of the volunteers between those with a high response (high levels of metabolites), medium response or no-response (individuals that are not able to produce metabolites). Future research in the area should pursue meaningful stratification of the sample population following their degree of response.

RESEARCH DISSEMINATION

Publications & Communications

Paper co-authors of the POSITIVE team from the University Antwerp (Belgium)

vel Szcic et al. *Clinical Epigenetics* (2015) 7:33  
DOI 10.1186/s13148-015-0068-2



CLINICAL  
EPIGENETICS

REVIEW

Open Access

## From inflammaging to healthy aging by dietary lifestyle choices: is epigenetics the key to personalized nutrition?

Katarzyna Szarc vel Szcic<sup>1</sup>, Ken Declerck<sup>1</sup>, Melita Vidaković<sup>2</sup> and Wim Vanden Berghe<sup>1\*</sup>

This recent article by Szarc vel Szcic et al. (*Clin. Epigenetics*, 2015) is a joint publication of COST FA1403 POSITIVE partner University of Antwerp, Department of Biomedical Sciences (Belgium) and CM1406 EPICHEM partner University of Belgrade (Serbia). In this review, the researchers summarize the epigenetic effects (i.e. changes in DNA methylation, chromatin, microRNA, noncoding RNA patterns) of dietary components, including phytochemicals, and macro- and micronutrients as well as metabolites, which attenuate low-grade systemic inflammation during physiological aging, also known as 'inflammaging'. The heterogeneity in biological aging, chronological age, and aging-associated cardiovascular disorders in humans have been related to choices in dietary lifestyle.

In relation to POSITIVE main objectives, this article highlights important aspects related to both WG1 (bioavailability of bioactives) and WG2 (individuals response to bioactives intake) with a special focus on the role of epigenetics on variability: For some bioactive nutrients individuals can be categorized into poor, intermediate, or extensive absorbers or metabolizers based on the presence of genetic

single-nucleotide polymorphisms (SNPs) in enzymes with known relevance to drug pharmacokinetics, such as detoxification enzymes and transporters. However, pharmacogenomic studies alone are insufficient to explain the large interindividual variation in nutritional responses. In recent years, evidence has accumulated that epigenetic changes in key ADME genes (genes related to drug absorption, distribution, metabolism, and excretion) involved in the metabolism and distribution of phytochemicals also contributes to interindividual variations in the nutritional response.

Personalized nutrition is an increasingly recognized paradigm in nutri-epigenetic research. Therefore, some population subgroups may gain more benefit than others from the consumption of plant foods and their bioactives. The further determination of environmental-epigenetic factors responsible for interindividual variations in the endocrine system, metabolism, microbiome communities and the identification of 'susceptibility profiles' in response to plant bioactive consumption could lead to targeted dietary advice and use of functional foods customized for different population subgroups.

## POSITIVE DISSEMINATION

POSITIVE was presented to the general public at a **EUROPE DIRECT** (<http://europa.eu/europedirect/>) meeting held at the European Centre for Industry and Innovation (CEEIM, University Campus of Murcia, SPAIN) on the 3<sup>rd</sup> of March (2015). The EUROPE DIRECT service **aims to:**

i) enhance the visibility of the EU actions in matters of education, mobility, employment, citizenship, R+D, environment, etc,

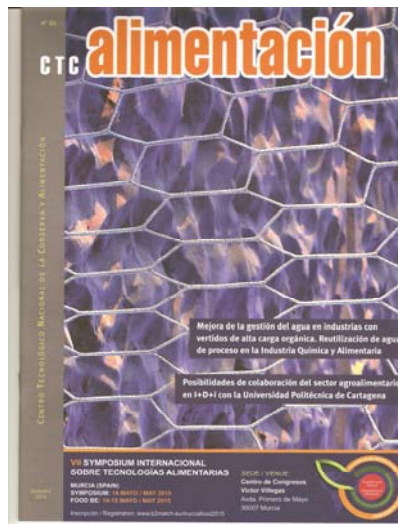
ii) encourage citizens' participation stressing the relevance and impact of the European institutions in everyday life.

The Europe Direct office in Murcia has launched several campaigns in this direction ("Me, European citizen") to strengthen the sense of the EU membership. The past meeting celebrated at the University of Murcia was part of this strategy and included invitations to researchers from Murcia taking part in European programs and projects. Dr. María-Teresa García-Conesa attended this meeting and explained to the audience the objectives and relevance of the COST Action POSITIVE.



*Dr. Maria-Teresa Garcia Conesa, FG leader of POSITIVE, during her presentation of POSITIVE at the Europe Direct meeting in Murcia (SPAIN)*

POSITIVE was announced at the December-2014 edition of the local Spanish journal 'CTC Alimentación'. The CTC is the National Technological Centre for the Food and Canning Industry (<http://www.ctnc.es>) located in Molina de Segura, Murcia, SPAIN. CTC's main aim is to promote research, innovation, competitiveness and internationalization of the Spanish Agrofood sector. CTC activities are related with technology transfer, training and dissemination.



# INFOGEST

POSITIVE was introduced to members of the COST Action INFOGEST. On the occasion of the final conference of the COST Action INFOGEST, held in Naples from the 17<sup>th</sup> to 19<sup>th</sup> of March 2015, Dr. Christine Morand was invited to present the outline and objectives of POSITIVE to the members of the INFOGEST network. At present, several participants involved in INFOGEST and working on the digestion of food bioactives have joined POSITIVE.

## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS

- **What is the focus of your research?**

Nutrigenetics: Identifying dietary strategies to counteract the impact of an 'at-risk' genotype and the genetic determinants of highly heterogeneous physiological responses to dietary change, with a particular focus on *APOE* genotype.

- **In what countries/organisations have you studied or worked?**

BSc in Nutrition and Biochemistry at University College Cork (UCC), Ireland, 1988-1992

PhD at the Institute of Food Research, Norwich, UK, 1992-1996

Hugh Sinclair Nutrition Group, University of Reading, UK, 1997-2009

School of Medicine, University of Auckland, NZ, 2009-2010

Norwich Medical School, UEA, Norwich, UK, 2010-present

- **What has been the greatest achievement in your career?**

Being offered two professorial posts in the one week in March 2010.

- **Which is your favourite paper you have written/co-authored and why?**

Minihane AM, et al, *APOE* polymorphism and fish oil supplementation in subjects with an atherogenic lipoprotein phenotype (ALP). *Arteriosclerosis, Thrombosis and Vascular Biology* 2000;20:1990-7

Good study and team and the first indication that *APOE* genotype influences responsiveness to n-3 fatty acid supplementation.

- **Who is/was your most influential mentor/colleague and why?**

Prof. Christine Williams, University of Reading. Christine taught me so many of the skills needed to progress in academia such as accurate and succinct scientific writing, 'political skills' and how to be an effective manager and leader whilst always being respectful.



Prof. Anne Marie Minihane  
Norwich Medical School,  
University of East Anglia, UK

- **What is your advice for young scientists?**

- \* Stay as focused as you can and avoid being a 'Jack/Jill of all trades and master of none',
- \* Develop critical skills early on. Present a balanced view of the evidence,
- \* Prepare for interview, by reading books on interview techniques and availing of practice interviews when offered. In my experience scientists are notoriously bad at interview, faltering at the most obvious of questions.

- **Where is your favourite place in the world and why?**

San Francisco.....got a vibe, which cannot really be described.

- **What is your favourite music/book?**

Not really in to music. My favourite author is *Haruki Murakami* and individual book is *The Old Man and the Sea* (Hemingway)

- **What is your favourite sport(s)?**

Basketball. In my youth (now several decades ago!). I used to play for the Irish National Team. These days I run.



## GET TO KNOW YOUR POSITIVE

### EARLY STAGE RESEARCHERS



Laurent-Emmanuel Monfoulet

Human Nutrition Unit

- **What is the focus of your research?**

My main research interest is the characterization of the mechanisms by which polyphenols may regulate cellular interactions between vascular endothelium and circulating immune cells. This research is mostly based on primary endothelial cells under static and hemodynamic conditions and is part of the research program carried out at the MicroCard Group (INRA - Human Nutrition Unit) looking at the role of plant foods, particularly of the plant bioactive compounds, in the prevention of cardiovascular diseases.

- **In what countries/organisations have you studied or worked?**

I did my PhD in Cellular Biology and Physiopathology at the team of the French Institute for Health and Medical Research (INSERM) at the University of Bordeaux (France). My work was focused on the role of extracellular matrix protein in natural bone repair processes. Subsequently, I joined the Osteoarticular Bioengineering and Bioimaging (B2OA) laboratory, affiliated to the National Center for Scientific Research (CNRS) and Paris Diderot University (France). In this laboratory I worked on the engineering of artificial bone graft using osteoprogenitor cells in association with a bioglass scaffold. In 2012, I was recruited as a permanent researcher at the French National Institute of Agronomic Research (INRA) and joined the Human Nutrition Unit (Clermont-Ferrand, France).

- **What has been the greatest achievement in your life?**

It has been 5 years since I got my PhD. Therefore, I think that in this still short career the greatest achievement was to obtain a permanent position in a leading European agricultural research institute.

- **Which is your favourite paper you have written/co-authored and why?**

My recent paper on the impact of lipid-activated receptor deficiency on osteoarthritis (OA) is my favourite, as OA is a major public health issue and its treatment still remains a challenge because of the low capacity of the cartilage to regenerate. Using a combination of in vivo- and in vitro-models of OA, I have shown for the first time that the lipid-receptor deficiency leads to an extended OA phenotype providing evidence that increasing the activity of this receptor by natural (i.e dietary lipids) or synthetic ligands could be a new strategy in the management of OA.

- **Who is/was your most influential mentor/colleague and why?**

My most influential mentors are the very renowned scientists Clemens van Blitterswijk (Netherlands), Nicolas L'Heureux (Canada) and Didier Letourneur (France) who were involved in my research on osteoarticular tissue health and engineering. Each of them coordinates multidisciplinary and interdisciplinary research in tissue engineering from the production of the scaffold to its association with stem cells. They have tested their products in vitro and have all succeeded to implant their 3D-engineered bone or vessels in pre-clinical, clinical studies and even in patients. To me, they constitute three successful examples of how to transfer academic research into clinical applications.

- **Where is your favourite place in the world and why?**

Among all the places I have visited or those where I have lived in, my favourite is still the beach I recall from my childhood.

- **What is your favourite music/book?**

One of my favorite songs is Elephant by Damien Rice.

- **What is your favourite sport(s)?**

... volley-ball that I practice every week.



Mireia Urpi Sarda  
Nutrition & Food Science Dept , Pharmacy School  
University of Barcelona

- **What is the focus of your research?**

My research is focused on the discovery and evaluation of biomarkers of food intake and biomarkers associated with cardiovascular risk factors, such as diabetes, through targeted and untargeted metabolomic approaches within the Biomarkers and Nutritional & Food Metabolomics research group (University of Barcelona) ([www.nutrimetabolomics.com](http://www.nutrimetabolomics.com)).

- **In what countries/organisations have you studied or worked?**

I did my PhD with the Biomarkers and Nutritional & Food Metabolomics research group of the Food Science and Nutrition Department in the University of Barcelona (Spain). My thesis was focused on the study of the bioavailability of polyphenols, mainly resveratrol and cocoa flavanols, in human volunteers for clinical intervention trials using mass spectrometry techniques. During 2006–2008, I undertook a stay in the *Unité Nutrition Humaine (Centre de Recherche INRA, Clermont-Ferrand, France)*, studying the bioavailability of isoflavones in biological fluids and tissues (i.e. human mammary glands). After the PhD, I undertook a postdoctoral study at the University of Perugia, where I studied the association between the consumption of polyphenol-rich diets and frailty status and other illnesses related with aging. Afterwards, I worked for three years as a postdoctoral researcher at the Hospital Clinic of Barcelona (Barcelona, Spain) in the Internal Medicine Department. The main objective of the research was to evaluate inflammatory biomarkers for atherosclerosis after a Mediterranean dietary pattern for the prevention of cardiovascular diseases. In 2010, I spent six months at the University of Aberystwyth (Wales, United Kingdom) studying endogenous biomarkers of cardiovascular risk associated with a Mediterranean dietary pattern in the PREDIMED study through a metabolomic approach. In 2012, I came back to the Biomarkers and Nutritional & Food Metabolomics research group as Associate Scientist on the ‘Ramon y Cajal programme’ to work within on my current area of research and to start teaching Nutrition and Food Sciences at Bachelor and Master Degree level.

- **What has been the greatest achievement in your life?**

Achieving in 2012 the position of Associate Scientist on the ‘Ramon y Cajal programme’ supported by the Spanish Ministry.

This has allowed me to continue developing my research and consequently conduct two projects as principal investigator. In addition, I have directed two PhD theses (and currently directing two ongoing ones) and several master degrees.

- **Which is your favourite paper you have written/co-authored and why?**

My favourite papers are those from my PhD in which resveratrol metabolites such as glucuronides and the entire profile of resveratrol sulfates were identified for the first time in human LDL after moderate red wine intake (*Anal. Chem.* 2005, 77, 3149–3155 and *Clin Chem.* 2007, 53, 292–299). We were able to quantify very low amounts of metabolites (pmol/mg LDL) using validated analytical methods, including optimized solid-phase extraction and a precise, accurate, sensible and selective LC-MS/MS methodology. I am also very proud of a recent paper in the field of polyphenols and their application, where high levels of bifidobacteria were associated with increased levels of anthocyanin microbial metabolites (*Food Func.* 2014, 5, 1932). This study confirmed the important role of polyphenols as bacterial substrates and their modulatory capacity. This is of importance in the field of finding new products with prebiotic and probiotic characteristics for the food industry.

- **Who is/was your most influential mentor/colleague and why?**

From each of the scientists with whom I have worked, I have tried to learn as much as possible. With their input, each and every one of them have contributed to developing my knowledge, which has increased accordingly and allowed me to improve from day to day as a researcher. They are: Dr Claudine Manach from INRA-Clermont-Ferrand, who introduced me to the techniques for studying the bioavailability of polyphenols; Dr Antonio Cherubini, from the University of Perugia, who initiated me into the hospital clinic environment dealing with aging-related diseases and epidemiological studies, such as INCHIANTI; Dr Ramon Estruch from the Hospital Clinic of Barcelona and IP of the PREDIMED study, who introduced me to the field of clinical biomarkers related to cardiovascular diseases; and Dr John Draper from the University of Aberystwyth, with whom I worked in metabolomics and computational techniques. My most influential mentor has been the leader of the research group, Dr Cristina Andres-Lacueva, who taught me from the start of my career in laboratory research (as my PhD supervisor) through to helping me to acquire other basic elements of a researcher, such as learning to teach, supervise, direct and lead.

- **Where is your favourite place in the world and why?**

The area where I was born and still live in - the Penedès area. Its stunning and characteristic landscape of vineyards provides a relaxing environment brimming with nature in a rural area.

- **What is your favourite music/book?**

I love listening to opera, mainly the song “Madame Butterfly” sung by Maria Callas.

- **What is your favourite sport(s)?**

I love swimming sports.... When I was young, I belonged to a swimming club in which we competed in group and individual championships.

## CHAIR'S CORNER

Dear partners,

POSITIVE is the unique European scientific network aiming to address interindividual variation in bioavailability and physiological responses to consumption of plant food bioactives in relation to cardiometabolic health. A crucial strength of POSITIVE is to gather and structure for the first time top level experts in human nutrition and plant food bioactives, in cutting edge omics technologies and in forefront research fields, such as human gut microbiota or personalised nutrition, together with experts from regulatory agencies and representatives from industry.

POSITIVE is committed to:

- gather and analyse existing data in an integrated way
- coordinate research efforts in the field across Europe
- foster exchange and collaborations for the emergence of cutting-edge projects
- pave the way for future translation of scientific findings into applications.

The challenge addressed by POSITIVE is undoubtedly of great interest for the European scientific community as evidenced by the large number of participants, more than 70 Research Institutions and 7 National Federations of the Agro-Food Sector from 31 participating COST countries.



*Dr. Christine Morand (POSITIVE Chair)  
and Prof. Francisco Tomas Barberan (POSITIVE Co-Chair)*

We are truly excited to serve as Chair and Co-Chair of such a dynamic multidisciplinary and multisectorial network that will be at the foreground of innovative strategies to optimize the benefit of plant food consumption for everyone.

We will all do our best during the four coming years for the success of POSITIVE!

Christine & Francisco

## CONTACT US



### Contact us:

**Chair:** Dr. Christine MORAND, INRA - France, e-mail: [christne.morand@clermont.inra.fr](mailto:christne.morand@clermont.inra.fr)

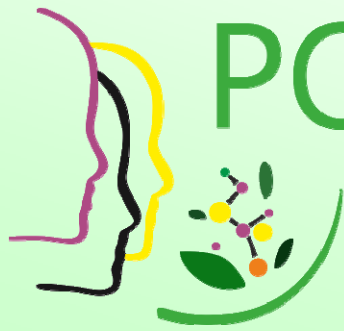
**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain, e-mail: [fatomas@cebas.csic.es](mailto:fatomas@cebas.csic.es)

**COST Science Officer:** Dr. Luule Mizera, e-mail: [luule.mizera@cost.eu](mailto:luule.mizera@cost.eu)

**COST Administrative Officer:** Christophe Peeters, e-mail: [christophe.peeters@cost.eu](mailto:christophe.peeters@cost.eu)

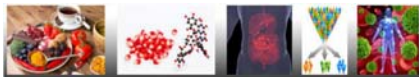
### Webpage:

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)



# POSITIVE

ISSUE 2



SPECIAL ISSUE , SEPTEMBER

## FA-1403 - POSITIVE COST Action

### Interindividual variation in response to consumption of plant food bioactives and determinants involved

**ANNOUNCEMENT OF THE:**  
**1<sup>st</sup> POSITIVE SCIENTIFIC WORKSHOP**  
**October 26-27, 2015 , Tours (FRANCE)**  
<https://colloque.inra.fr/workshop-cost-positive-2015/Registration>



The workshop will be held in satellite to the 7<sup>th</sup> International Conference in Polyphenols and Health (ICPH).



Dear all,

As the Chair of the POSITIVE COST Action I would like to invite you to attend our 1<sup>st</sup> Scientific Symposium.

The aim of this symposium is to raise awareness of the scientific community to the relevance of interindividual variability in the bioavailability and physiological responses to the consumption of plant food bioactives in relation to the prevention of cardiovascular and metabolic disorders.

Several excellent scientists leaders in the area will review and present state-of-the-art information on the topic, as well as their views and perspectives in this emerging field. You may see the program of this workshop and information about the speakers in the next pages. All the information is also available on the website: <https://colloque.inra.fr/workshop-cost-positive-2015>.

We believe that this workshop is of great interest to all scientists working on polyphenols and health and thus we encourage you to attend the workshop. Participation to this workshop is subjected to registration at <https://colloque.inra.fr/workshop-cost-positive-2015/Registration>.

**Please, register and join us in this excellent and exciting workshop!!!**

Kind regards



**Dr. Christine MORAND**  
**CHAIR OF POSITIVE COST Action**

## Scientific Program

### COST POSITIVE - 1st Scientific Workshop

October 26-27th, 2015 - Vinci Congress Center, Tours - FRANCE

<b>Monday, 26th 2015</b>	
3:00 - 3:15 p.m.	Introduction of the COST Action POSITIVE <b>Dr. Christine Morand</b> (INRA - Clermont-Ferrand, France)
3:15 - 4:15 p.m.	"Inter-individual differences in polyphenols gut microbiota metabolism. Can they affect human health?" <b>Pr. Francisco Tomas-Barberan</b> (CSIC - Murcia, Spain)  "Single nucleotide polymorphisms associated with carotenoid bioavailability" <b>Dr. Patrick Borel</b> (INRA - Marseille, France)
4:15 - 4:30 p.m.	<i>Break</i>
4:30 - 6:00 p.m.	"Differences in vascular response to cocoa flavanol intake according to age and sex" <b>Dr. Ana Rodriguez-Mateos</b> (Univ. Duesseldorf - Germany)  "From inflammaging to healthy aging by dietary lifestyle choices: is epigenetics the key to personalized nutrition?" <b>Pr. Wim Vanden Berghe</b> (Univ. Antwerp - Belgium)  "Genetic polymorphisms and response to polyphenols/Mediterranean diet" <b>Dr. Dolorès Corella</b> (Univ. Valencia - Spain)

<b>Tuesday, 27th 2015</b>	
9:00 - 10:45 a.m.	"Interindividual differences in metabolism of plant food bioactives: impact on dietary recommendations" <b>Pr. Joanna Lampe</b> (Univ. Washington - Seattle, USA)  "Cofactor mapping: a model for the plant bioactives" <b>Dr. Jim Kaput</b> (Nestle Institute of Health Science - Switzerland)  "Lessons from Food4Me about opportunities and challenges for personalized nutrition" (Title to be confirmed) <b>Dr. Eileen Gibney</b> (Institute of Food and Health - Dublin, Ireland)
10:45 - 11:00 a.m.	<i>Break</i>
11:00 - 12:00 a.m.	Round table with all speakers " <b>The future for plant food bioactives in personalized nutrition</b> ". <i>Chairman: Pr. F. Tomas-Barberan</i>



# POSITIVE



## Speakers

### Prof. Francisco TOMÁS BARBERÁN Co-Chair of the POSITIVE Action



Prof. Francisco Tomas Barberán (CSIC Murcia, Spain) got a PhD in Pharmacy at University of Valencia and works currently as a Research Professor at CSIC in Murcia (Spain). He is co-author of more than 300 publications in scientific journals in the areas of Phytochemistry, Agricultural Chemistry, and Food Science and Nutrition. These articles have been cited over 12000 times. His main interest is deciphering the role of phenolic phytochemicals on food quality and health. His current research aims to the identification of those food constituents that provide health benefits, the mechanisms by which they exert their effects, their bioavailability and efficacy in humans and the role of gut microbiota on polyphenols metabolism and inter-individual variability. He has carried out research in laboratories from England (Reading), Switzerland (Lausanne), France (Lyon), and the USA (Davis). His research has also been oriented to the transfer to industry and he has registered 6 patents of which 3 have been licensed and derived products are actually in the market.

### Dr. Patrick BOREL

Dr. Patrick Borel (INRA Marseille, France), obtained his PhD in Molecular Biology at Marseille University, 1988. He works for INRA in a joint research unit with INSERM (the French national institute of health and medical research) and Aix-Marseille University. The research unit, NORT (“Nutrition, Obesity and Risk of Thrombosis”) is located at the Faculty of Medicine de la Timone in Marseille (France). Since 2002, Dr Borel leads the research group “Bioavailability of fat soluble micronutrients” composed of various experts on lipid micronutrients, postprandial lipid metabolism, cellular and molecular biology and genetics. He is member of the scientist board of the nutrition department of INRA and vice-chairman of the SFVB (Société Francophone Vitamines & Biofacteurs ; French society on Vitamins). In 2002 he won the research award on vitamins research from the CEIV (Centre d’Etudes et d’Information sur les Vitamines; the French center for information on vitamins). Dr Borel has published some highly cited papers on the metabolism of carotenoids and vitamin E in humans and on factors that modulate their bioavailability. He is currently focused on the identification of intesti-



### Dr. Ana RODRIGUEZ-MATEOS



Dr. Ana Rodríguez Mateos (Univ. Dusseldorf, Germany) is a Research Group Leader at the Division of Cardiology, Pulmonology and Vascular Medicine of the University of Dusseldorf, Germany. She received her PhD and conducted her postdoctoral studies at the Department of Food and Nutritional Sciences of the University of Reading, UK, where she began to investigate the absorption, metabolism and excretion of dietary flavonoids and their impact on vascular function in Professor Jeremy Spencer’s research group. Her research included development and validation of analytical methods for the identification and quantification of polyphenol metabolites in biological fluids using liquid-chromatography and mass spectrometry; design and undertaking of randomized controlled trials investigating the effects of polyphenol-rich foods on cardiovascular function and investigations on mechanisms of action using animal and cell models. Currently, her main research interests include investigating the factors affecting the bioavailability and bioactivity of dietary polyphenols, such as food matrix, processing, age or sex, and their mechanisms of action in the vascular system.

## Speakers



### Prof. Wim VANDEN BERGHE

Prof. Wim Vanden Berghe (Univ. Antwerp, Belgium) is professor of Epigenetic Signaling (PPES) at the University of Antwerp and University of Ghent (Belgium). His research focuses on crosstalk of kinases and hormone signaling with epigenetic reprogramming in cancer-inflammation, CVD and neuroplasticity in response to medicinal phytochemicals. He holds a PhD degree in Chemistry-Biotechnology from the University of Ghent (LEGEST, UGent, Belgium). He received postdoctoral training at the Nuclear Signaling Lab of Prof. L. Mahadevan (Oxford, UK, 2000) and at the Department of Biochemistry lab of Prof. J. Hapgood & Prof. A. Louw (Stellenbosch, South Africa, 2001).

### Dr. Dolores CORELLA

Dr. Dolores Corella is Full Professor of Preventive Medicine and Public Health at the University of Valencia since 2009. She has been Director of the Genetic and Molecular Epidemiology Laboratory since its creation in 1998. Since 2003, Dr. Corella has participated in the PREDIMED Study (PREvención con DIEta MEDiterránea) as principal investigador and from 2006, in the CIBER of Fisiopatología de la Obesidad y Nutrición. Her studies have generated more than 270 papers in peer-reviewed journals. Dr. Corella's interests are focused on the study of genetic and epigenetic determinants of cardiovascular diseases, diabetes, obesity and other cardiovascular risk factors. She has developed research methodology for analyzing gene-environment interactions. Within the gene-environment interaction study, gene-diet interactions have constituted the main research line giving rise to the development of Nutritio-



### Dr. Joanna LAMPE



Prof. Joanna Lampe (Univ. Washington Seattle, USA), PhD, RD is a Full Member and Associate Division Director in the Public Health Sciences Division at Fred Hutchinson Cancer Research Center and a Research Professor in the Department of Epidemiology at the University of Washington in Seattle, USA. She received her PhD in nutritional sciences, with a minor in biochemistry, from the University of Minnesota and trained as a post-doctoral fellow in epidemiology at the University of Minnesota before joining the faculty at Fred Hutchinson Cancer Research Center in 1994. Dr. Lampe's research focuses on the effect of diet constituents on cancer susceptibility in humans and the effects of genetic variation on response to diet. Her group uses controlled dietary interventions to evaluate cancer biomarker-response to diet and specific phytochemicals. In addition, her lab studies the modifying effects of the gut microbiome on diet and disease risk. Dr. Lampe's research has been supported by the US National Cancer Institute for the past 15 years and she has published over 200 papers related to diet and human health. In 2014, Dr. Lampe received the American Society for Nutrition's Mary Swartz Rose Senior Investigator Award for research on the safety and efficacy of bioactive compounds for human health.



## Speakers



### Dr. Jim KAPUT

Dr. Jim Kaput currently works at Nestle Institute of health Sciences (Lausanne, Switzerland) as the Head of the Clinical Transaltion Unit. He's got his PhD at the University of Colorado in Biochemistry and Molecular Biology. He is an expert in Translational Genomics and Personalized Nutrition for Health Care. His research focuses on human genetics molecular studies and association with the diet.

### Dr. Eileen GIBNEY

Dr. Eileen Gibney (Institute of Food and Health, Dublin, Ireland) Dr. Eileen Gibney is a lecturer in Human Nutrition at University College Dublin, Ireland. She is an active member of the UCD Institute of Food and Health, and a Registered Nutritionist. She graduated with a degree in human nutrition from the University of Ulster at Coleraine, she then obtained her PhD from the Dunn Nutrition Unit, University of Cambridge in 2001.

Her current research interests lie in the molecular aspect of nutrition and disease, an area of nutrition research called Personalised Nutrition. Dr Gibney has successfully obtained funding for several research projects including 'Examination of the effect of genotype (PTC/PROP) on fruit and vegetable intake in children' ([www.ucd.ie/foodandhealth/projects/geneticsofhealthyeating/](http://www.ucd.ie/foodandhealth/projects/geneticsofhealthyeating/)) and more recently is involved in both the National Adult and Nutrition Survey (NANS) and National Phenotype Database ([www.ucd.ie/JINGO](http://www.ucd.ie/JINGO)) in Ireland. Eileen is a PI on the FP7 funded food4me project ([www.food4me.org](http://www.food4me.org)), which examined opportunities and barriers to personalised nutrition.



## CONTACT



EUROPEAN COOPERATION IN THE FIELD OF SCIENTIFIC AND TECHNICAL RE-



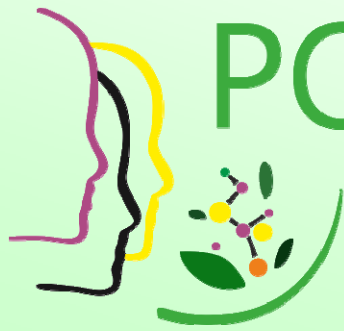
**PLEASE contact us for further information:**

**Chair:** Dr. Christine MORAND, INRA - France, e-mail: [christine.morand@clermont.inra.fr](mailto:christine.morand@clermont.inra.fr)

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain, e-mail: [fatomas@cebas.csic.es](mailto:fatomas@cebas.csic.es)

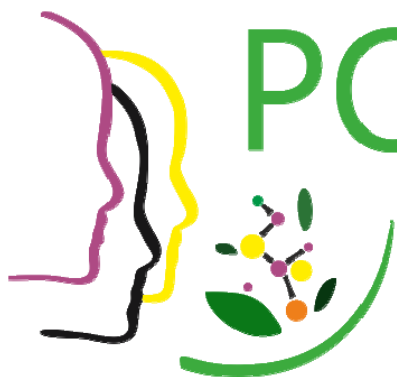
**Webpage:**

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)



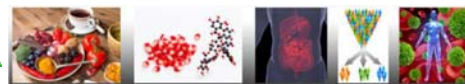
# POSITIVE

ISSUE 3



# POSITIVE NEWSLETTER

**cost**  
EUROPEAN COOPERATION IN SCIENCE  
AND TECHNOLOGY



ISSUE II, DECEMBER 2015

## WELCOME



To introduce this 2<sup>nd</sup> newsletter of POSITIVE, I would like to first express my satisfaction with the high success of the scientific events and activities that have been organised by the network during this first year. This is also an opportunity for me to express all my gratitude to the leaders and co-leaders of WGs and to the STSMs coordinator for the excellent work they have done for bringing together POSITIVE partners around the scientific objectives of the Action and organising the networking activities. Of course, the success of POSITIVE in the coming years will also tightly depend upon the active involvement of the

large community of POSITIVE partners. I'd like to thank all of them in advance for pursuing their efforts to reach the objectives of the Action.

In 2016, POSITIVE will organise two WG meetings, the first one in Bucharest (Romania, 15-17, March) and the second in Norwich (UK, 14-16 September). This latter will be joined with the 2<sup>nd</sup> Scientific Workshop of the Action, which will be also a part of the 1st International Conference on Food Bioactives and Health (13-14 September, Norwich). As previously, a special attention will be given to the Early Career Investigators involved in POSITIVE to favour building of their capacity and exchanges between partner groups.

Yours sincerely  
*Christine Morand, PhD*  
Action Chair

## NEWS FROM THE ACTION

### 2<sup>nd</sup> COST Action POSITIVE Meeting 22<sup>nd</sup>-23<sup>rd</sup> September 2015, Murcia, Spain

The second WG1, WG2 and FG meeting of the COST Action POSITIVE FA1403 took place during the 22<sup>nd</sup> and 23<sup>rd</sup> of September in Murcia (SPAIN) with the participation of 57 partners. The major aims of this meeting were to i) evaluate and discuss the progress of the already initiated tasks, ii) to delineate the following activities to ensure the successful continuation of the work and iii) to reinforce the interchange and collaboration between all partners. In addition, the WG3 held its first working meeting to debate and decide the tasks to be further developed in the next period.

The meeting took place in the pleasant environment of the Scientific Park, University Campus of Espinardo (Murcia) under the frame of a very cordial and friendly atmosphere accompanied by a sunny and warm weather. Participants also had the opportunity to stroll around the city in the evening and enjoy a relaxing outdoor dinner next to the beautiful cathedral of the city.



## 2<sup>nd</sup> POSITIVE Meeting cont.



Within the working groups, various subgroups have been working on different key issues, i.e. families of bioactive compounds, analytical methods, metabolomics, specific databases, microbiota, genetic variants, and specific cardiovascular and metabolic target biomarkers affected by flavanols. All these topics have been carefully discussed and evaluated and a vast literature search for articles related to the specific objectives

of WG1 (human variability in bioavailability) and of WG2 (human variability in the response regarding CVDs) conducted. This search was done using standard criteria for systematic reviews and specifically-designed templates shared through Google docs. The search is now almost complete and has gathered a substantial number of the most relevant articles. The next steps will involve the extraction of data to evaluate inter-individual variation. Review and positions papers are being outlined.

The participants of the WG2 were also separated into two sections : 1) one that was further divided in various subgroups and will initiate a literature search looking at metabolic and cardiovascular effects in humans of various other bioactives (ellagitannins, flavonols, phytosterols, anthocyanins) and 2) the Cell & Molecular Target section which will conduct a literature search looking at relevant studies on the impact of bioactives on cardiometabolic disease with the final aim of identifying potential cell and molecular targets, to then create a list of potential candidate genes and to investigate the available omics data from clinical studies. Three groups were formed and will focus on human, animal and *in vitro* studies.

The FG had an initial meeting to recapitulate on the work done but also to start planning further dissemination ways for 2016. Part of this work will be done in collaboration with the WG3 which has already started to develop some of its main tasks such as the preparation of a specific questionnaire directed to stakeholders and end-users with the aim of identifying which of the POSITIVE findings and developments may have the greatest commercial and/or health impact.

## SAVE THE DATE

**15<sup>th</sup> - 17<sup>th</sup> March, 2016**

**WORKING GROUPS 1 & 2, AND FOCUS GROUP MEETING  
THINK-TANK GROUP & STEERING COMMITTEE MEETINGS**

**Venue: University of Agronomic Sciences and  
Veterinary Medicine of Bucharest (ROMANIA)**

Organized by **Dr. Liliana Tudoreanu, Dr Mario Codreanu,  
& Dr. Alin Birtoiu** from the University of Agronomic Sciences and  
Veterinary Medicine of Bucharest - Faculty of Medical Veterinary



## RESEARCH HIGHLIGHTS

### Work Group 1

The 2<sup>nd</sup> WG1 meeting in Murcia counted with the presence of 26 partners. Dr. Tom van De Wiele (chairman of WG1) presented an overview of the goals and tasks of the 1<sup>st</sup> year of POSITIVE within this working group: creating databases on interindividual variability (IVA) in absorption and metabolism of plant bioactives, identify genes that may affect this variability, and collect knowledge on the role of gut microbiota on IVA in bioavailability. There were a total of 8 subgroups that have conducted a vast literature search and selected the relevant information on a number of plant bioactive compounds: carotenoids, ellagitannins/tannins/lignans/phenolics, phytosterols, catechins, anthocyanins, flavonols & flavanones. The subgroup leaders reported on the results of the search, the problems found and the potential preparation of review or position papers. Critical issues were further discussed such as the need to improve the screening templates, when and how to obtain individual raw data or the inclusion of food processing as an additional factor that can affect IVA in bioavailability of special interest for the food industry.



Within the WG1, the metabolomics sub-group led by Dr. Claudine Manach also presented the main tasks of this working section: 1) evaluation and improvement of the analytical methodology of plant bioactive compounds and metabolites for the development of a consensus method or combination of complementary methods with a wide coverage for plant food bioactive metabolites; 2) help with the identification of metabolites in non-targeted analytical approaches *via* the enrichment of currently available databases, the establishment of the metabolic pathways involved, the creation of tables with known analytical features for specific metabolites,

and the contribution of partners to virtual chemical libraries such as FoodComeEx; 3) organization of a training school on metabolomics (see announcement later on in this issue). A general request for more partners to contribute to the tasks of WG1 was stated during the meeting.

The subgroup looking at genes and variants implicated in IVA in bioavailability has few active members and the need for more people involved was also highlighted. These genes still need to be identified and listed. In the microbiota subgroups, a few compounds formed by the gut microbes have been identified but these microbes and the specific microbial enzymes need to be identified and listed. Once again, help from further collaborators and experts is needed and requested.



A general discussion of all the tasks, achievements, problems to solve, future steps, preparation of future papers and reviews, etc, were further discussed under the leading of Dr. Rikard Landberg. On the last morning of the meeting, Dr. Tom van De Wiele demonstrated the use of Dropbox to all partners and summarized the specific activities to accomplish before the next meeting in March in Bucharest. In addition, two potential topics for future STSMs related to the WG1 work were proposed: one at INRA (Clermont-Ferrand) on database information on the metabolism of specific model compounds and a second one at PAN in Olsztyn on metabolomics analysis. During 2016, literature extracted about factors affecting inter-personal variability in ADME for the 8 selected compound groups will be processed and dissemination activities will be initiated. Reviews and opinion papers as well as publically available data are expected.

**Prof. Tom Van de Wiele**  
**WG1 Leader**

**RESEARCH HIGHLIGHTS**

**Work Group 2**



The second WG2 meeting in Murcia counted with 28 participants distributed into 2 subgroups: the human meta-analysis subgroup and the cell and molecular targets subgroup. In the human meta-analysis subgroup, Mar Garcia-Aloy updated the status of the flavanol meta-analysis initiated after the meeting in Belgrade and showed the work is progressing satisfactorily. The lessons we learnt from this first “feasibility” project were discussed and changes will be made in future work accordingly. A discussion on the protocol and templates to conduct meta-analysis for assessment of inter-individual variability in selected clinical and molecular biomarkers of cardiometabolic risk in response to plant food bioactives consumption was discussed next. The template for data extraction was critically reviewed, and it was decided which information was needed to be included in it. The factors affecting inter-individual variability in the response to plant food bioactives were also discussed. POSITIVE will focus on: bioavailability, age, sex, ethnicity, country of origin, genetic polymorphisms, health status, dietary background, gut microbiota, drug/supplements consumption, baseline physical activity level, BMI, waist circumference and smoking. It was also decided which bioactives will

be investigated next, and 3 working subgroups were created on anthocyanins and ellagitannins, flavonols and phyosterols.

During the meeting, Professor Jose Ordovas gave a lecture on his research on interindividual variability of plant bioactives and gave very useful insights for future work.

The cell and molecular targets group major aim for this meeting was to initiate the work on the identification of cellular and molecular targets of plant food bioactives in vivo (human and animal studies) and in vitro. The identified targets will be used to examine inter-individual variability in nutrigenomic response and also genes of interest for future nutrigenomic studies. Regarding the literature search for human studies and due to the limited number of papers available, all plant food bioactives both isolated molecules as well as foods



rich in these molecules will be reviewed.

The following criteria will be applied: 1) target tissues: PBMCs (peripheral blood mononuclear cell), whole blood, liver and adipose tissue; 2) impact of bioactives on gene expression only (although later on it could be extended to miRNA and epigenetic impact). The group also discussed the criteria to search for molecular targets of bioactives in animal studies. It was decided that different animal models will be included: rats, mice, mini-pigs and dogs but only wild-type species with diet-induced metabolic/physiological dysfunctions related to cardiometabolic diseases (obesity, hypertension, insulin resistance, atherosclerosis, etc). The nutrigenomic effects will be reviewed only in the following tissues: aorta, adipose tissue, liver, PBMCs/immune cells where gene expression had been evaluated using different approaches (microarray, macroarray, sequencing, TLDA). For in vitro studies, it was decided to only include studies with primary cells (endothelial cells, adipocytes, immune cells) exposed to circulating metabolites at physiologically relevant concentrations. In order to progress in these tasks, a monthly video-conference will take place between the people involved in each task.

**Dr. Ana RODRIGUEZ-MATEOS**

**WG2 Leader**

## RESEARCH HIGHLIGHTS

### Work Group 3

The first COST Action POSITIVE Working Group 3 meeting was organised in September in Murcia, Spain. During this fruitful meeting, we discussed the initiation of a range of activities to be carried out during the next 2-3 years, and we are currently looking for members who would be interested in leading these activities or in contributing otherwise.



A **'dissemination' subgroup** will be formed next year to distil the relevant information from WG1 and WG2 reviews on the scientific basis for dietary recommendations for stratified groups and development of innovative and healthy foods targeted at population subgroups. This information can then be made available in a powerpoint presentation to be displayed at different meetings, such as Vitafoods, Food Matters Live, etc., either in a specific 'COST Action POSITIVE' session or otherwise. In addition, we will publish a (technical) white paper dedicated to stakeholders and end-users, which will be available from our website (pdf) or as a booklet. These activities are going to be co-ordinated with the members of the Focus Group.



An **'on-line tool' subgroup** will be also formed next year to develop a computational on-line decision-tree-like tool that allows stakeholders and end-users to select from a large range of foods, moving to the bioactives available in

these foods, to the physiological health outcomes these bioactives can modulate, to the actors that determine the variability in response. Whilst navigating through the structure, links to relevant papers and reviews can be provided. The information required to set up this tool will be coming from the reviews published as a part of WG1 and WG2 reviews/position papers. Considering the nature of this work, it may be worthwhile to carry it out through an exchange project involving 1-3 early career researchers.



A **'success stories' subgroup** will be formed next year to aid in the development of short movies/webinars where individual POSITIVE members will highlight their 'success stories' in order to inspire stakeholders and end-users working in a particular field. The movies/webinars will be produced in collaboration with the Focus Group and made available on POSITIVE website and through other (national) websites of interest to the food industry.

A **'roadmap' subgroup** will be formed during the 3-4 years of the project to aid in the development of a roadmap for future research projects and innovative initiatives in Europe, based on the results obtained in WG1 and WG2. In addition, we will continue to work on the questionnaire (to be translated into different languages) to collect the views and expectations of various stakeholders and end-users with respect to POSITIVE outcomes.

The next WG3 meeting will be held in September 2016 and will be particularly open to the WG3 members who are going to play an important role in the subgroup activities proposed above to allow them to further develop their ideas.

**Dr. Baujke DE ROOS**  
WG3 Leader

## RESEARCH HIGHLIGHTS

### Think Thank Group

During this first period of the POSITIVE Action, the group of Early Career Investigators (ECIs) coordinated by Mireia Urpi Sarda and Laurent-Emmanuel Monfoulet have fully accomplished the plans agreed during the 1<sup>st</sup> Think-Tank Group meeting in Belgrade. They have created an on-line forum using LinkedIn as the social network. Currently, 45 ECIs-POSITIVE' participants have joined the forum to share their professional experience and skills, especially those related to the objectives of POSITIVE. They have also organized three on-line meetings (every two-three months) using the Going-to-meeting application.

The 1<sup>st</sup> online meeting took place on the 10<sup>th</sup> of July and gathered 10 participants who discussed several topics related to the bioavailability and bioactivity of tea polyphenols in human and animal tissues. The 2<sup>nd</sup> online meeting was organized the 18<sup>th</sup> of September and gathered 6 participants who reviewed several recent papers proposed by Rodrigo Feliciano (Univ. Düsseldorf). These articles were about how genetic polymorphisms of specific enzymes can affect polyphenols bioavailability and bioactivity. Lastly, a 3<sup>rd</sup> online meeting was held the past 2<sup>nd</sup> of December with 8 participants who discussed amongst other issues a proposal raised by Baukje de Ross (WG3 leader): the creation of an on-line tool that follows a decision-tree-like model. This tool will allow for the selection of a large range of foods and will provide information on the bioactives present in them for which robust physiological health outcomes have been shown in randomized-controlled human intervention trials, as well as proven actors that may determine the variability in response. The information required to set up this tool will be coming from the reviews published as part of WG1 and WG2 reviews/position papers. If you are interested in this project, please contact one of your Think-Tank Group (TTG) representatives.

Overall, involved ECIs have met to debate and learn on some key variables, i.e. genotype and microbiota that influence the response to the consumption of plant food bioactives.

The next face-to-face meeting of the TTG will be held in Bucharest 15-17<sup>th</sup>, March.

This letter is an opportunity to strongly invite the ECIs of POSITIVE to participate in the dynamic of the TTG and to be a source of proposals for next year. All propositions will be welcomed!

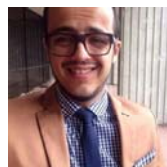
You can contact the coordinators of the Think-Tank group:

Mireia Urpi Sarda, [murpi@ub.edu](mailto:murpi@ub.edu),

Laurent-Emmanuel Monfoulet,  
[laurent-emmanuel.monfoulet@clermont.inra.fr](mailto:laurent-emmanuel.monfoulet@clermont.inra.fr)

or through the forum of the TTG at <https://www.linkedin.com/grp/home?gid=8311680>

### ECIs participants in on-line meetings in 2015



Rodrigo Rodrigo Feliciano  
Heinrich-Heine-Universität Düsseldorf  
GERMANY



Antonia Kaltsatou  
University of Thessaly  
GREECE



Geoffrey Istas,  
Universität Düsseldorf  
GERMANY



Mireia Urpi Sarda,  
Univariad de Barcelona  
SPAIN



Laurent-Emmanuel  
Monfoulet, INRA,  
FRANCE



Antonio González-Sarriás  
CEBAS-CSIC, Murcia  
SPAIN



Aleksandra Konić-Ristić  
Institute for Medical  
Research-Belgrade  
SERBIA



Pedro Mena  
University of Parma  
ITALY



Mar Garcia-Aloy  
University of Barcelona,  
SPAIN



## 1<sup>st</sup> POSITIVE Scientific Workshop 26-27 October 2015, Tours, France



The 1st Scientific Workshop of the Cost Action FA1403 POSITIVE was held on the 26<sup>th</sup> and 27<sup>th</sup> of October 2015 in Tours, France, as a satellite symposium of the 7th International Conference on Polyphenols and Health, 2015 (ICPH: [www.icph2015.com](http://www.icph2015.com)). The aim of this symposium was to raise awareness of the scientific community to the relevance of interindividual variability in the bioavailability and physiological responses to the consumption of plant food bioactives in relation to the prevention of cardiovascular and metabolic disorders. The workshop was attended by over 80 participants from throughout the world, providing a platform for presentation of state-of-the-art research results related to the topic by renowned scientific leaders, including POSITIVE members: Dr. Christine Morand, Prof. Francisco Tomas Barberan, Dr. Patrick Borel, Dr. Ana Rodriguez Mateos, Prof. Wim Vanden Berghe, Dr. Jim Kaput, Dr. Eileen Gibney, and invited speakers: Prof. Joanna Lampe (USA) and Prof. Dolores Corella (Spain)<sup>1</sup>.



Following the individual presentations, all the speakers invited to the workshop gathered on the stage for a general discussion on the issue of 'human variability' and the main problems that still need to be sorted in order to move forward in the research area of 'health benefits of plant dietary bioactive compounds'.



Many of the factors that can have a critical effect on human responses have now been identified: bioavailability, age, sex, ethnicity, genetic polymorphisms, epigenetic, health status, gut microbiota or dietary habits among others. Each one of these factors constitutes itself a complex research area where multiple aspects still need to be unravelled. This is the case, for example, of gut microbiota, epigenetic mechanisms or genetic make-up. It is now well established that the microbiota plays an essential role on human metabolic and immune health and that diet, in general, and dietary components such as plant food bioactives, in particular, can interact with the microbiota affecting its composition and metabolic functionality. The metabolites produced by the gut bacteria are many and need to be identified as well as their potential health effects. Further, although changes in the microbiota are clearly associated with health effects, the microbiota population is largely unknown, and the groups of beneficial bacteria and the mechanisms of interaction between them and the host need to be established.

## 1<sup>st</sup> POSITIVE Scientific Workshop cont.



Dietary components can also affect our genetic imprint through a range of epigenetic mechanisms such as the methylation or acetylation of the DNA. These epigenetic modifications can have an impact on gene transcription and the subsequent cellular responses. The epigenetic effects of some plant



natural bioactives have now been shown but important questions such as the reversibility and tissue-specificity of these epigenetic changes remain to be answered. In addition, the host itself exhibits a great variability in the genetic characteristics, especially associated with millions of single nucleotide polymorphisms (SNPs) some of which can have an effect on the expression and function of many molecules and subsequently in the response of the cells, tissues and the organism. It has also been shown now that the genotype has an important influence on the response to the Mediterranean diet or to specific diet components such as carotenoids in relation to cardiovascular responses. SNPs can affect the translatable regions of the genes but also the binding site of regulatory microRNAs making the picture even more complex. The search

for genotypes affecting human responses to diet has just started and will be further developed in the coming years.

It is because of the complexity of the research that studies cannot be focused only on a few targets and the use of computational and network multiple analyses are becoming essential to help in the understanding of human responses to diet. Larger cohort trials must be encompassed and, importantly, these studies need to be replicated. In addition, the results analysis and data presentation from these studies is moving from statistical average values to stratification of the individuals. We can no longer look at human results under the umbrella of average total values but rather mean values of



responsive groups. Stratification of the population is the way to go in order to understand human responses. It remains to elucidate whether this stratification must be based on microbiota composition (metabotypes), genetic make-up (genotypes), epigenetic differences, or a combination of all.

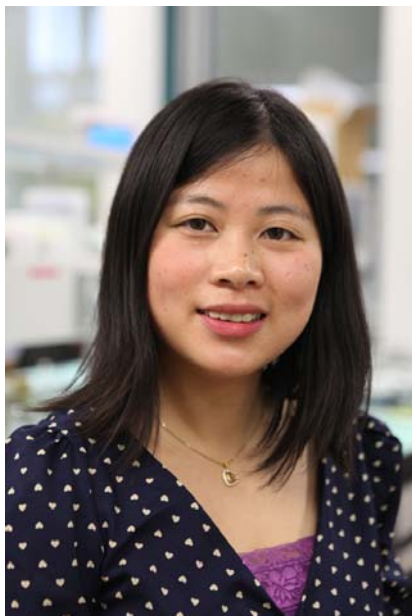
A very relevant question still to be answered is the translation of the results to the general public: is personalized advised including phenotypic and (or) genetic information really making an impact on improving dietary habits and their health consequences? The evidences are still limited.

The final conclusion to be drawn is that researchers in the area of plant bioactives and health effects face a vast and complex task to further understand the influence of human variability and factors implicated on the response to diet and its link to health. Nevertheless, the tools are now available, the ways to go have been depicted and the collaboration and communication with other research areas have been initiated.

<sup>1</sup>You can find the pdf files of some of the presentations given at the Workshop in the restricted area of the website of POSITIVE.

## SHORT TERM SCIENTIFIC MISSIONS

### STSM Topic: Analysis of metabolic markers of dietary phytosteryl conjugates in plasma



The POSITIVE Short Term Scientific Missions (STSM) grant enabled me to gain knowledge on nutritional metabolomic techniques under the supervision of Prof. Lars Ove Dragsted in the group of Bioactive Foods and Health in the University of Copenhagen. Currently, I am an early stage postdoc in the Laboratory of Food Biochemistry at ETH Zurich under the supervision of Prof. Laura

**Dan ZHU**

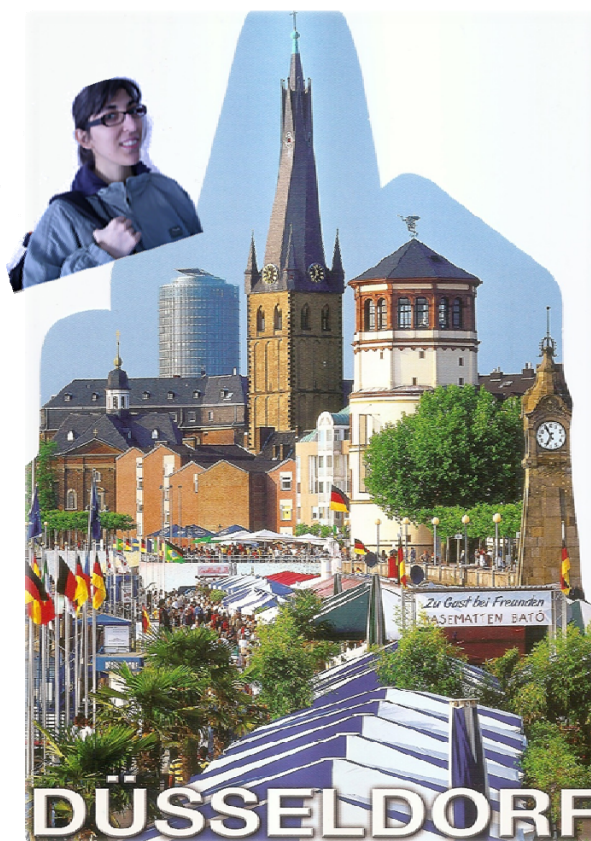
Myström. My research objective is to develop highly accurate detection methods for phytosteryl conjugates in natural sources as well as to study their bioactive properties and intestinal absorption. Phytosteryl conjugates have a high potential to reduce cholesterol levels. However, the exact mechanism hasn't been yet fully understood. Metabolomic techniques may facilitate exploring both metabolites of phytosteryl conjugates after the intake, and other metabolites related to their cholesterol lowering effect. During my STSM, I got familiarized with untargeted LC-MS-based metabolomic techniques to investigate the metabolites after the food intake, including the sample preparation (plasma, urine and fecal samples), LC-MS analysis (UPLC-Q-TOF), data analysis (MZmine and MatlabPLS\_Toolbox) and metabolite annotation. In addition, I had access to specific biological samples and data analysis methods not currently available in my institution. All of the techniques learnt will be applied in my future project on phytosteryl conjugates. Furthermore, this stay has contributed to the development of new ideas which will be the base for future joint projects as I had a chance to meet and collaborate with excellent researchers from Lars's group.

Apart from scientific work, I very much enjoyed the beautiful city of Copenhagen.

### Elsa MECHA

#### STSM Topic: Identification of metabolites by MS following the consumption of common beans: interindividual variation study

I could say my mission in Düsseldorf began in August 2015, when I took the flight at 08:40 a.m., however my journey started pretty earlier when in May 2015 my PhD supervisor invited me for a short term scientific mission (STSM) within the framework of a COST action and I committed myself to the task. I just had around two months to prepare several details related to the experimental assay and collect all the samples to analyse. The task was very challenging and unique, therefore I put myself to the test and my choice was to embark in Düsseldorf's mission. Looking back this was one of my best choices.



The proposal was undeniable because this was an opportunity to improve my PhD with bioavailability assays and an occasion to collaborate with an European partner. Despite the reduced time to prepare and implement an experimental assay with humans, a great team allowed the development of all the work.

Staying during two months in Düsseldorf, was more than a chance to perform a great amount of work, it represented a challenge to grow at a personal level. It gave me the chance to work in a different lab with new colleagues, learn and cope with new cultural habits (gastronomy, language, and schedules), understand my own limitations and capabilities, enhance self-confidence and most of all enjoy a lovely place with beautiful landscapes. Indeed an experience to recommend and to appreciate from

the first until the last day.

## SHORT TERM SCIENTIFIC MISSIONS

**Marina NIKOLIC**

**STSM Topic: Inter-individual variability in platelet function in response to plant bioactives – DATA ANALYSIS**



Internships are exciting by definition. You are going to live and work somewhere abroad and it always brings new challenges and opportunities. My Short Term Scientific Mission was held at The Microsoft Research – University of Trento Centre for Computational and System Biology (COSBI) in Italy. I have chosen to apply for a STSM at COSBI because it was the perfect combination of two of my favourite things: data analysis and Italian lifestyle.

The STSM grant was a great opportunity. The multidisciplinary team at COSBI is one of the most renowned groups in the

field of nutritional/genomic data analysis using advanced techniques and software. I had not used many of those and thus, this was a great opportunity for me to learn new methods of multivariate analysis and data visualisation better and more powerful than the ones I used before. This was a unique opportunity for me to upgrade my knowledge by interacting with professionals, and for sure it will put an impact on my future work. The young and international COSBI team made me feel great in and out of the offices. It's very easy to become Italian in a short time. You just need to get used to very tasty food, perfect wine and a "domani" life style.



Trentino, as a perfect fusion of the Italian life style and German discipline, is a very nice place to live. I would definitely suggest, to all POSITIVE young researchers, to find a place abroad among many of the project partner's institutions, where they could improve knowledge in their field and to apply for the STSM.

**Mar GARCIA-ALOY**

My enthusiasm to contribute to the activities of the COST Action POSITIVE was the driving force of my application for the STSM in the 1<sup>st</sup> Call, with the project closely linked to the objectives of the WG2. The initial collaboration of my team led by Prof. Cristina Andres-Lacueva from the Nutrition and Food Science Department of the University of Barcelona with the scientists from the Institute of the Food and Health at the University College Dublin on developing the guidelines to perform the systematic review on the impact of plant bioactives on cardiometabolic biomarkers, was an excellent background to continue the work we started with the direct supervision of Dr. Eileen Gibney, leader of the UCD team. This was an exceptional opportunity to enhance the communication between the two research groups and to ensure the best use of our skills to deal with the tasks that were being developed, enabling us to discuss specific points in depth, as well as to decide more efficiently on the details of the stages involved in the design of review guidelines.

Beyond the successful completion of the mission that enabled further progress in joint work on WG2 objectives in future, the collaboration with UCD team continued fruitfully since then, within POSITIVE activities and beyond.



The constant support from the host scientist and her team, both on scientific issues and in social part, the memories of a beautiful summer in Dublin and the impact of knowledge I gained during the mission on my future research, definitely make my STSM one of the best decisions. Based on my experience that overcame the expectations, I would recommend young colleagues from the POSITIVE network to use the opportunity of the STSM grand and apply!

## METABOLOMICS TRAINING SCHOOL



**Dr. RAFAEL LLORACH**

*University of Barcelona, SPAIN*

Metabolomics constitutes a powerful approach to investigate food derived metabolome (nutrimetabolomics) and its impact on human health. It is also a promising tool to unravel the complexity of interindividual response to plant bioactives consumption. Despite the interest in nutrimetabolomics and its applications to agro-food production, food technology, food intake, etc most food & health researchers lack both the necessary knowledge and skills to perform nutrimetabolomic studies. In this context, the metabolomics training school will combine e-learning lectures and hands-on training to provide sufficient theoretical knowledge and practical skills to all participants so that they can develop their own metabolomics experiments.

**The school will be split in two types of courses:**

### BASIC AND THEORETICAL ASPECTS OF METABOLOMICS

Webinars

**Date:** April—May 2016

A series of one-day webinars (2-3 hours) will cover the different steps in a nutrimetabolomics experiment including aspects such as data acquisition, metabolite identification and biological interpretation as well a session devoted to show successful studies related to the discovery and identification of new biomarkers of food intake by metabolomics approach.

**Learning objectives:**

- Introduce the importance of metabolomics in nutrition studies.

- Discuss the specific use of non-targeted and targeted approaches in nutrimetabolomics studies.
- Introduce the main technical aspects (including analytic, processing and analysis) for the nutrimetabolomics studies.
- Identify advantages and drawbacks of the different platforms applied to nutrimetabolomics experiments.

The complete list and schedule of these webinars will be announced in early January 2016.

### PRACTICAL METABOLOMICS TRAINING SCHOOL

At place

**Place and Dates:** Barcelona 5-8 July 2016. Campus de l'Alimentació Torribera (Santa Coloma de Gramanet (<http://www.ub.edu/campusalimentacio/en/index.html>)).

**Target audience:** The course is aimed at 15 experienced participants in the use of metabolomics tools.

**Overview:** This practical module will be focused on the annotation and identification of metabolites and on data analysis strategies to improve the predictive capacity of food intake by multimetabolite combined models. To this purpose, the seminars will combine theoretical lectures with hands-on training sessions.

**Learning objectives**

- Analyze the complexity of LC-MS metabolomics data.
- Assess the *in silico* strategies to annotate mass features.
- Practice the skills to carry out the computational-assisted identification of biomarkers.
- Discuss the relationship between dietary information and food metabolome
- Evaluate the ability to predict food intake using Nutrimetabolomics data

**Facilities:** All the sessions will be developed in an informatics room. Each participant will have a computer to carry out the training activities

Due to the limited number of participants, a pre-registration period will be open in March. The selection procedure will be announced during this period. The final agenda will be announced in May.

SCIENTIFIC EXPERT'S OPINION



*Lifestyle, (poly)phenolics, food source,  
gut microbiota & epi(genome):  
A complex cocktail of interplaying  
actors*

Many investigations suggest that the intake of (poly) phenolic compounds might help to prevent degenerative disorders, such as cancer, cardiometabolic and neurodegenerative diseases. But these non-nutrient compounds promote dissimilar responses in different individuals. This is, at least in part, the reason why despite intense research the evidences regarding the role of polyphenols in human health are not conclusive. It is becoming evident that some variables contribute to this story. Some can be classified as 'inherent' to the individual whereas others can be considered as 'external' variables and can affect the former ones. Some of the most important variables that can determine the individuals' response to polyphenols consumption follow.

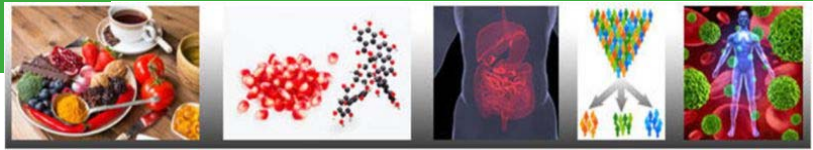
The role of our genetic makeup is essential in this story. Certain point mutations in the genotype, such as SNPs can modulate the absorption, conjugation and subsequent potential effect of polyphenols on human health. Another important actor is our epi-genome. We all are hu-

*Prof. JUAN CARLOS ESPIN*  
*Dep. Food Sci. & Technol., CEBAS-CSIC,*  
*Murcia, SPAIN*

mans but obviously not identical. There is regulatory information superimposed on the genome that can change the expression of our genes without alteration of the genetic code. The lifestyle (diet, sedentarism, smoking, alcohol drinking, pollutants, stress...) can modify our genome. Amazingly, epigenetic changes can be inherited from our parents. Therefore, we inherit not only their genetic characteristics but somehow also their lifestyles... And thus, one's experiences may have consequences for subsequent generations. Polyphenols are not out from this entire context. Curcumin, resveratrol, epigallocatechin gallate and other derived metabolites have been reported to induce epigenetic changes such as histone acetylation/deacetylation, DNA demethylation and miRNA modulation.

The gut microbiota is also emerging as a key player for the maintenance of health. It interplays with the host organism from birth to senescence and it is settled during childhood. The gut microbiota contributes to the regulation of multiple metabolic pathways through a complex series of interactive and symbiotic host-microbiome signaling systems. Furthermore, the gut microbiota produces molecules that can directly or indirectly influence epigenetic modifications involved in essential cell processes (apoptosis, inflammation, etc.). In the specific context of polyphenols, the double-way interaction between polyphenols and gut microbiota has been well established. It is becoming clearer that individuals' gut microbiota can determine the response to polyphenols consumption. This is the case of iso-flavones where equal producer and non-producer subjects have been described; also ellagic acid where three urolithin metabolites have been recently reported (A, B and O) and also citrus flavanone rutinosides where individuals can be stratified as low-, medium- and high flavanone excretors as a function of their gut microbiota rhamnosidase activity. Known and (mostly) unknown microbial species can metabolize these (and possibly other) polyphenols to yield specific metabolites which can exert stronger or milder effects than their parent compounds. Therefore, individuals respond differently depending on their gut microbiota and should be stratified in intervention trials that address the response to polyphenols consumption. This is an exciting research area to be explored.

## SCIENTIFIC EXPERT'S OPINION



Are there other variables that can affect the absorption, metabolism, microbiota interaction and further effects of polyphenols? We can envisage a number of important 'external' variables (although often forgotten) that may also affect (indirectly) the individuals' response to polyphenol consumption. For example:

- the type of (poly)phenol-containing food (fruit, vegetable, cocoa, olive oil, tea, coffee, etc.).
- the food matrix (solid, liquid, purée, raw, cooked...).
- the type of (poly)phenol (thousands of molecular structures).
- the intake as individual compounds or (more likely) forming part of dietary mixtures (synergy and/or addition and/or counteractions in their effects?).

In addition to these specific aspects, it is also difficult not only to ascertain the individuals' response to polyphenols within some healthy dietary patterns but also the specific role of these polyphenols on human health. For example, strictly speaking, the 'Mediterranean diet' does not exist. It was indeed a 'way of life' followed by people who lived in that wide geographic area long ago (Spain, Italy, Morocco, France, Greece...). Nowadays, a number of 'Mediterranean-like dietary patterns' could be identified in all these countries. Individuals adhered to different 'Mediterranean diets' can respond very differently to the polyphenolic content consumed. One more example: The 'five a day' campaign to consume at least five portions of fruits and/or vegetables a day. Two 'five a day' diets with even the same type of fruits and/or vegetables can differ in 10 or more the amount of phenolic compounds because of the cultivar chosen. This could yield confounding results in observational studies to correlate health effects with the polyphenolic content. In this regard, it is essential the use of food databases such as 'Phenol Explorer' which try to cover this important gap.

Last but not least, the evaluation of the effects. Apart from the different individuals' response, the inconclusive evidences found in the literature regarding the effects of polyphenols on health can also be partly due to the different approaches followed: analytical procedures (including '-omics'), clinical/dietary intervention trial protocols (type of trial and follow-up, healthy voluntaries and/or patients,

suitable markers to measure a 'preventive action' in healthy people)... Moreover, should different groups try to follow the same protocol trial with the same analytical procedures and with the same type of polyphenol? In other words, how many times the same specific intervention study has been repeated by the same and other research groups? Is the 'ethical' issue the real problem? For example, there are 'ring-tests' to validate analytical procedures. Should we do something similar with intervention trials dealing with polyphenols?

Overall, it seems reasonably that Nutri(epi)genomics and gut microbiota both should be jointly investigated to understand the health benefits of dietary polyphenols. In addition, the often forgotten 'food side' of this story should be also considered. And finally, dietary intervention protocols on polyphenols and health lack of enough consensus to reach consistent evidences... After finishing this document I wonder whether polyphenols really exert healthy beneficial effects!

Undoubtedly, there is a huge task ahead for POSITIVE COST action.



**Volunteers need to be stratified for citrus flavanone absorption in clinical**

JOURNAL OF  
AGRICULTURAL AND  
FOOD CHEMISTRY

**Encapsulation and Micronization Effectively Improve Orange Beverage Flavanone Bioavailability in Humans**

María Tomás-Navarro,<sup>†</sup> Fernando Vallejo,<sup>†</sup> Francisco Borrego,<sup>§</sup> and Francisco A. Tomás-Barberán<sup>\*†,§</sup>

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**Volunteer Stratification Is More Relevant than Technological Treatment in Orange Juice Flavanone Bioavailability**

María Tomás-Navarro<sup>†</sup>  
Fernando Vallejo<sup>\*†</sup>  
Enrique Sentandreu<sup>§</sup>  
Jose L. Navarro<sup>§</sup>  
Francisco A. Tomás-Barberán<sup>†</sup>

<sup>†</sup>Quality, Safety and Bioactivity of Plant Foods, Food Science and Technology Department, CEBAS-CSIC Campus de Espinardo, 30100 Murcia, Spain  
<sup>§</sup>IATA-CSIC, Agustín Escardino 7, 46980 Paterna, Valencia, Spain



**Prof. FRANCISCO A. TOMÁS-BABERÁN,**  
**CEBAS-CSIC,**  
**Murcia, SPAIN**

There is an increasing interest in the study of dietary citrus flavanones as they are associated with health benefits. In the recent 7<sup>th</sup> International Conference on Polyphenols and Health held in Tours (October 2015), evidence from prospective studies and clinical trials on the role of citrus flavanones on human health was presented. Importantly, a large inter-individual variability in the gut metabolism and absorption of citrus flavanones was highlighted at the 1<sup>st</sup> Scientific Workshop of this POSITIVE COST action. Although citrus flavanones have been repeatedly shown relevant for the vascular protective effects of orange juice, some studies did not find statistically significant benefits on cardiovascular health. This could be partially explained by the large inter-individual variability observed in flavanone bioavailability. One relevant source of variability may be the fact that citrus flavanones cannot be absorbed as they are present in the fruit, i.e. conjugated rutinoides [rhamnosyl (1-6) glucosides] or neohesperidosides [rhamnosyl (1-2) glucosides] and need to be hydrolyzed before absorption. The intestinal cells do not have rhamnosidase activity and thus, the citrus flavanones can only be absorbed after the hydrolysis by the gut microbiota enzymes. This is seen in hesperidin pharmacokinetic studies where hesperetin conjugates appear in plasma 3-4 h after intake indicating absorption in the distal portion of the GI

tract, after the involvement of gut microbiota. Hence, the plasma levels of hesperetin conjugates will largely depend on the availability of gut microbiota able to de-conjugate hesperidin. Other sources of variability may be differences in intestinal transporters, accessibility of the gut microbiota to the flavanones and solubility of these compounds. Some of these can be improved by technology, i.e. ultra-homogenization, particle size reduction, increased dispersion through encapsulation.

We jointly investigated the effects of flavanone solubility and gut microbiota metabolism on flavanones absorption. We compared freshly squeezed, pasteurized and ultra-homogenized orange juice. We evidenced that the volunteers could be stratified in high, medium and low flavanone absorber/excretors and that the high excretors took advantage of the increased flavanone accessibility from ultra-homogenized juices. The low excretors that do not have appropriate microbial activity to release and facilitate hesperetin absorption did not benefit from increased solubility while those that have the rhamnosidase-active microbiota exhibit higher absorption when flavanone accessibility is enhanced. When the aglycone hesperetin was given to the same volunteers to overcome the need of the rhamnosidase hydrolysis, the low excretors displayed absorption levels close to those of the high excretors supporting the role of the microbiota enzyme activity.

Thus, if circulating flavanones are responsible for the health effects associated to citrus consumption, stratification of volunteers needs to be taken into consideration. If the health benefits are due to phenyl acetic and phenyl propionic metabolites and related compounds also produced by the gut microbiota then the knowledge of the gut microbiota role becomes even more relevant to understand the benefits of citrus consumption. Microbiota metabolism can affect the phenolic profile that is finally found in plasma and in relevant target tissues. There are still important questions very relevant for POSITIVE that need to be answered: Is it possible to differentiate responders and non-responders in clinical intervention trials with citrus juices or derived flavanones? If so, can they be associated with different events during flavanone absorption and (or) with the gut microbiota composition of the volunteers? Furthermore, can we modulate the plasma flavanone levels after the intake of citrus products by modifying the gut microbiota composition?



**RESEARCH DISSEMINATION**

**Dr. CHRISTIAN HEISS,  
University of Dusseldorf,  
GERMANY**

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**Cocoa flavanol intake improves endothelial function and Framingham Risk Score in healthy men and women: a randomised, controlled, double-masked trial: the Flaviola Health Study**

Roberto Sansone<sup>1</sup>, Ana Rodriguez-Mateos<sup>1</sup>, Jan Heuel<sup>1</sup>, David Falk<sup>1</sup>, Dominik Schuler<sup>1</sup>, Rabea Wagstaff<sup>1</sup>, Gunter G. C. Kuhnle<sup>2</sup>, Jeremy P. E. Spencer<sup>2</sup>, Hagen Schroeter<sup>3</sup>, Marc W. Merx<sup>1</sup>, Malte Kelm<sup>1,4</sup> and Christian Heiss<sup>1\*</sup> for the Flaviola Consortium, European Union 7th Framework Program

<sup>1</sup>Division of Cardiology, Pulmonology, and Vascular Medicine, Medical Faculty, University Dusseldorf, 40225 Dusseldorf, Germany

<sup>2</sup>Department of Food and Nutritional Sciences, University of Reading, Reading, UK

<sup>3</sup>Mars Inc., McLean, VA, USA

<sup>4</sup>Cardiovascular Research Institute Dusseldorf, Medical Faculty, Univer

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DOI 10.1007/s11357-015-9794-9



**Cocoa flavanols increase vasodilation and lower blood pressure improving blood vessel function in healthy people**

**Impact of cocoa flavanol intake on age-dependent vascular stiffness in healthy men: a randomized, controlled, double-masked trial**

Christian Heiss • Roberto Sansone • Hakima Karimi • Moritz Krabbe • Dominik Schuler • Ana Rodriguez-Mateos • Thomas Kraemer • Miriam Margherita Cortese-Krott • Gunter G. C. Kuhnle • Jeremy P. E. Spencer • Hagen Schroeter • Marc W. Merx • Malte Kelm • for the FLAVIOLA Consortium, European Union 7th Framework Program

As we age, our blood vessels become less flexible and less able to let blood flow normally increasing the risk of hypertension. These events are linked with cardiovascular diseases (CVDs) — the number one cause of deaths worldwide. These two studies funded by the EU research consortium FLAVIOLA and led by Dr. Christian Heiss demonstrate that cocoa flavanols improves cardiovascular health and lessens the burden on the heart that comes with the ageing and stiffening of arteries. Earlier studies have shown that cocoa flavanols improve the elasticity of blood vessels and lowers blood pressure in high-risk individuals (smokers and people diagnosed with hypertension and coronary heart disease). These two new studies are first to show that cocoa flavanols can also modulate age-related changes in blood vessels in healthy individuals and may help to prevent the risk of CVD.

In the study published in *Age*, two groups of young ( $26 \pm 1$  y) and older ( $60 \pm 2$  y) healthy men consumed either a flavanol-containing drink or a flavanol-free control drink twice a day for 2 wks. Vasodilation (the extent to which blood vessels dilate in response to nitric oxide) was significantly improved (~30%) in the young and old age groups that consumed flavanols. In the older age group, a statistically and clinically (~ 4 mm Hg) significant decrease in systolic blood pressure over control was also seen. In the study published in *BJN*, these researchers extended their investigations to healthy middle-

aged men and women (35–60 years, n=100). The participants consumed either a flavanol-containing drink or a flavanol-free control drink, twice a day for 4 weeks. Flavanols significantly increased flow-mediated vasodilation by 21%, decreased blood pressure (~ 4 mm Hg) and improved blood cholesterol decreasing LDL cholesterol (by 0.17 mmol/L) and increasing HDL cholesterol (by 0.1 mmol/L). Flavanols may reduce the 10-y risk of being diagnosed with CVD by 22% and the 10-y risk of dying from coronary heart disease or CVD by 37% (this Framingham Risk Score estimation must be taken cautiously since the duration of the study and the sample population do not reach the scale of the Framingham studies).

Concerning the aims of POSITIVE, these results indicate that the improvement in vasodilation, diastolic blood pressure, pulse wave velocity, and cholesterol by cocoa flavanols appear to be independent of age and sex in healthy individuals whereas the lowering of systolic blood pressure and aortic augmentation seems to be associated with stiffer blood vessels in the aging population. Other longer-term studies, such as the 5-year COcoa Supplement and Multivitamin Outcomes Study (COSMOS) with 18,000 men and women, are now underway to investigate the health potential of flavanols on a much larger scale and should help to confirm these results.

## POSITIVE DISSEMINATION

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The checklist below summarizes the corresponding COST branding elements that should be included in the different dissemination documents prepared by POSITIVE partners.

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## SAVE THE DATE



The 1st International Conference on

# FOOD BIOACTIVES & HEALTH



Demonstrating the health benefits of food bioactives: challenges and opportunities

13-15 September 2016

Norwich Research Park, UK



### Aim

To provide an open forum that brings together researchers from various scientific communities to present the latest research and discuss common themes and challenges to understanding the impacts of food bioactives on health.

### Themes

The conference will be organised around a series of themes that are relevant to all food bioactives, including:

- Bioavailability and metabolism
- Inter-individual variation in response to bioactives
- The role of the gut flora
- Impact on health, healthy ageing and disease
- Latest research on mechanisms of action
- Health claims
- Safety and formulation / delivery

### Who should attend?

Researchers from academia and the agri-food sector with interests in the health benefits of food bioactives, health claims, functional foods and nutraceuticals.

### Chair

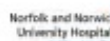
Dr Paul A Kroon  
Institute of Food Research,  
Norwich, UK, NR4 7UA

### Contact

dawn.rivett@ifr.ac.uk  
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14<sup>th</sup> - 16<sup>th</sup> September

4<sup>th</sup> POSITIVE COST MEETING  
and 2<sup>nd</sup> POSITIVE SCIENTIFIC WORKSHOP

*Institute of Food Research  
hosted by Dr. Paul Kroon  
Norwich, UK*

## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHER

#### What is the focus of your research?

Food phytochemicals with particular contribution to flavonoids, their metabolism and bioavailability, tissue distribution and passage through biological barriers, i.e. blood-brain and blood-cerebrospinal barriers.

#### In what countries/organisations have you studied or worked in?

1978 - 84 — M.Sc. in Chemistry, Technical University of Gdansk, Chemistry Faculty, Poland

1987 - 91— Ph.D. University of Agriculture and Technology, Olsztyn, Poland

1988 - present — Institute of Animal Reproduction and Food Research, PAS, Olsztyn, Poland;

1991— National Food Research Institute, Tsukuba, Japan

1995 - 97— National Food Research Institute, Tsukuba, Japan

1997 - 99 — Nikkoman Corporation, Noda, Japan

Plus several short term trainings/internships lasting from a few weeks to 3 months in Central Institute for Nutrition, Potsdam, East Germany (!!!); SIK Food Research Institute, Gothenburg, Sweden; TNO Nutrition and Food Research, Zeist, The Netherlands; The University of Tokushima, Tokushima, Japan.

#### What has been the greatest achievement in your career?

Being invited to contribute to the 'Get to know your POSITIVE partner' newsletter column, SENIOR RESEARCHER section (!!!). And seriously, it has been climbing through all the ranks at my Institute, from the bottom position as a technologist to Professor and Director.

#### Which is your favourite paper you have written/co-authored and why?

There are a few. It is always nice to be the first to report something, e.g. to demonstrate that soy aglycones are absorbed from the stomach while their glucosides are not; that aglycones are absorbed better than their respective glucosides and this strongly depends on the food matrix or that in biphasic systems as liposomes, flavonoids locate on the border of phases.

#### Who is/was your most influential mentor/colleague and why?

No doubt, Junji Terao (Japan). During our life we interact with other people often by chance and we cannot predict

how these interactions can influence us. It was no different with how I met Junji Terao. His openness to a request from an unknown PhD graduate from a country newly liberated from the communist system to accept him for a post-doc almost 25 years ago was the most im-

portant moment in my career development. He offered me a lot of research freedom and excellent conditions to work. It has influenced also my family in a positive way to an extent that is difficult to estimate.

#### Where is your favourite place in the world and why?

Wherever it is sandy, sunny, warm and with plenty of colourful fish.

#### What is your favourite music/book

Book - Patrick Süskind "Perfume: The Story of a Murderer". There is a lot of chemistry in it! I have read it in the Junji Terao's lab between chromatographic runs, we had no autosampler.

Music - Pat Metheny, in particular the "Falcon and the Snowman" album, its fragment serves as a ringtone in my mobile.

#### What is your favourite sport(s)?

Handball. A fast contact game. I was introduced to it already in the Grammar school and used to play it through university years. As I was brought up near a lake, for a couple of years I was practicing kayaking. Now, cycling and snorkelling on the reefs.



**Prof. MARIUSZ PISKUŁA**  
*Institute of Animal Reproduction  
 and Food Research, PAS,  
 Olsztyn, POLAND*

## GET TO KNOW YOUR POSITIVE

### EARLY STAGE RESEARCHERS

#### What is the focus of your research?

I am interested in understanding the potential bioactivity of polyphenol metabolites as far as reduction of the cardiovascular disease risk is concerned. Specifically, I am focused on the effect of berries intake on the cardiovascular health and a correlation with ADME. Recently, I have been working on the development of a high throughput sample analysis methodology, mainly for the analysis of human fluids by mass spectrometry using a targeted metabolomics approach.

#### In what countries/organisations have you studied or worked in?

I obtained my 6-year pharmaceutical sciences degree in Lisbon, Portugal, and worked for 5 years in different pharmaceutical industries as well as in the Food Science research lab in Portugal (IBET). Subsequently, I received my PhD in food science from the University of Wisconsin-Madison, USA. Currently, I am working as a Postdoctoral Fellow at the University of Düsseldorf, Germany, at the Division of Cardiology, Pneumology and Vascular Medicine.

#### What has been the greatest achievement in your career?

I was granted the Fulbright Scholarship in 2008, which was a great opportunity to pursue my PhD in the US. I also received the Daryl Lund Fellowship (College of Agricultural and Life Sciences) awarded to an Outstanding Graduate Food Science Student in 2012. During my PhD I was also able to fill in a patent as a co-inventor of "Addition of tannin formulations to enteral nutrition to counteract impairment of or improve immune function (P120201US01)".

#### Which is your favourite paper you have written/co-authored and why?

During my PhD I published a paper entitled "Deconvolution of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry isotope patterns to determine ratios of A-type to B-type interflavan bonds in cranberry proanthocyanidins", which highlighted the importance of MALDI-TOF as a crucial tool to characterize proanthocyanidins. My recent review about "Methods to determine effects of cranberry proanthocyanidins on extraintestinal infections: Relevance for urinary tract health" was also of a significant importance to me as it summarized the state-of-the-art knowledge in the field of cranberries and urinary tract infections.

#### Who is/was your most influential mentor/colleague and why?

I started to get interested in Food Science in 2000 by doing a research project with Prof. Maria do Rosário Bronze who taught me a lot about chromatography, as well as fruit and

vegetables polyphenols. My PhD supervisor, Prof. Jess Reed was undoubtedly a very important person in my career due to his extensive knowledge and his help in improving my scientific writing skills. Dr Ana Rodriguez-Mateos, whom I currently work with, has been giving me a lot of help and insight about my current research topic.

#### Where is your favourite place in the world and why?

I am absolutely passionate about the ocean and the beach. I really like Central America, specifically Costa Rica due to its immense natural beauty and amazing tropical fruits. I think some of the best beaches in the world can be found in Panama, Costa Rica and Nicaragua.

#### What is your favourite music/book?

I really enjoy jazz and blues like Nina Simone, Chet Baker, Dee Dee Bridgewater, Blossom Dearie but also other types of music such as The Smiths, Edith Piaf, Serge Gainsbourg, Hot Chip, Future Islands, Arvo Pärt, Erik Satie, Bach, Sparks, The Drums. Generally, I prefer watching movies to reading books, but I have recently read a great book by a Portuguese poet Adília Lopes titled "Manhã".

#### What is your favourite sport(s)?

I really enjoy swimming and playing badminton.



*Dr. RODRIGO FELICIANO, PharmD, PhD  
University of Dusseldorf, GERMANY*



**Dr. ROCÍO GARCÍA VILLALBA**  
*Food Science & Technology Dept.*  
*CEBAS-CSIC, Murcia, SPAIN*

**What is the focus of your research?**

My research is focused on the development, validation and application of advanced analytical techniques, mainly based on the coupling of separation techniques (LC or GC) with mass spectrometry (IT, QQQ, QTOF), to study the metabolism and bioavailability of dietary polyphenols and their interaction with the gut microbiota.

**In what countries/organisations have you studied or worked?**

I did my PhD in the Department of Analytical Chemistry at the University of Granada (Spain) during the years 2006 to 2010. My work was devoted to the evaluation of the potentialities of different analytical platforms to characterize olive oil phenolic compounds and their metabolites in biological fluids. During this period I did three 4-months stays at: i) Institute of Industrial Fermentations (IFI-CSIC, Madrid, Spain), 2007; ii) Bruker Daltonik (Bremen, Germany), 2008; and iii) Leiden University Medical Centre (LUMC, Leiden, The Netherlands), 2009. For the past five years I have been developing a post-doctoral stage in the department of Food Science and Tech-

nology of CEBAS-CSIC (Murcia, Spain).

**What has been the greatest achievement in your life?**

The greatest achievement of my career was to get my current post-doctoral position in Murcia just after finishing my PhD. This allowed me to carry on working on what I like and, at the same time, it gave me the opportunity of starting a new life in this pleasant city together with Pedro, my husband.

**Which is your favourite paper you have written/ co-authored and why?**

One of my favourite papers has been recently published in the Journal of Chromatography A: "Chromatographic and spectroscopic characterization of urolithins for their determination in biological samples after the intake of foods containing ellagittannins and ellagic acid". It is an analytical work of great importance for the determination of urolithins in biological samples. We report, for the first time, the most relevant chromatographic and mass spectrometry characteristics of a wide variety of synthesized urolithins. It is, in my opinion, an important contribution for the reliable identification and accurate quantification of these interesting metabolites in future works when standards are not readily available.

**Who is/was your most influential mentor/colleague and why?**

My most influential mentor is Prof. Francisco Tomás Barberán, whose wide knowledge and experience in the area of Food Science and Nutrition, the scientific discussions with him and his valuable advice and encouragement help me to grow scientifically. Prof. Tomás Barberán and also Prof. Juan Carlos Espín have contributed to improve my knowledge in the field of metabolism, bioavailability of polyphenols and their relation with human health and to develop other important scientific skills needed to progress in my research career. I would like also to mention Dra. Alegría Carrasco Pancorbo who initiated me in the research field and taught me during my PhD all what I know about analytical techniques.

**Where is your favourite place in the world and why?**

My favourite place is Granada, the city where I was born and grew up. It's a beautiful city with many historical places and charming areas to go for relaxing walks.

**What is your favourite music/book?**

I love novels based on historical events. One of my favourites is "The Century Trilogy" by Ken Follet: "Fall of Giants", "Winter of the World" and "Edge of Eternity".

**What is your favourite sport(s)?**

One of my favourite sports is trekking. I try to practice it as often as I can. It helps me to relax and discover amazing natural sights.

## CHAIR'S CORNER

Dear partners,

The first year of the POSITIVE network is almost completed, so it is an appropriate time for a short review of the tasks and goals accomplished.

The scientific activities of the network were launched last March with the Opening meeting held in Belgrade (Serbia). This meeting welcomed 69 participants (including 1/3 ECIs) from 31 COST countries to initiate the activities of the WG1, WG2 and FG of POSITIVE. Then the dynamic of POSITIVE was further strengthened in Murcia (Spain) in September with its 2<sup>nd</sup> WG meeting gathering 57 participants. During this 1<sup>st</sup> year, four short-term missions between POSITIVE partners have been successfully completed. This number will increase next year, particularly for those aiming to support the Action in achieving its objectives. The first scientific workshop of POSITIVE organised in October in Tours (France), as a satellite to the 7th International Conference on Polyphenols and Health, was highly successful. The quality of the lectures was excellent as well as that of the exchanges during the subsequent roundtable between the speakers and the audience. This workshop welcomed more than 80 participants from worldwide research institutions and industry (Europe, USA, Canada, Japan, Brazil...) including many that are not current partners of the Action. This high rate of attendance clearly illustrates both the interest of the international community for the questions addressed by POSITIVE and

the broad visibility of the Action. First connections between POSITIVE and other international networks (ISEKI-Food Association; Micronutrient Project) have also been initiated. These contacts will be strengthened and many others initiated during the coming years.

At the onset of the 2<sup>nd</sup> year of POSITIVE, our primary wish is to get increasingly involvement from POSITIVE partners in networking activities in order to reach the ambitious objectives of the Action, always within a very cordial and friendly atmosphere.

With our best wishes for Christmas and the New Year

Christine and Paco



## CONTACT US

### Contact us:

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: christine.morand@clermont.inra.fr

**Vice-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: fatomas@cebas.csic.es

### Webpage:

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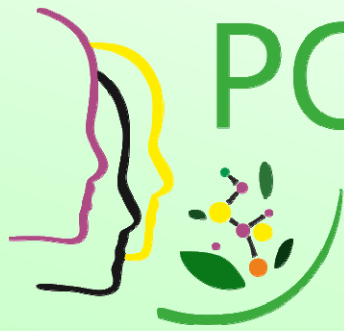
**COST Science Officer:** Dr. Luule Mizera,

E-mail: [luule.mizera@cost.eu](mailto:luule.mizera@cost.eu)

**COST Administrative Officer:** Christophe Peeters,

E-mail: [christophe.peeters@cost.eu](mailto:christophe.peeters@cost.eu)

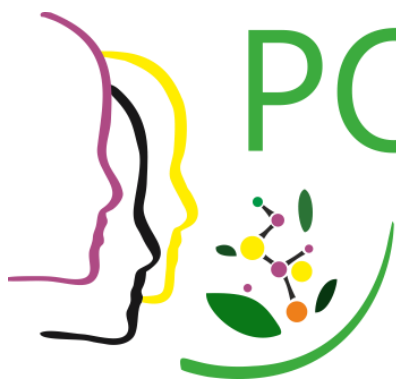
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# POSITIVE

ISSUE 4

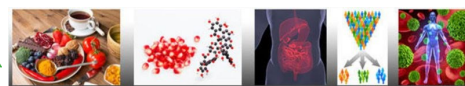




# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE III, JUNE 2016

## WELCOME

**Salut!** Welcome back to all the POSITIVE partners. As ever, thanks so much to all of you who have helped and contributed with reports and information to be included in this new edition of our newsletter. As usual we have many activities to report on, group meetings, publications, future conferences, introducing POSITIVE partners, etc. which have been listed in our new initial List of Contents. We are now approaching the equator of the COST Action and

we would like to encourage you to further increase your participation in the production of our next editions, so that we may include new sections and any information that may be of interest to all POSITIVE partners.

We hope you enjoy this June edition and, please, do send us your comments and suggestions for the future editions. We look forward to hearing from all of you!

*The FG*

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## NEWS

### POSITIVE meeting in Bucharest, Romania

The third WG1, WG2 and FG had a special round table with meetings of the COST Action ISEKI Food Association, four POSITIVE FA1403 was on this occasion organized by Dr. Liliana TUDOREANU and took place in the University of Agronomic Sciences and Veterinary Medicine of Bucharest (UASVMB) Romania, from the 15<sup>th</sup> to the 17<sup>th</sup> of March 2016.

As in previous meetings the objectives were to i) evaluate and discuss the progress of the on-going tasks, ii) to define future activities and ensure the successful continuation of the work and iii) to continue reinforcing the interchange and collaboration between all partners. In addition to the WG meetings, we

had a special round table with presentations given by scientist leaders in different topics of relevance to the main aims of POSITIVE as well as a poster session. Last but not least, the Think-Tank group had its second gathering to debate and decide the tasks to be further developed in the next period by the young scientists. Summaries of the main activities developed in Bucharest collecting the work carried out so far by POSITIVE may be viewed in the following section of this newsletter.



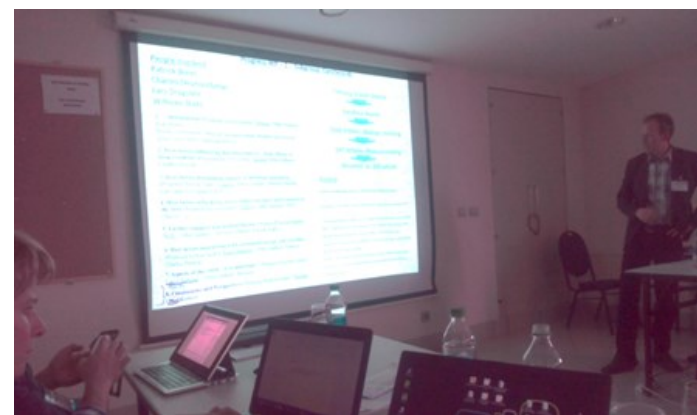
## RESEARCH HIGHLIGHTS

### Work Group 1

Leader: Tom Van de WIELE

Co-leaders: Richard LANBERG & Claudine MANACH

The WG1 3<sup>rd</sup> meeting commenced with a status update of the work carried out by the different subgroups presented by each subgroup coordinator. They have now collected and selected a considerable amount of articles and some subgroups have started writing up some of the reviews focusing of the factors influencing bioavailability. Some key questions remain to



be answered such as: Is the material collected sufficient to prove inter-individual variability? With this information, can we determine which factors are really causing this variability? Efforts should also be directed to prepare the outlines of the metabolic pathways.

#### Metabolomics subgroup

General presentation by Dr. Claudine Manach. She informed the audience about the current state of the recollection of representative standards and metabolites covering a range of masses and polarities, the preparation of a 'ring test' with a selection of these compounds coordinated by Dr. Maria Bronze, and the development of consensus analytical semi-targeted methods for



importance of *in vitro* mechanistic studies involving microorganisms. A number of compounds have been selected to focus on and microbial gene variability will be identified in the gene catalogue (INRA).

a wide cover of plant bioactive metabolites.

Dr. Rafael Manach introduced the program of the 1<sup>st</sup> Training School on Metabolomics that consists of a series of webinars and practical sessions (Barcelona). A summary of the webinars is reported later on in this newsletter (page 16).

Progress on the contribution of POSITIVE members to data entering into PhytoHub was also reviewed during the meeting. An STSMs carried out by Andreia Bento da Silva at INRA Clermont-Ferrand is dealing with the collection and up-

loading of known metabolites to this database.

#### Microbiome subgroup

General discussion on the Literature survey conducted with a stress on the im-

## RESEARCH HIGHLIGHTS

### Work Group 2

Leader: Ana RODRIGUEZ-MATEOS

Co-leaders: Eileen GIBNEY & Dragan MILENKOVIC

#### Human Meta-analysis group

During the WG2 meeting the progress on the human meta-analyses was reviewed. The protocols and templates for data extraction have been completed and a method paper prepared (see status on the Publications section). This methodology has been applied to some groups of bioactive compounds during the course of two STSMs in Glasgow under the supervision of Dr. Emilie Combet (for details on these STSMs check the corre-



sponding section of this issue). The possibility of obtaining raw data and its use was also discussed in this meeting. Dr. Arno Greyling and Dr Eileen Gibney will investigate the best practices and agreements to do this.

In addition, a general discussion on how to report interindividual variability in publications led to the possibility of preparing a paper with guidelines to do so and that may be offered to COST members who are part of Editorial boards for its publication.



sponding section of this issue). Data on specific biomarkers are being introduced in the Comprehensive Meta-Analysis software to investigate the weight of the current human evidence and the factors affecting it.



#### Cell and Molecular targets group

The revision of gene expression studies in humans has been launched under the supervision of Dr. María-Teresa García Conesa. Criteria will be more flexible than initially suggested in order to get as many articles as possible dealing with gene expression in human intervention studies. The aim will be to try to understand the impact of the intake of bioactive compounds on gene expression, the variability and the problems that need to be solved for future intervention studies. Equally, studies in animals (led by Dr. LE Monfoulet) and *in vitro* (led by Dr. Marika Massaro) have also been initiated. The specific models, conditions, biomarkers and compounds to be considered have been discussed and established.



During the course of this meeting a number of critical issues regarding meta-analysis were discussed. The progress on the different sub-groups (different compounds) was presented.

## RESEARCH HIGHLIGHTS

### Focus Group

Leader: *María-Teresa GARCÍA CONESA*

Co-leader: *Iwona KIEDA*

Attendants: Dr. María-Teresa García Conesa (FG leader), Ms. Iwona Kieda (FG co-leader), Dr. Liliana Tudoreanu,



Dr. Emilie Combet, Ms. Vanessa Boissery, Dr. Christos Kontogiorgis, Dr. Baujke de Roos (WG3 leader) and Dr. Christine Morand (POSITIVE Chair). On this occasion, we welcomed to two newcomers that have recently joined the FG: Dr. Adriana Birca, Professor at the Technical University of Moldova and at the University 'George Baritiu' of Brasov (Romania) and Dr. Van Droogenbroeck Bart, Senior Researcher at ILVO Institute for Agricultural and Fisheries Research, Belgium.

The tasks agreed on to be completed during this period of the Action were the release of the POSITIVE newsletter (the current June issue), the updating of the website with new publications, links to Facebook and Twitter, and a photo gallery including pictures of the different meetings and presentations.



You may see now some pics from the meeting in Bucharest! (<https://www6.inra.fr/cost-positive/Events/3rd-WG-meeting-Bucharest-2016>)

Other issues discussed were the possibility of collecting the posters presented at the meeting and preparing an on-line ISBN registration and publication (Dr. Liliana Tudoreanu). Importantly, we initiated some discussions about dissemination of information to Food Industry in collaboration with the WG3. A specific questionnaire has now been prepared in English by Dr. Baujke de Roos and translated to other languages and it is ready to be sent around. The results may be used in the elaboration of an informative leaflet directed to Food Industry representatives. A poster with updated information about POSITIVE will be prepared and presented at Norwich 'Bioactives & Health Conference' in September 2016. During this Conference, POSITIVE flyers will be once again distributed to all partici-

pants and some short videos will be recorded with interviews to some academic and industrial partners. Further, a 3 slides Power-Point presentation of POSITIVE has been prepared and it is available to all partners who may want to use them to introduce the Action in meetings and conferences.

## RESEARCH HIGHLIGHTS

### Think Thank Group

"Low participation but very productive" might be the best way to headline this 2<sup>nd</sup> Think-Tank meeting in Bucharest, Romania. A total of eight Early Career Investigators (ECIs) involved in POSITIVE attended the meeting on



site. The meeting was led by Dr. Rodrigo Feliciano since due to technical problems it was not possible to establish a GotoMeeting connection with Dr LE Monfoulet (France) and other ECIs who have registered to attend it via Internet connection .

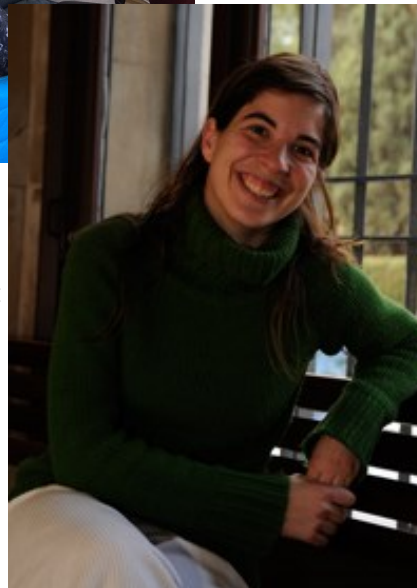
The meeting started with a short introduction of all the members since some were new in the COST Action. For more than two hours, several proposals were discussed and new aims were proposed with the main goal of increasing the participation of the ECIs and reverse the trend observed since the beginning of the COST Action in Belgrade:

- To stop using the LinkedIn ECIs-POSITIVE group since there has been hardly any activity in the past year. The members decided to create a new group in a different platform called Unison. All the participants present in the meeting were invited to join this group and it was decided to give it a try to see if this platform would work better than LinkedIn. With Unison, members will be able to share files and probably also to establish video connection replacing the

GotoMeeting platform.

- To keep organizing webinars once a month where one member in each webinar will present a short introduction of the research they perform in their lab along with the COST actions that they are involved. The remaining time of the webinar will be dedicated to discuss the progress of the tasks within this group.

- To lay down a draft that will be circulated to senior authors of the COST-POSITIVE for their input before the next meeting to be held in Norwich, UK. This draft corresponds to a systematic analysis of parameters dealing with inter-individual variability data presentation that will culminate in a paper publication. This goal will be obtained through two main interrelated tasks: (1) establish a quality index to express inter-individual variability in response to plant food bioactives and (2) propose suggestions/recommendations for how to report data concerning inter-individual variability.



- To look for experts in pharmaceutical research and how inter-individual variability data reporting is dealt with in that field and try to establish a parallel approach. Try to establish connections that could provide useful and even have a lecture of an invited speaker in a symposium satellite in the next two years.

Finally, it was decided by unanimity that the new representatives for the following year would be Dr. Mar Garcia-Aloy and Dr. Antonio González-Sarrías from the University of Barcelona (Barcelona, Spain) and CEBAS-CSIC (Murcia, Spain), respectively. They will represent to ECIs in the Steering Committee (SC).

## RESEARCH HIGHLIGHTS

### Round table with ISEKI



Integrating Food Science and Engineering  
Knowledge Into the Food Chain

*'Inter-individual variation in response to consumption of plant food bioactives as influenced by technologies, matrix interaction and formulation'*

The ISEKI Food Association (IFA) was introduced to all POSITIVE partners attending the meeting in Bucharest. The round table was celebrated at the Hotel Parliament during the afternoon of Tuesday the



15<sup>th</sup> and counted on the presence of Dr. Gerhard Schleininger, from BOKU - University of Natural Resources and Life Sciences, Vienna and general secretary of ISEKI. We also had the opportunity to listen to ISEKI's president, Dr. Paola Pitia by means of a webinar.

ISEKI Food gathers universities, research institutions and food industries and associations from all over the world with the aim of promoting continuous learning and education in the food area both in the academia and industry sectors. Among others, this network includes a special group with specific interest on Bioactive Compounds chaired by Dr. Manuela Pintado. You may see all the information related at <https://www.iseki-food.net/>.

15<sup>th</sup> and counted on the presence of Dr. Gerhard Schleininger, from BOKU - University of Natural Resources and Life Sciences, Vienna and general secretary of ISEKI. We also had the opportunity to listen to ISEKI's presi-

dent, Dr. Paola Pitia by means of a webinar. POSITIVE and ISEKI have many things in common and can learn from each other by means of collaborations and interaction between the two networks.

## Oral presentations

In the morning of Wednesday the 16<sup>th</sup> of March the meeting was opened with four oral presentations about specific subjects of great relevance for POSITIVE aims.

The session commenced with the intervention by Dr. Marion Leclerc (INRA Jouy en Josas, France) who presented her talk entitled 'Gut microbiota diversity, functions and individual variability' which dealt with the human metagenome large variability, the association between the loss of microbial genes and diseases like inflammatory bowel disease and obesity and the role of nutrients and diet components such as protein and fibre in the increase of gene richness for some individuals.



## RESEARCH HIGHLIGHTS

### Oral presentations cont.

Following with the prominent role of microbiota in human individual variability, Dr. Francisco Tomás-Barberán (CEBAS-CSIC, Murcia, Spain) spoke about 'Inter-individual variability on the biological response to ellagitannins' and presented his current view on the stratification of individuals based on their 'metabotypes', in particular, on the metabotypes responsive to the consumption of ellagitannins and the relationship with microbiota dysbiosis and metabolic diseases.

The third talk of the morning was presented by Dr. Claudia Nunés Dos Santos (IBET-ITQB, Oeiras, Portugal) who talked about 'Insights into the cytoprotective potential of phenolic sulfates metabolites'. During her talk, Dr Nunés Dos Santos introduced us to the issue of the variability of plasma sulfate metabolites from catechol and pyrogallol as well as some interesting mechanistic studies with *in vitro* models of the blood brain barrier and 3D models of neurons and astrocytes.

Last, but not least, Dr. Arno Greyling (Unilever R&D Vlaardingen, The Netherlands) talked about 'Best practices when investigating health effects of food bioactives' with a focus on the importance of health claims.



### Poster session

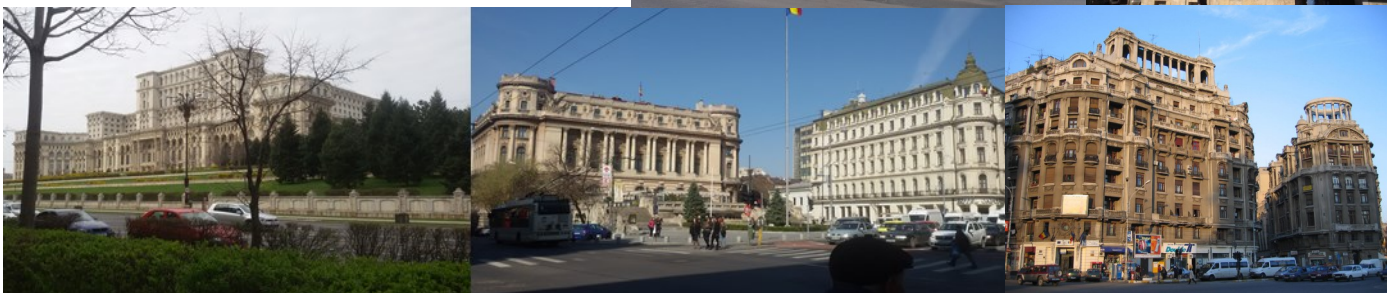
The poster session was successfully held during the lunch time on Wednesday the 16<sup>th</sup> so that all partners had the opportunity to walk around and have a look at them. Up to 17 posters were presented. They dealt with a broad range of research areas related to POSITIVE main objectives including *in vitro* and *in vivo* methods to test the bioactive properties and health benefits of different bioactive compounds, metabolomic approaches to investigate biomarkers of exposure, molecular mechanisms of action and nutrigenomic studies, synthesis of metabolites, etc.



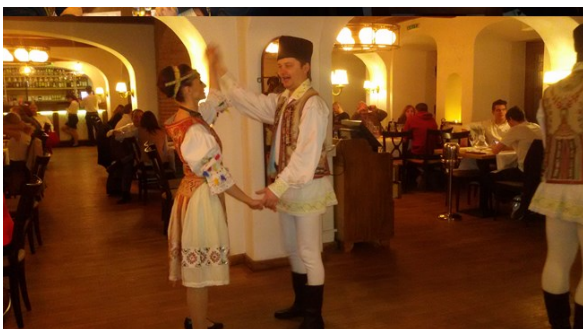
## RESEARCH HIGHLIGHTS

### Social events

The meeting took place under a very friendly atmosphere accompanied by a surprising sunny and not too cold weather which gave the participants the opportunity to stroll around the old Bucharest city centre, visit the Parliament palace (*Ceausescu* palace)...



... and enjoy a typical Romanian dinner and dancing.



**Mersi! La revedere!**

## SAVE THE DATE

### FOOD BIOACTIVES & HEALTH CONFERENCE

1 3-15 September 2016

Registration at: <http://www.fbhc2016.com/>

&

### COST JOINT MEETING

2<sup>nd</sup> POSITIVE Scientific workshop

«Inter-individual variation in response to food bioactives»

15<sup>th</sup> September (morning session)

&

4<sup>th</sup> WG, FG, SC & 3<sup>rd</sup> MC MEETINGS

September 15-16, 2016

The 1st International Conference on

## FOOD BIOACTIVES & HEALTH



13-15 September 2016

Norwich, UK

Demonstrating **COST** EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY food bioactives: challenges and opportunities



Norwich, United Kingdom



## Short Term Scientific Missions

ANDREA FILIPA ALMEIDA



### STSM Topic: Confirmation of the presence of acetylcysteinyl phenolic metabolites in human cells media

This short term scientific mission at CEBAS-CSIC in Murcia (Spain) allowed me to learn new techniques used to analyze metabolites in different biological samples under the supervision of Dr. Francisco Tomás-Barberán and Dra. Rocío García-Villalba. The acetyl-cysteinyl phenolic metabolites have been identified in human volunteers after the intake of a polyphenol-rich juice and, recently, it has been shown that they may have beneficial effects against neurodegenerative diseases. New approaches and analytical techniques are very important skills that I need for my research since they will help me to identify metabolites of polyphenols conjugates present in biological samples. These samples were analyzed using an UPLC-MS-NMR after they were specifically prepared for HPLC

analysis. The metabolites of interest were retained and concentrated using an automatic SPE extraction system and then eluted from the SPE system with deuterated solvents and directly analyzed in the 500MHz instrument.

This STSM allowed me to develop new ideas and work with new colleagues in different areas of knowledge which may be the base for the development of future projects. My stay at CEBAS was an opportunity to improve my skills and knowledge and to collaborate with news partners. Staying during two weeks in Murcia was an opportunity to develop at a personal level and I encourage others young colleagues of the COST action to use the STSM opportunity in the same way.

## Short Term Scientific Missions

**ANTONIO GONZÁLEZ-SARRÍAS & PAULA PINTO**

This STSM took place at the University of Glasgow under the supervision of Dr. Emilie Combet. The mission was fully dedicated to gain skills and knowledge of the tools needed for meta-analysis and was applied to the objectives planned within POSITIVE COST Action, i.e. evaluating the effects of bioactives compounds and the assessment of inter-individual variability on specific cardio-metabolic biomarkers.

During two hardworking weeks in Glasgow, we learned how to prepare the data for analysis, define specific subgroups for analysis of interindividual variability and run the meta-analysis using the Comprehensive Meta-Analysis software. During the working day, we were able to relax and enjoy hot chocolate and coffee from a machine nearby!



lovely lunch in an excellent restaurant in Glasgow and ended it with Emilie's group having dinner and a Scottish



### STSM Topic: Meta-analysis tools and guidelines to assess the impact of ellagitannins and anthocyanins & Meta-analysis on flavonols

By the end of the two weeks, we had completed most of the analysis of flavonols effects and started the analysis of the flavanols effects. This visit became a great opportunity to enhance the interaction and communication between our respective research groups.

It was cold most of the time but, fortunately, we could enjoy a few sunny days. We also enjoyed our visit to the city center and the views of some beautiful landscapes during weekend. We started our STSM with a

beer in Drygate bar. We would like to highly recommend the STSM to other scientists as we felt it provided us with many new experiences and increased our knowledge in other research areas.

With many thanks to Dr. Emilie Combet and her team. Full STSM reports can be read at:

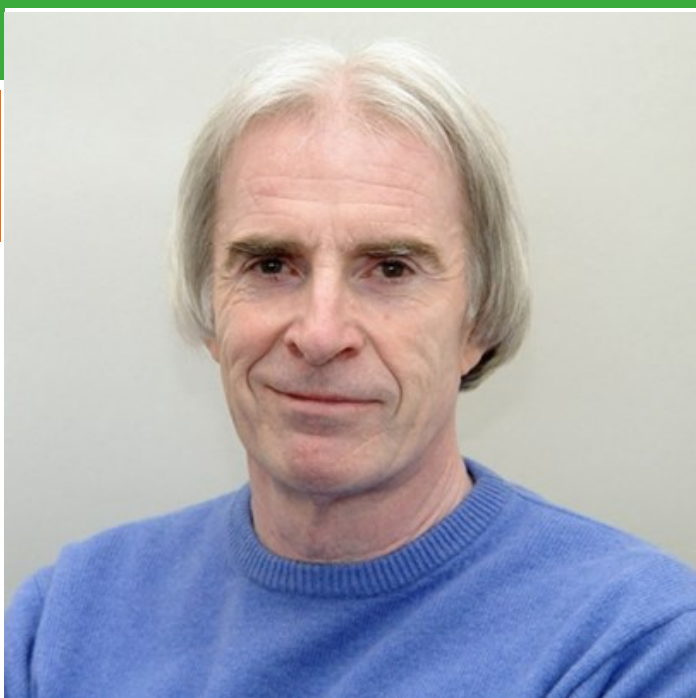
<https://www6.inra.fr/cost-positive/Trainings-STSMs/STSMs/STSMs-2016>

**SCIENTIFIC EXPERT'S OPINION**
***NEARLY 30 YEARS  
OF POLYPHENOL RESEARCH***

It all started for me when we asked ourselves what compounds in vegetable and fruit are responsible for the epidemiological observations that a diet rich in vegetable and fruit is associated with reduced cancer risk. Professor Daan Kromhout, an outstanding epidemiologist and principle investigator of the Dutch Zutphen Study, then mentioned the work of a pathologist, Lee Wattenberg, who showed that a whole variety of compounds was able to inhibit the development of tumours induced in mice. Remarkably, common compounds of plants sometimes showed to be potent inhibitors of the progression of cancer, e.g. the flavonol quercetin.

So, could quercetin play a role in the beneficial effects of vegetables and fruits? To answer that question we had to know the dietary intake of quercetin, but at that time, data on quercetin contents in foods were not available. Consequently, we embarked on a project to develop an analytical method for quercetin (and other flavonols) in foods, measure their contents in common foods, determine their intake in the Zutphen Study, and relate this intake to health outcomes in Zutphen. This project was successfully completed and we were very proud to be able to publish the very first epidemiological evaluation of flavonoids. Because of our novel findings, the Lancet accepted our manuscript (Hertog et al., Lancet, 1993;342(8878):1007-11), and the paper has been very highly cited since (citations >2850). However much to our surprise, we did not find an effect on cancer, but showed that flavonols reduced the risk of coronary heart disease by some 60%.

These positive findings boosted the interest of the research community in flavonoids, and a myriad of research questions were waiting to be answered. To name a few: what is the bioavailability of flavonols, what are determinants of their bioavailability, what are potential mechanisms of beneficial effects, what about the health



*Prof. Peter Hollman  
Nutrition and Health, Wageningen University,  
The Netherlands*

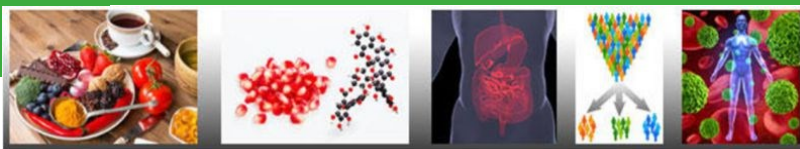
effects of other flavonoids, or more generally of polyphenols? In these past years we were very happy to be able to contribute to the answer to these questions which was quite challenging because each of these various topics required different types of expertise.

As an analytical chemist, it was quite a thrill when I began to realise that polyphenols are a huge group of related compounds: tens of thousands of different polyphenols are estimated to occur in plant foods. But, how could we ever try to address this complexity? Therefore, acknowledging their similarities in chemical structures, the major question of my research always has been: "Can we link the chemistry to biological activity?" Obviously, the phenolic hydroxyl group is the basic chemical structure characterising polyphenols. This structure causes their outstanding antioxidant properties. So, is their antioxidant activity possibly protecting against oxidative damage in the body, really biologically relevant? If true, measuring the total antioxidant activity (TAC) of a food or a full diet would predict their favourable biological activity, and also would greatly reduce the complexi-

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## SCIENTIFIC EXPERT'S OPINION



ty because all polyphenols would be combined into a single value. This so-called antioxidant hypothesis became very popular, and the United States Department of Agricultural (USDA) even published a

among others enzymes involved in cellular protection or signalling pathways involved in inflammation. In addition, because the largest proportion of the polyphenols will reach the colon, the role of microbiota potentially will offer new insights in their biological activity. This activity may not be possibly caused by the small polyphenols produced by ring



food table with TAC values. However, it became clear that the TAC of a food is not a predictor for systemic antioxidant effects at all because of the poor absorption and extensive metabolism of polyphenols (Hollman et al., J Nutr, 2010;141:989S-1009S). This example shows that knowledge of the bioavailability and metabolism of polyphenols is crucial to be able to understand their biological effects. I am therefore happy to contribute to the activities of the WG1 within this POSITIVE COST Action which is reviewing published information on these aspects of e.g. polyphenols.

As it is clear now that circulating concentrations of polyphenols are in the nM range rather than the mM range, new hypotheses for their biological activity have to be tested. Potentially of interest are signal transduction pathways that regulate

fission because until now there is little evidence of their biological effects. However, an emerging and exciting



new topic could be to investigate changes in gut microbiota composition and the potential link between those and the benefits for the human host health.

## SAVE THE DATE

21-23 February, 2017



### POSITIVE Working Groups Meeting

Organized by Prof. Mariusz Piskula, Dr. Wiesław Wiczowski, Iwona Kieda from the **Institute of Animal Reproduction and Food Research PAS in Olsztyn, Poland**

**RESEARCH DISSEMINATION**
**PUBLICATIONS**

Plant food bioactives can be absorbed in the small intestine, but most of the glycosylated, polymeric or esterified native plant compounds are hydrolyzed and metabolized by the gut microbiota. The bioactive compounds and their microbial metabolites undergo Phase I (oxidation/reduction reactions) and Phase II ( $\beta$ -glucuronidation, sulfation, methylation, glutathione conjugation) metabolism. In the case of polyphenols, phase II metabolism prevails because of their polyhydroxylated structures. Several metabolizing phenotypes, or "metabotypes", exist depending on the concentration and activity of intestinal carriers, phase I and phase II enzymes, and of the composition and activities of the microbiota. Thus, for the same dietary intake, exposure to bioactive metabolites can largely differ



Kateřina Purchartov, Vladimr Křen & Kateřina Valentov

We have recently developed preparatory methods for chemoenzymatic synthesis of sulfated flavonoids using two types of aryl sulfotransferases (AST). Recombinant mammalian sulfotransferase IV from rat liver (EC 2.8.2.1) can be used to catalyze the transfer of a sulfate group from phenolic sulfate esters to a phenolic acceptor substrate employing the 3'-phosphoadenosine-5'-phosphosulfate (PAPS) cofactor regeneration system by whole transformed cells. Another sulfotransferase, e.g. bacterial aryl sulfotransferase from *Desulfito-*

*bacterium hafniense*, previously proved to be suitable for preparatory syntheses of respective aryl sulfates and also its regioselectivity seems to be rather close to the mammalian enzyme. Here a cheap sulfate donor, e. g. *p*-NPS, can be used. In the present paper, we focused on sulfated metabolites of common flavonoids - quercetin, taxifolin, isoquercitrin and rutin. The rat liver enzyme was able to sulfate only quercetin and taxifolin, quercetin glycosides remained intact. *D. hafniense* enzyme sulfated isoquercitrin and rutin selectively at the position C-4' of the quercetin moiety in very good yields. Taxifolin was sulfated at C-4' and minor amount of C-3' isomer was formed. Sulfation of quercetin proceeded preferentially at C-3' but a lower proportion of C-4' isomer was formed as well. Bacterial AST from *D. hafniense* was identified as a perfect tool for the biotransformation of the whole array of the flavonoids; it is stable, highly efficient and high yielding (50-80%). The isolation and full characterization of the sulfated products from both ASTs found that their sulfated products were identical. The sulfates can therefore be used as authentic standards in further metabolic studies, especially for the metabolomics group of the POSITIVE network.



DOI: 10.1002/cctc.201500298

**CHEMCATCHEM**  
Full Papers

### Prokaryotic and Eukaryotic Aryl Sulfotransferases: Sulfation of Quercetin and Its Derivatives

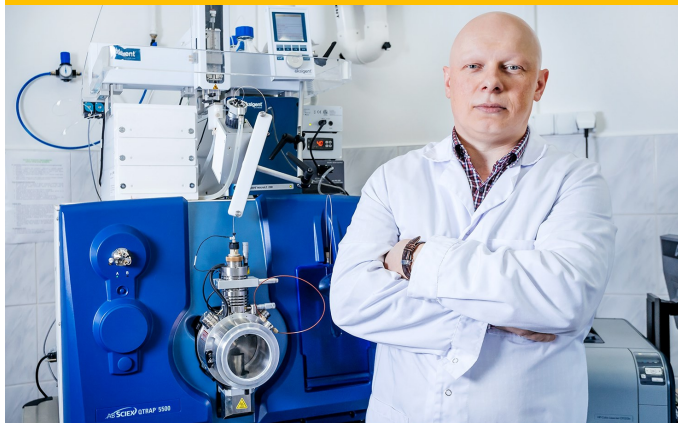
Kateřina Purchartov,<sup>[a, b]</sup> Kateřina Valentov,<sup>[a]</sup> Helena Pelantov,<sup>[a]</sup> Petr Marhol,<sup>[a]</sup> Josef Cvačka,<sup>[c]</sup> Libor Havlček,<sup>[d]</sup> Alena Křenkov,<sup>[a]</sup> Eva Vavřikov,<sup>[a]</sup> David Biedermann,<sup>[a]</sup> Christopher S. Chambers,<sup>[a]</sup> and Vladimr Křen<sup>\*[a]</sup>

between individuals and must be characterized in depth.

The exact identification of bioactive metabolites in human samples strongly depends on the analytical procedures used (mostly HPLC-MS/MS analyses) and the use of authentic, pure and fully structurally characterized standards of the metabolites. Commonly used MS techniques seldom provide structural information allowing for the determination of the exact structure. This is important for polyphenols, where region-isomers are hard to distinguish. NMR spectroscopy is the only reliable method (besides X-ray spectroscopy) to determine the site(s) of e.g. sulfation. However, even here the task is not trivial as the place of sulfate substitution can be determined only indirectly (no couplings available) from the shifts of the carbons in the aromatic ring. We propose the methylation of flavonoid sulfates as a novel approach for the direct and unequivocal determination of the position of sulfates (and possibly also other groups lacking direct interactions) in polyphenols. Replacement of hydroxyls by easy detectable methoxyl singlets enabled – based on the HMBC correlations - to locate methoxyl groups and clearly deduce the site of sulfate attachment.

## RESEARCH DISSEMINATION

## PUBLICATIONS



Dr. Wiesław Wiczkowski, IAR&FR, Polish Academy of Sciences

There is something fascinating about the mechanisms taking place in the human body. It has to be admitted even by people not engaged in the scientific study on daily basis. This enormity and complexity of processes and substances involved is astonishing and not fully recognized yet. So it is in case of nutrition. Today we know that the a reasonable nutrition, from the first days of our life up to old age, may be one of the main factors positively influencing our health status. In addition to physical activity, a proper diet containing elements essential for the human body, diversified depending on age, gender and lifestyle, is a prerequisite for the prevention of many diseases, including so called civilizational diseases. Recent research has shown that the consumption of cereals, legumes, fruit and vegetables is crucial for a proper human nutrition. They are the source of many valuable components, including carbohydrates, proteins, fats, vitamins and minerals, as well as a number of non-nutritive substances having biological activity. Investigation of the metabolism of these bioactive substances present in food with respect to their interindividual variability remains a vital phenomenon to be further considered. And this is one of the main issues POSITIVE is dealing with.

The recent article by Wiczkowski *et al.* (Food Chemistry, 2016, 190, 730-740) was focused on the anthocyanin profile in red cabbage, widely appreciated for its attractive dietetic and taste values. Apart from being responsible for the intense purple/red color of cabbage, anthocyanins have a number of biological properties that may be advantageous to human health. The study in focus showed that red cabbage cultivated in Poland is a source of 20 different anthocyanins with the main structure of cyanidin triglucosides defining the color of this vegetable. The glucoside residues of anthocyanins found were nonacylated and acylated with sinapic, ferulic, caffeic and *p*-coumaric acids. The process of fermentation applied during the study reduced the total content of anthocyanins in red cabbage at the level of 15%. After fresh and fermented red cabbage consumption, the



The impact of red cabbage fermentation on bioavailability of anthocyanins and antioxidant capacity of human plasma

Wiesław Wiczkowski\*, Dorota Szawara-Nowak, Jerzy Romaszko

Institute of Animal Reproduction and Food Research of the Polish Academy of Sciences in Olkztyn, Tuwima 10, 10-748 Olkztyn, Poland

HPLC-MS/MS analysis of human blood plasma and urine collected showed that 30 cyanidin derivatives were present in physiological fluids. Apart from 18 native cyanidin compounds, the presence of 12 cyanidin metabolites, including methylated, glucuronidated and sulfated forms, were found. However, the cyanidin derivatives, present in the blood plasma and excreted with the urine after consumption of fresh and fermented red cabbage, were mainly represented by native compounds (above 75% of anthocyanins found). In the case of blood plasma, among native compounds, cyanidin 3-(sinapoyl)-diglucoside-5-glucoside was the main compound, while in urine cyanidin-3-diglucoside-5-glucoside predominated. Among 12 metabolites of cyanidin found, methylated cyanidin (sinapoyl)-triglucoside was predominant in blood plasma, while methylated cyanidin monoglucuronide in urine. Generally, upon absorption, most of anthocyanins appeared in the body fluids in unmetabolized forms. On the other hand, among the metabolic routes, methylation constituted the major path, with glucuronidation and sulfation playing a minor role in the metabolism of red cabbage anthocyanins in humans.

In the study described, the bioavailability of anthocyanins from fresh red cabbage was higher than from fermented red cabbage. This difference was determined by various food matrices and the saturation of anthocyanins absorption mechanisms. In addition, accumulation of these compounds in the urine after the consumption of red cabbage was affected by the particle size and anthocyanins affinity for water. Furthermore, the antioxidant capacity of human plasma water-soluble substances analyzed by PCL ACW method was also examined in this study. Volunteers' plasma exhibited a higher antioxidant capacity upon the consumption of fresh cabbage than after the intake of fermented cabbage.

In conclusion, the study in focus demonstrated that the fermentation process affects the bioavailability of red cabbage anthocyanins and the antioxidant capacity of human plasma. This indicates that red cabbage is a rich source of bioavailable derivatives of cyanidin and may be used as a natural food ingredient and/or dietary antioxidant, especially when the prophylaxis of diseases associated with oxidative damage is considered. Taking into account the aims of POSITIVE, further studies are now needed to investigate the gut metabolism of red cabbage anthocyanins with respect to the issue of interindividual variability.

## RESEARCH DISSEMINATION

### PUBLICATIONS

#### New rule for funding Open Access

#### Publications

The Steering Committee (SC) has submitted to the MC a rule aiming to govern the funding of Open Access publications in POSITIVE. COST provides financial support for the production of dissemination material (website, material for display or distribution, multimedia content, publications). To be eligible for funding, this material must be a direct result of work performed by the Action and must be authored by several participants from different Participating countries. Dissemination material must reflect the Action's objectives, detailed in the Action's MoU. COST encourages Open Access in order to promote the availability of results published thanks to COST funding, as a way to boost the visibility and accessibility of publicly funded European science and technology worldwide. More specifically, COST participates in the funding of Open Access publishing strategies.

Considering the expectations of COST and the annual budget of the Action, the rule proposed by the SC for funding Open Access publications in POSITIVE is as follows:

*"In order to help in publication of papers resulting from the COST Action FA1403-POSITIVE in Open-Access journals and in respect with the annual budget of the Action, it is proposed that the COST Action POSITIVE takes in charge open access fees for publications involving Institutions from at least 5 participating countries and directly resulting from the discussions of the WGs. This will be done in the limit of the budget available for Dissemination for the Grant Period. However, the MC could be asked by the SC to re-allocate underspent budget for the Open Access licenses later on in the Grant Period".*

By way of indication, such a rule could help in funding 2 to 4 open access publications per grant period (GP), (2 for GP2 and 4 for GP 3 and for GP4). It is important to note that the publication of articles in Open access journals of the work carried out in a COST action is **encouraged but not mandatory**.

From a practical perspective, the procedure will be as follows:

- Prior to submission, the corresponding author should inform the Steering Committee (SC) about the willingness of all the co-authors to publish in an Open Access Journal. Considering both the topic of the paper, the impact of the Journal and the assumed REF score of the paper, the SC will render its decision and inform the Grant Holder of its approval.
- The open access publications fees should be paid to the Journal by the institute/university of the corresponding author, who will be reimbursed for the full amount, by the Grant Holder of the COST Action (INRA) in receipt of an invoice.

*This rule for funding Open Access publications has been approved by the MC (June 23, 2016).*

## SAVE THE DATES

### FURTHER CONFERENCES and CONGRESSES in September 2016

#### Black Sea Association of Food Science and Technology Congress (B-FoST Congress)

22 -24 September 2016 in Ohrid, Macedonia <http://keyevent.org/CongressComittees>

#### Conference "Modern technologies in food industry" MTFI-2016, Chisinau, Republic of Moldova,

20-22 September, 2016



For more information, please, contact **Dr. Adriana BIRKA** (University of Moldova; [birca.adriana1@gmail.com](mailto:birca.adriana1@gmail.com))

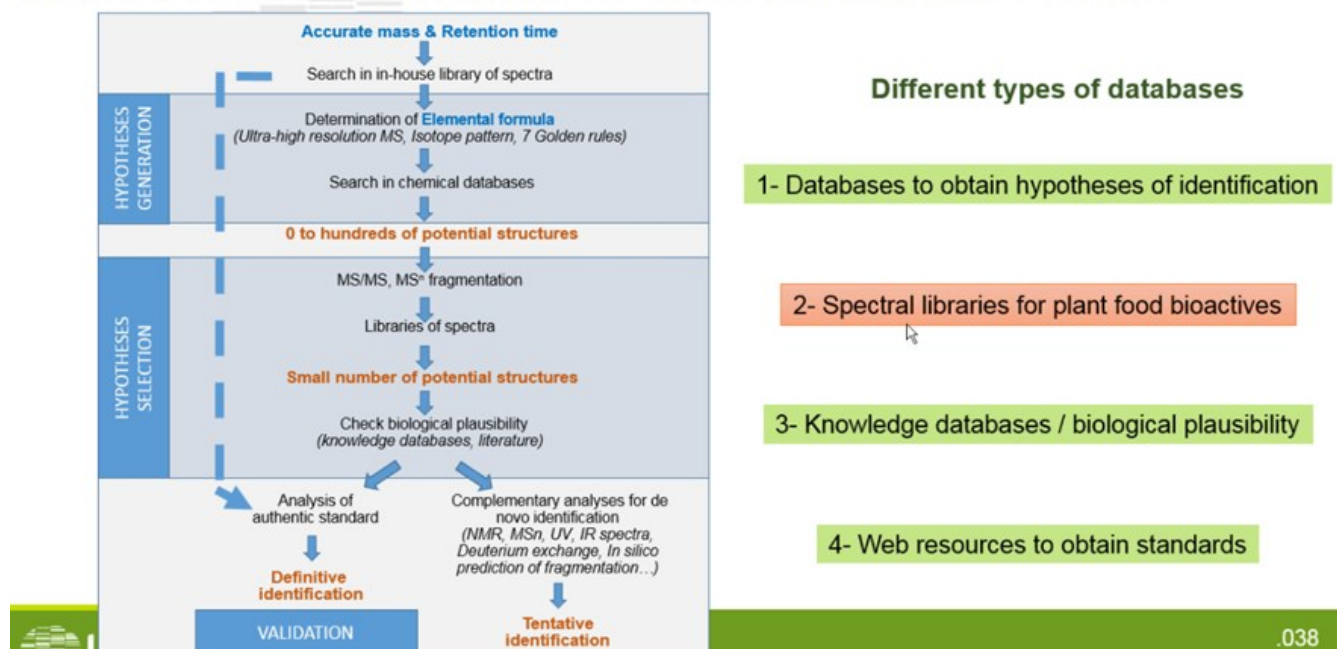
## RESEARCH DISSEMINATION

### TRAINING SCHOOL

The first training school on the "Use of Metabolomics in Nutrition Research" has been celebrated in three sessions on the 24<sup>th</sup>, 26<sup>th</sup> and 30<sup>th</sup> of May 2016. Each session consisted of a webinar that lasted about two hours and a half and included different lectures followed by a short time for questions. At the beginning of each session Dr. Liliana Tudoreanu (University of Agronomic Sciences and Veterinary Medicine of Bucharest) explained how to use the GoTOWebinar tools and then Dr Ra-

Manach, INRA Clermont-Ferrand). The last session was dedicated to applications of nutrimetabolomics using different analytical platforms and consisted of four lectures: "Discovery of biomarkers of whole grain intake using non-targeted LC-MS metabolite profiling" (by Dr Kati Hanhineva, University of Eastern Finland), "Characterization of microbial metabolism of polyphenols using GCxGC-TOFMS" (by Dr Anna-Marja Aura, Technical Research Centre of Finland), "Host-microbe co-metabolism assessed by LC-MS and NMR metabolomics" (by Dr Sofia Moco, Nestle Institute of Health Sciences), and "Clinical phenotype clustering in cardiovascular risk patients for the identification of red wine polyphenol intake" (by Dr

## IDENTIFICATION WORKFLOW FOR MS-BASED METABOLOMICS STUDIES



*Identification workflow explained by Dr. Claudine Manach in her lecture about databases used in Nutrimetabolomics.*

fael Llorach (University of Barcelona) and coordinator of the metabolomics training school, made a short introduction about the session.

The first session was an "Introduction to metabolomics" with basic concepts, applications in nutrition (by Dr Lars Ove Dragsted, University of Copenhagen) and a description of the analytical workflow (by Dr. Rafael Llorach, University of Barcelona). The second session included three lectures about strategies for data processing and analysis (by Dr Carl Brunius, Swedish University of Agricultural Sciences), strategies for metabolite identification (by Dr. Estelle Pujos-Guillot, INRA Clermont-Ferrand) and databases in nutrimetabolomics (by Dr Claudine

Rafael Llorach, University of Barcelona). Webinars were followed on average by 50 people per session with an active participation and plenty of interesting questions and discussion after each lecture. The main initial goals of the webinars have been achieved: 1) to understand the importance of metabolomics in nutrition studies, 2) to know their applicability, 3) to become familiar with the main metabolomics platform techniques and 4) to get first insights into data processing and interpretation.

*Videos of the metabolomics webinars can be accessed through the website at the restricted area:*

<https://www6.inra.fr/cost-positive/Restricted-Access/Videos-1st-Training-School>



## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHER



**Dr. Adriana Mihaela Tudose**

*Carol Davila University of Medicine & Pharmacy, Bucharest*

#### What is the focus of your research?

I am a doctor first, and specialize in allergic diseases.

#### In what countries/organisations have you studied or worked?

I graduated from Carol Davila University of Medicine and Pharmacy (Romania) in 1999. I did a year of internship as a general practitioner in Bucharest University and Emergency Hospital. Subsequently, I got specialized in clinical immunology and allergy. Since 2008, I have been the Assistant Professor in the Department of Allergology at Carol Davila University of Medicine and Pharmacy. I carry out my clinical work in Nicolae Malaxa Hospital in Bucharest. I am a member of the Romanian Society of Allergology and Clinical Immunology, European Academy of Allergy and Clinical Immunology, and World Allergy Organisation.

#### What has been the greatest achievement in your career?

The greatest achievement in my career was the out-

come of my research in genetic profile of patients with autoimmune urticaria and hypersensitivity to NSAIDs. Once the research results were obtained, I was granted a PhD in medical sciences.

#### Which is your favourite paper you have written/co-authored and why?

My favourite paper is "The safety profile of etoricoxib in autoreactive urticaria" since it investigates therapeutic alternatives for patients with autoreactive urticarial.

#### Who is/was your most influential mentor/colleague and why?

The person who influenced me most in my career is Prof. Florica Popescu, the PhD coordinator. She has taught me perseverance and patience, so crucial for a successful research career.

#### What is your advice for young scientists?

Do not give up!

#### Where is your favourite place in the world and why?

My favorite place in the world is my home with my husband and my child. Here I find peace of mind and I am surrounded by love.

#### What is your favourite music/book?

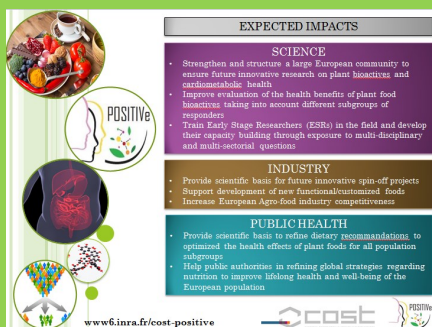
Loreena McKennitt, a Canadian musician who writes, records and performs world music with Celtic and Middle Eastern themes.

#### What is your favourite sport(s)?

hiking trails

## POSITIVE SLIDES

Interested in introducing POSITIVE at your Institution or at any Conference or Meeting that you may be attending?



**EXPECTED IMPACTS**

**SCIENCE**

- Strengthen and structure a large European community to ensure future innovative research on plant bioactives and cardiometabolic health
- Improve evaluation of the health benefits of plant food bioactives taking into account different subgroups of responders
- Train Early Stage Researchers (ESRs) in the field and develop their capacity building through exposure to multi-disciplinary and multi-sectorial questions

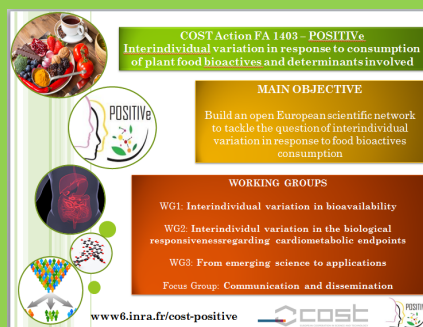
**INDUSTRY**

- Provide scientific basis for future innovative spin-off projects
- Support development of new functional/customized foods
- Increase European Agro-food industry competitiveness

**PUBLIC HEALTH**

- Provide scientific basis to refine dietary recommendations to optimised the health effects of plant foods for all population subgroups
- Help public authorities in refining global strategies regarding nutrition to improve lifelong health and well-being of the European population

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**COST Action FA 1403 - POSITIVE**  
Interindividual variation in response to consumption of plant food bioactives and determinants involved

**MAIN OBJECTIVE**

Build an open European scientific network to tackle the question of interindividual variation in response to food bioactives consumption

**WORKING GROUPS**

WG1. Interindividual variation in bioavailability  
WG2. Interindividual variation in the biological responsiveness regarding cardiometabolic endpoints  
WG3. From emerging science to applications

Focus Group: Communication and dissemination

www6.inra.fr/cost-positive

Contact us to get the POSITIVE slides: [i.kieda@pan.olsztyn.pl](mailto:i.kieda@pan.olsztyn.pl)

## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHERS



**Desislava Abadjieva**  
IBIR-BAS, Sofia, Bulgaria

#### What is the focus of your research?

The focus of my research is the impact of biologically active substances of non-hormone origin on the reproductive potential of farm animals, and elaboration of novel methods and approaches on the reproduction in animals to facilitate a maximum use of their reproductive capacity.

#### In what countries/organisations have your studied or worked in?

I work and finished my PhD thesis in the Institute of Biology and Immunology of Reproduction, but when I was a PhD student I visited the Group of Human and Animal Physiology at the Wageningen University, Department of Anatomy, Martin Wuther University- Halle, Germany (Training school of RGB- COST Action) and the University of Veterinary Medicine, Murcia, Spain (Epigenetic Training school of COST Action 1203).

#### What has been the greatest achievement in your career?

...upgrading my career skills, as mastering molecular methods.

#### Which is your favourite paper you have written/co-authored and why?

“Tribulus terrestris Alters the Expression of Growth Differentiation Factor 9 and Bone Morphogenetic Protein 15 in Rabbit Ovaries of Mothers and F1 Female Offspring”, these are the results of my thesis.

#### Who is/was your most influential mentor/colleague and why?

Oh, undoubtedly, prof. E. Kistanova is my most influential mentor, because she is “Uhuu” .... very conceptual.

#### Where is your favourite place in the world and why?

Brazil – but I've never been there, just a dream....

#### What is your favourite music/book?

My favorite music is evergreen and typical national Bulgarian music “horo”.

My favorite book is “Love” of Elif Safak.

#### What is your favourite sport(s)?

My favorite sport is volleyball and riding a bike.

## JOIN US ON TWITTER



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[www.twitter.com](http://www.twitter.com)

## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHER

#### What is the focus of your research?

My research interest is the organic synthesis with application in the biological area. Mainly, synthesis and identification of polyphenolic metabolites presence in human and cellular samples after biological processes.

#### In what countries/organisations have you studied or worked in?

I obtained my degree in chemistry at the University of Lisbon and now I'm doing my PhD with the Molecular Nutrition and Health group in Instituto de Biologia Experimental e Tecnológica (Portugal). My work is focused on the development of new methodologies for synthesis and identification of the different types of polyphenols metabolites, mainly sulfates, glucuronides, acetylcysteine and glutathione derivatives. These compounds were identified in human volunteers after polyphenols-rich juice consumed and recently has been demonstrate an interesting result in cell models of neurodegenerative diseases. In March 2016, I worked at CEBAS-CSIC (Spain) where it was possible to learn a new analytical technique of identification these metabolites in biological samples.

#### What has been the greatest achievement in your career?

I think that in my short career my greater achievement was to obtain a grant of PhD in research institute that to

allow continue developing my research career.

#### Which is your favourite paper you have written/co-authored and why?

My favourite paper is my first paper in Organic Letters about work developed in my degree because was the starting point of my research career.

#### Who is/was your most influential mentor/colleague and why?

My most influential mentors are the scientists with whom I have worked that has allowed to learn as much as possible. With their experience and knowledge in different areas each and every one of them have allowing to improve my knowledge and others important skills needed to progress in my research career.



*Andrea Filipa Almeida*  
Molecular Nutrition and Health Lab.,  
iBET, Portugal

#### Where is your favourite place in the world and why?

My favorite place is Lisbon, the city where I was born and live. It's perfect city because have a beautiful sun and near of beach.

#### What is your favourite music/

#### book?

I don't have one favourite artist, but I like Florence and the Machine, Adele, Matt Simons, Aurea and others. Recently, I read a book by Dan Brown "The lost symbol" but I prefer watching movies.

#### What is your favourite sport(s)?

One of my favourite sports is trekking that I try to do in my free time.

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## CHAIR'S CORNER

Dear POSITIVE partners,

The networking activities within POSITIVE are now very well running, with the first collaborative papers resulting from the work of the WGs ready for submission or in preparation. These are for sure the beginning of a long series!

During the last meetings it has become evident the complexity of the topic studied within POSITIVE, and the need for a multidisciplinary approach to reach the Action objectives and training to share knowledge and skills.

As detailed in a previous section of this newsletter, the COST Action POSITIVE organises this year its 1<sup>st</sup> Training School focused on the Use of Metabolomics in Nutrition Research. The aim of this TS is to help in promoting new research in the field of the Action using innovative approaches. We have initiated a new formula of TS in a COST Action by combining open webinars for a broad audience (May 2015) together with a hands-on part dedicated to the training of a dozen ECIs and experienced researchers of the Action (5-8 July 2016, Barcelona). This formula has been very successful since it has allowed more than 60 POSITIVE partners to benefit from the theoretical part of the TS (webinars are now available on the website of the Action). We would like to take the opportunity of this newsletter to thank all the partners involved in this TS, including the organisers and the trainers. The organisation of the TS is coordinated by Dr. Rafael Llorach (University of Barcelona) for the scientific aspects and by the Prof Liliana Tudoreanu (University of Bucharest) for the technical dimension of the webinars. Of course, we also warmly thank the eight experts in metabolomics in the POSITIVE community who have

accepted to be trainers in this TS. The high involvement of all these POSITIVE partners has led to the success of this theoretical part of the webinar.

The next step of the TS will be the practical course that will take place in a few days in Barcelona, under the lead of the Barcelona Group on Biomarkers & Nutrimetabolomics Research of the Pharmacy School-University that will make available all its expertise and equipment for trainees. We wish a huge success to this TS...

Before ending, once again we would like to encourage all the partners of POSITIVE to take an active contribution in the scientific activities of the WGs. If not already done there is still time to contact the WG leaders who will be very happy to include you in the ongoing or following activities of the network.

Looking forward to seeing you at the next meeting.

Christine & Paco



## CONTACT US



EUROPEAN COOPERATION IN THE FIELD OF  
SCIENTIFIC AND TECHNICAL RESEARCH

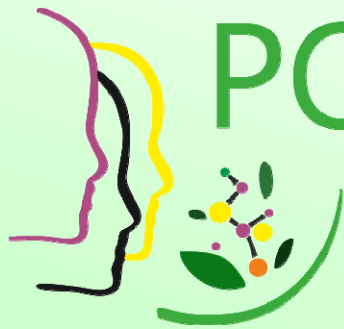
### Contact us:

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: [christne.morand@clermont.inra.fr](mailto:christne.morand@clermont.inra.fr)

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: [fatomas@cebas.csic.es](mailto:fatomas@cebas.csic.es)

### Webpage:

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)



# POSITIVE

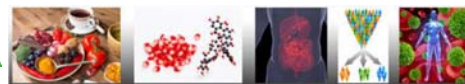
ISSUE 5



# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE IV, DECEMBER 2016

## WELCOME

We have got to the 4<sup>th</sup> edition of our POSITIVE newsletter, December 2016 !!!! Right in the mid-period of the Action. We would like to use this occasion to wish you all a joyful Christmas time and a wonderful New Year full of happiness. We also want to congratulate everybody for the huge amount of work carried out so far and the many contributions that have been done and have promoted the excellent progress of the Action.

As listed in our index, this issue summarizes the past recent conferences & activities of the Action, presents the STSMs carried out by the ECIs this year, as well as some of the latest publications. It also brings to your attention some coming meetings and the new training school. We can also read a new and interesting opinion of our Scientific Expert and Get to Know some more of our partners in the Action.

**We hope you enjoy it!**



## NEWS

### FOOD BIOACTIVES AND HEALTH CONFERENCE 13-15, September, 2016, Norwich, UK

The 1<sup>st</sup> Conference on Food Bioactives & Health (FB&H) was held at the John Innes Conference Centre, Norwich Research Park, Norwich (UK), from the 13<sup>th</sup> to the 15<sup>th</sup> of the past September (2016). The Conference was chaired by Dr Paul Kroon from the Institute of Food Research (IFR) and was designed to put together the latest evidence that supports the benefit of consuming food derived bioactive compounds as well as the challenges that still need to be solved and the opportunities for future research and development on functional foods.

The FB&H Conference also hosted the 2<sup>nd</sup> Scientific Workshop of the COST Action POSITIVE. The complete programme, gallery of pictures and the main presentations of the conference can all be seen at: <http://www.fbhc2016.com/>.

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## RESEARCH HIGHLIGHTS

Briefly, the talks presented at this FB&H conference dealt mostly with the effects of food bioactives on cardiometabolic health, brain function, cancer, gut health, etc, with a main focus on human intervention studies. The mechanisms of absorption, metabolism and their connection with the potential mechanisms of action were also covered by different presentations. Of special interest, there were also some presentations about the important interaction between colonic microbiota and the metabolism of food bioactives as well as about the human metabolic variability and differences in the responses from different groups of individuals.

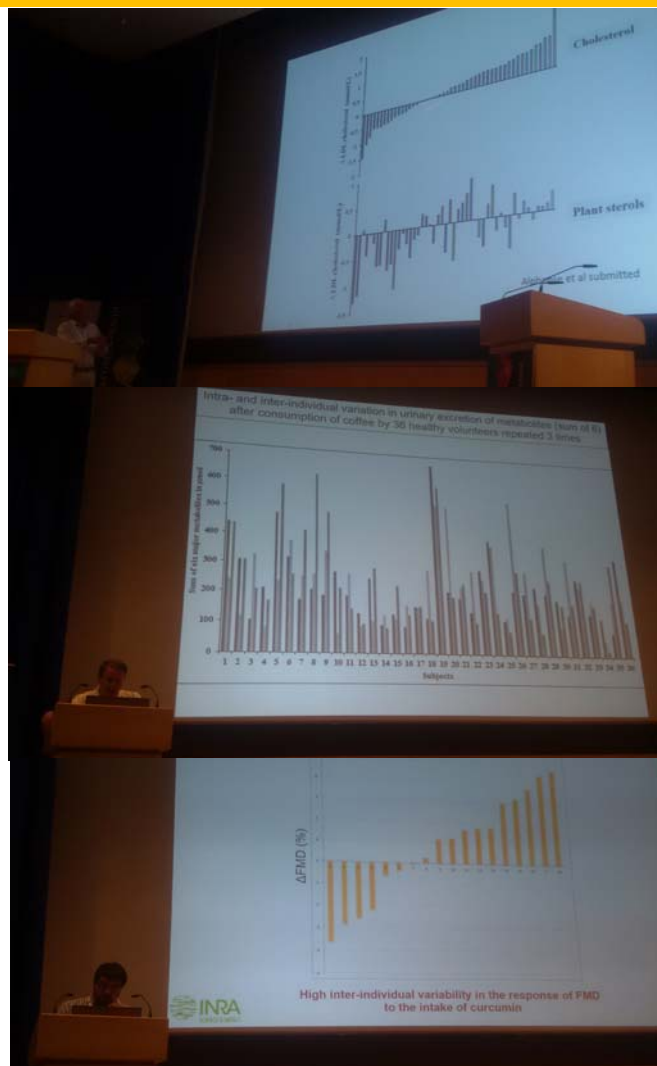


### 2<sup>nd</sup> POSITIVE Scientific Workshop (Norwich, UK, 15 September 2016) "Inter-individual variation in response to food bioactives"

On Thursday the 15<sup>th</sup> of September the FB&H conference was entirely devoted to '*Inter-individual variation in response to food bioactives*', a session that constituted the 2<sup>nd</sup> Scientific Workshop of the POSITIVE COST Action. The detailed programme of this scientific session can be found at :

<https://www6.inra.fr/cost-positive/Events/2nd-Scientific-Workshop-Norwich-2016>

The first talk of this workshop was offered by Dr Peter Jones, invited speaker from the University of Manitoba, who presented some of their latest results on inter-individual variation in response to lipid-lowering sterols and PUFAS with a focus on genetic factors, i.e. genes and SNPs, that have an impact on this response. Following his talk, several members of POSITIVE also presented their research dealing with inter-individual variation and factors affecting it. For example, Dr Anne Marie Minihane from the UEA in Norwich spoke about the role of the APOE genotypes in cardiovascular health in response to fish oil intake or, Dr Gary Williamson from the University of Leeds spoke about intra- and inter-individual variability in the metabolism of coffee phenolics. Several other partners also presented some of their latest results and some of the work carried out within POSITIVE in relation to inter-individual variability in metabolism and responses.



## RESEARCH HIGHLIGHTS

4<sup>th</sup> COST Action POSITIVE Meeting, 15-16 September, 2016

Institute of Food Research, Norwich, UK

## Work Group 1

Leader: Tom VAN DE WIELE

Co-leaders: Claudine MANACH &  
Rikard LANDBERG

As in previous occasions, the 4<sup>th</sup> WG1 meeting started off with several presentations by partners with an update of the progress carried out in their respective tasks. The leaders of different subgroups, Torsten Bohn (Carotenoids subgroup), Claudia Santos (Flavonols subgroup) and Rikard Landberg (Lignans subgroup), presented summaries of the reviews completed and the draft papers that are already submitted, ready or nearly finished. These articles review the current literature on carotenoid, flavonol and lignan metabolism and the factors affecting ADME for these compounds. Of particular interest, an important role of the microbiota in the lignan metabolism has been established. Additionally, future topics to deal with were also introduced by the subgroups leaders, such as the continuation of the initiated meta-analysis, the need to clarify the metabolic pathways for carotenoids or the progress of a study looking at factors affecting enterolactones concentration in plasma.

Maria Bronze (Metabolomic subgroup) informed about the *Multiplatform Coverage Test*. A list of 50 compounds will be used to prepare two

test-solutions. The mixtures and the SOP to follow will be sent to all the participants that will analyze the samples in their own laboratories. There was a general discussion about the final goal of this Cooperative Test which is to establish a consensus multiplatform methodology to cover the analysis of all phytochemical metabolites in future metabolomics studies. An additional outcome of these studies will be the comparison between NMR and MS approaches.

Tom Van de Wiele (Microbiome subgroup) exposed the difficulties found in the drawing of the complete metabolic pathways for the different compounds due to a general lack of information. Then, a reductionist approach has been proposed to focus only on the crucial rate limiting steps of these pathways. A template will be distributed to help with this task.

After constructive discussions within the group, it was concluded that the next actions within each subgroup will be to collect information on crucial absorption and metabolic steps and to identify biotransformation enzymes and transport proteins. Comparison to pharmacogenomics studies was proposed as a help.

Finally a STSM in the microbial variant subgroup was proposed.





## RESEARCH HIGHLIGHTS

### Work Group 2

Leader: Ana RODRIGUEZ-MATEOS

Co-leaders: Eileen GIBNEY &  
Dragan MILENKOVIC

#### *Meta-analysis subgroup*

Eileen Gibney initiated the 4<sup>th</sup> WG2 meeting in Norwich by presenting a summary of the ongoing activities, the current outputs and the future initiatives. Regarding the meta-analysis of cardio-metabolic variables, some papers have now been accepted (a position paper, a review on inter-individual variability in biological responses to the consumption of food bioactives) or submitted for publication (systematic review meta-analysis protocol, an article on inter-individual variability in cardio-metabolic markers in response to the intake of flavonols).



Other meta-analysis looking at specific groups of compounds and cardio-metabolic variables are still ongoing. Emilie Combet and others discussed various common problems occurring during data extraction and the need for independent double check of the data and changes in the data-extraction templates. During the meeting, Paula Pinto and Antonio González-Sarrías presented an update of the articles prepared or in preparation on the effects of flavonols, anthocyanins and ellagitanins on cardiometabolic endpoints. Other participants also presented an update of the progress of their respective meta-analysis on different group of compounds. It was agreed not to start any other



meta-analysis but to complete and publish the ones already initiated. Further, a Data Collaboration Agreement has been elaborated and circulated to everybody for comments. It was discussed how to approach the next stage of the analysis and how to access datasets. Datasets analysis was encouraged to be carried out through STSMs.

#### *Cell & Molecular Targets subgroup*

Dragan Milenkovic, leader of the *Cell & Molecular Targets* subgroup, also summarized the activities done so far. The three subgroups within this one: human, animal and *in vitro* studies have advanced in their work. In the animal group, all potential papers have been evaluated and those that complied with the criteria already selected. There will be a template prepared and circulated for data extraction. A similar point has been reached in the *in vitro* studies subgroup. In the human subgroup, an important number of papers have been identified and classified into an Excel file ready for the next step. A template for data extraction will also be prepared and circulated in the next months. There were several discussions on how to prepare this template and how to enhance the data extraction. Other issues such as the inter-species differential metabolic capacity, or how to tackle the analysis of the data including bioinformatics approaches were also commented.



## RESEARCH HIGHLIGHTS

### Work Group 3

Leader: Baujke DE ROOS

Co-leaders: Marina HEINONEN



The 2<sup>nd</sup> WG3 meeting took place in Norwich. There, Dr. Baujke De Roos had the opportunity to present to all the participants the main ideas and activities already initiated and those to be further developed by this group with regards to the preparation of strategies to disseminate the Action aims and results to different stakeholders and other end-user groups. A questionnaire which was already sent to different end-users has already provided a number of responses although many more are needed before it is possible to get a good overview of the opinions of these stakeholders and user groups. Hopefully, a lot more will be gathered and presented during the next meeting in Poland.

There were also some general discussions about other strategies such as the preparation of small videos and webinars describing successful interactions and projects between researchers and

industrial partners. There were several offers by various partners to prepare some of these videos that should be ready for February. In addition, other strategies presented and discussed were:

- the possibility of a COST scientist to present the scientific outcomes and deliverables of POSITIVE in a major meeting directed to stake-holders and end-users
- the preparation of a white paper to disseminate POSITIVE amongst the Agro-food industry, on-line forums, etc
- the development of an easy-to-use on-line tool to allow stakeholders find the information that relates foods-ingredients-bioactive compounds-proven beneficial effects-interindividual responses. This will be based on the results of all the meta-analysis and activities that are being developed within the Action
- the writing of a final 'roadmap' will be undertaken later on in the Action.

## OF INTEREST TO THE POSITIVE COMMUNITY

09 - 11 May 2017, Palexpo,  
Geneva, SWITZERLAND

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## RESEARCH HIGHLIGHTS

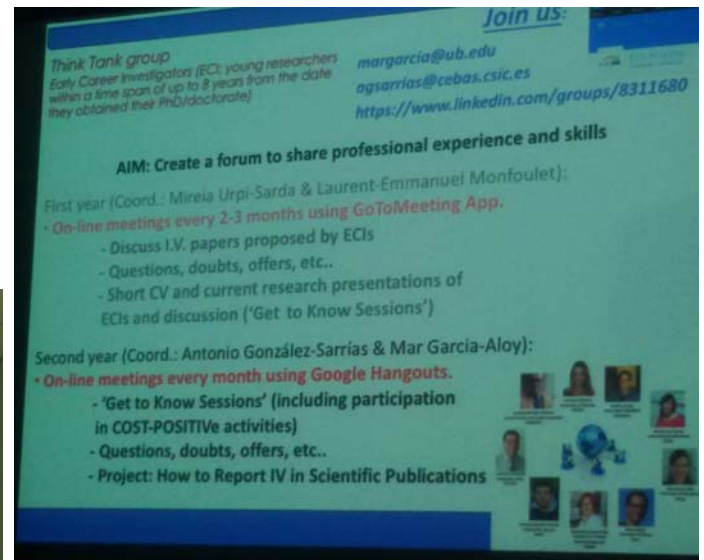
### Think Thank Group

Although there was not an official Think-Tank-Group (TTG) meeting in Norwich, the current coordinators of the TTG, Dr. Mar García-Aloy and Dr. Antonio González-Sarriás, attended the meeting and had the opportunity to present a summary about the progress of the Early Careers Investigators (ECIs) contributions to the general objectives of POSITIVE.



They specifically referred to the development of one of their current and very interesting projects: the elaboration of a manual on '*How to Report Interindividual Variability in Publications*' where one of the main goals is to propose and gather general guidelines, suggestions, recommendations and a checklist to cover the requirements

necessary to correctly report data concerning inter-individual variability in the most accurate way for future publications. Eventually, this information will be published as an opinion paper.



In addition to this, the activities of the TTG include monthly webinars where ECI members present a short introduction about the research that they are carrying out in their own institutions. These webinars allow for a nice and friendly interaction between the ECIs, while increasing their knowledge of the techniques and research areas of each participant. This information could be very useful to any ECI for future work and collaboration or should they be interested in applying for any specific STSM.

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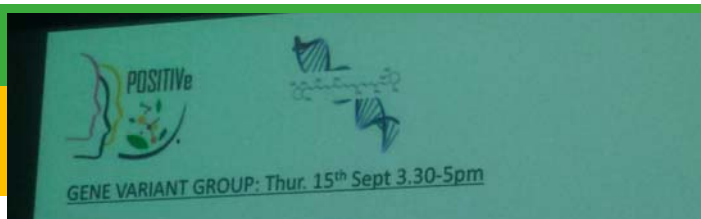
## RESEARCH HIGHLIGHTS

### Gene Variant Group Leader: Anne Marie MINIHANE

The gene variant group (GVG) led by Dr. Anne Marie Minihane had its first gathering *via* teleconference on the 8<sup>th</sup> of the past July. During this call Anne Marie presented an overview of the main issues that should be investigated and discussed within this subgroup of the Action. The GVG will focus on the impact of genetic variability of metabolic enzymes in the ADME of flavonoids. Genetic variation is also likely to have an effect on the specific targets of these compounds and biological responses triggered by their consumption. Nevertheless, the data in the literature about all this are still limited and need to be rechecked and expanded. There were a number of points and activities that were considered for further discussion in Norwich.



During the 1<sup>st</sup> meeting of the GVG in Norwich, Anne Marie Minihane initiated the session with a scientific overview of the relevance of genetic variance in the role of food bioactives intake on human health. After the short introduction, Anne Marie herself, Charles Demarchelier and Julie Dumont exposed to the audience their experiences with some of their respective human intervention trials investigating the impact of genotype, as well as with the different approaches and analyses applied.



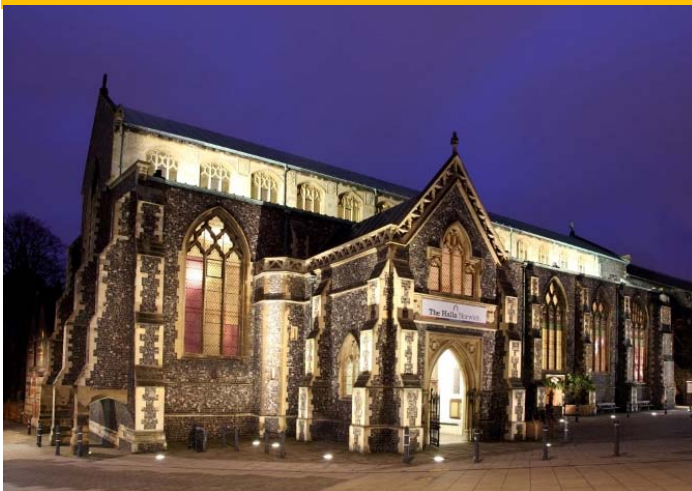
These presentations were followed by a general discussion about what may be the best future strategies to follow and how to focus the work and research to do. It was suggested to concentrate on a few compounds and specific metabolic enzymes. The GVG and the WG2 will collaborate in the preparation of a review article on already known genetic variants of relevance for bioactive compounds and cardiometabolic end-points and will establish a database of candidate genes. These genes and variants will be selected from the reviews and analyses currently being developed in the WG2 Cellular & Molecular targets subgroup.

The GVG will also collaborate with other Action members in the preparation of the second Training School next September.



## RESEARCH HIGHLIGHTS

## SOCIAL EVENTS



During the meeting in Norwich, a gala dinner was held at Saint Andrews Hall, a magnificent building located in the heart of Norwich.

On this occasion, the Hall offered to all the participants at the Food Bioactives & Health Conference as well as many of the POSITIVE partners that attended this conference a delightful meal that included, among other things, a tasty and 'healthy' super-broccoli soup. After the dinner, many brave participants volunteered to entertain the rest of the people with dancing. Great fun!!!!



## SAVE THE DATE



### 21-22, February 2017

### COST Action POSITIVE 5<sup>th</sup> Meeting

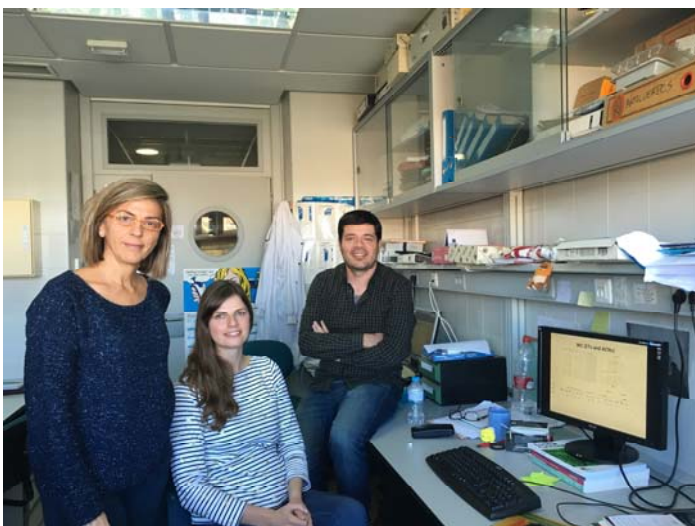
Organized by Prof. Mariusz Piskula, Dr.  
Wiesław Wiczowski, & Iwona Kieda

**Institute of Animal Reproduction & Food  
Research PAS  
Olsztyn, Poland**

## SHORT TERM SCIENTIFIC MISSIONS

**KAREN CHAMBERS** from the UK went to **CEBAS-CSIC, Murcia, SPAIN**

I took part in a STSM in November at CEBAS-CSIC, Spain with Dr. Mayte Garcia Conesa and Dr. Antonio Gonzalez. The STSM was undertaken in order to complete meta-analysis related to the working objectives planned within the COST Action. The meta-analysis included evaluating the effects of ellagitannins and anthocyanins on cardio-metabolic biomarkers and subsequently determining the effects of inter-individual variability.



I would recommend a STSM in order to foster collaboration and expand knowledge between groups. Although I could not speak Spanish, this was not a problem in the lab at least. Mayte took me on a night time tour of the city, which is very beautiful.



I also took a trip to nearby Cartagena to visit the Roman Theatre. By the end of the experience I had learnt a few essential phrases, like how to ask for wine (red of course), how to ask for tea with cold milk and most importantly how to say "can you speak English".

### STSM Topic: Training in meta-analysis to assess the impact of ellagitannins and anthocyanins on cardiometabolic biomarkers

Three weeks of solid data entry were undertaken to complete all of the outcomes for cardio-metabolic markers (BMI, WC, FMD, HOMA, Hb1ac, SBP, DBP, Insulin, Glucose, TGs, LDL, HDL and total cholesterol). A further week was spent determining subgroups for the inter-individual variability and performing the meta-analysis. The data was segregated according to several outcomes such as gender, smoking, and disease status. The STSM was a great opportunity for me to learn how to use the Comprehensive Meta-analysis V3 software. I have been inspired to further develop my statistics knowledge, particularly related to Bias.



**Muchas gracias Karen!!!!**

## SHORT TERM SCIENTIFIC MISSIONS

**NEVENA KARDUM from Serbia went to**



My STSM was placed at the Institute of Food Research (IFR), in Norwich, UK. My stay commenced the 12<sup>th</sup> of June 2016, but the arrangements for this visit started some time earlier. My main problems were related to the all the difficulties I had to overcome in order to obtain the Visa to be able to enter the UK. Because of this, my STSM had to be postponed more than once. But now, looking back to all this trouble I can happily say, it was all worthy. Coming to Norwich and IFR was indeed one of my best decisions and all the problems paid off as soon as I arrived. It was nice to know that Norwich is a twin city with my hometown Novi Sad and this helped me and made me feel less homesick.

Working at IFR has enriched my professional

methods and work with some equipment that is not currently available at my Home Institute. I went to the UK with some general misconceptions about this country: the bad weather and the very reserved English people. But, luckily, I was completely wrong.

My working experience at IFR brought me closer to the British people as well as to the people and culture of Poland, Italy, Mauritius, and other countries. I was also very fortunate to have the kindest Land Lord and Land Lady that I could ever wish for.



They provided me with a very nice and warm home environment and plenty of beautiful food. Tony and Dawn also shared with me their everyday life and showed me British traditions and beautiful landscapes around. Last, but not least, I had the opportunity to visit some good friends in the UK and

### STSM Topic:

**Bioavailability of Aronia juice polyphenols as determinant of inter-individual variation in their effects on platelet function**

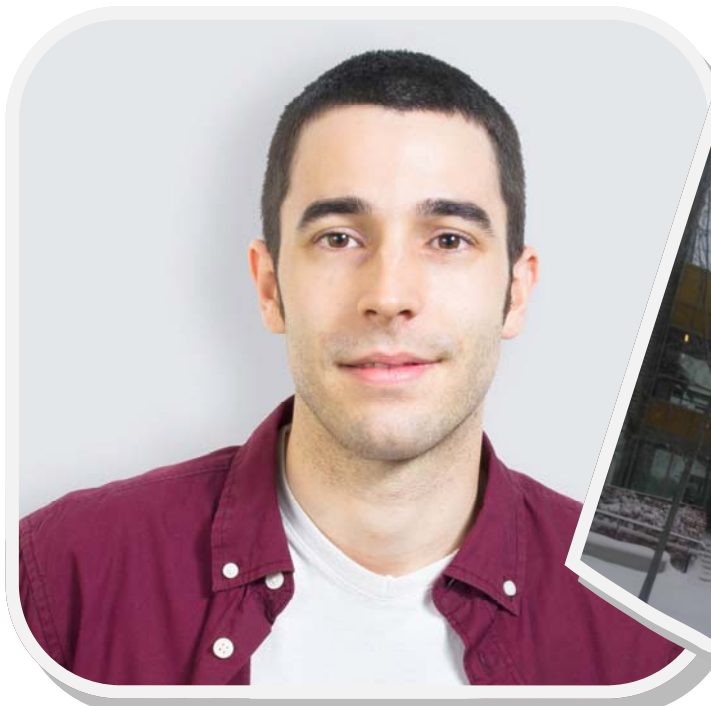
as well as my personal life. During this visit, the main task I had to accomplish was the analyses of a number of urine samples that were obtained during a RCT in which the volunteers were supplemented with Aronia juice. The work gave me the opportunity to be trained in advanced LC-MS/MS techniques. What's more, I had the opportunity to learn new

enjoy several weekends in Leeds, Reading, and London.

**Overall, a wonderful experience! Cheers.**

## SHORT TERM SCIENTIFIC MISSIONS

FRANCISCO MADRID-GAMBIN from Spain went to the Swedish University of Agric. Sciences, Uppsala, SWEDEN



### STSM Topic: Development of methodology for plasma samples in the study of metabolic phenotyping

The Short-Term Scientific Mission grant allowed me to gain expertise in the processing of small volume urine/plasma/serum samples and also in the robust data analysis of these samples using NMR-based metabolomics techniques. The STSM was placed at Department of Food Science at the BioCenter of the Swedish University of Agricultural Sciences, with Dr. Rikard Landberg and Dr. Carl Brunius, where we applied untargeted analysis to urine and plasma/serum samples for the discovery of new biomarkers of intake.

Furthermore, the work carried out during my stay contributed to optimize several steps in the NMR-metabolomics workflow exploiting resources of the FOOTBALL-JPI project, and also allowed the collaboration with the Swedish NMR center at the

University of Gothenburg which, all together, improved my analytical skills substantially. More specifically, I explored and optimized the development of peak alignment algorithms, the double cross-validation of data and a more focused version of the statistical total correlation spectroscopy (STOCSY).

Last, but not least, this opportunity allowed me to discover how nice was to work with Rikard and Carl and how wonderful is Uppsala, "fika" and the Scandinavian places....

**Statistics is fun!** as Dr. Carl Brunius often said.





## SHORT TERM SCIENTIFIC MISSIONS

The POSITIVE Short-term Scientific Mission (STSM) grant taken under the guidance of Dr. Dragan Milenkovic in the Unit of Human Nutrition at INRA, Clermont-Ferrand provided me with a huge experience in the analyses and understanding of complex data generated by Kinomic analysis as well as translating the results into a more meaningful biological interpretation using Metacore® pathway analysis tool. In addition to the pathway analysis software, I also had access to the *in silico* tool Nexus meteor® (Lhasam limited) that allows for prediction of the biotransformation of plant derived compounds in *in vivo* conditions. This may be relevant to understand the fate of plant compounds when not many experimental metabolic data are available.

My stay at INRA was not just limited to learning new *in silico* techniques, but also enabled me to perform some *in vitro* experiments. Using novel peptide microarray technology, we explored



**CHANDRA CHIRUMAMILLA from Belgium went to INRA, Clermont-Ferrand, FRANCE**

### STSM Topic: Biological interpretation of kinome generated data by Metacore® pathway analysis

the molecular mechanisms underlying the cardio-protective effects of some plant flavanol compounds like epicatechin in the context of protein kinase signalling. The knowledge accumulated during my STSM stay not only allowed me to learn, but also to put forward the results obtained during my STSM stay in the form of a recently submitted research article. Apart from the purely scientific and experimental work, I also enjoyed the intellectually stimulating talks and feedbacks received from Dr. Claudine Manach, Dr. Dragan Mienkovic and Dr. Christine Morand. They were really helpful.

Last but not the least, I want to mention our enthusiasm to walk to Puy de Dôme from Clermont Ferrand on foot (although, in truth, we were only able to walk from Panoramique des Dômes to Puy de Dôme) and also to explore the city of Clermont-Ferrand itself, in the company of our English-to-French translator Natalia and another STSM student, Andreia Bento da Silva.

**These were for me outstanding examples of cultural exchange !!!**

## FIRST ANNOUNCEMENT

**Week 18-22 September, 2017, Alexandropolis (GREECE)**

**6<sup>th</sup> POSITIVE WG meeting & 3<sup>rd</sup> Scientific Workshop**



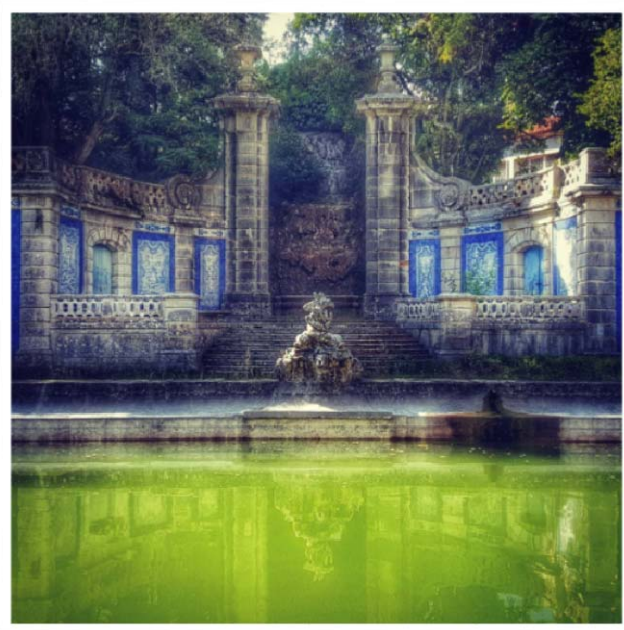
## SHORT TERM SCIENTIFIC MISSIONS

### VILLE KOISTINEN from Finland went to the University of Lisbon, PORTUGAL

I was sent for a short-term scientific mission to ITQB (Instituto de Tecnologia Química e Biológica) that belongs to the Universidade NOVA de Lisboa and is located in the city of Oeiras, about 15 kilometres from downtown Lisbon. My assignment was to prepare mixtures of phytochemical standards and carry out initial analyses on different Mass Spectrometry platforms in order to send the mixtures for further analysis in various analytical platforms across Europe. The idea was to create a small database of standards and their identification data along with information about their detection limit in each platform. Although the initial plan was to have at least some of this data ready by my arrival so that I could concentrate working on the data itself, the work was successful in forwarding the project and allowing me to get hands-on experience in working with various Mass Spectrometers.

Coming from the chilly Finnish October weather, +25 degrees in Portugal felt welcoming and like a small extension to the short summer I had in Finland. The stay was a very pleasant one with good food and inexpensive red wine, and my colleagues at the institute were awesome and helpful. I really felt like a special guest. I would especially like to thank Tiago who on my last day took me to see the historical city of Sintra and then drove me back to the airport with the heavy luggage full of wine.

**I will certainly visit Portugal again, either for leisure or for more work !!!**



## FIRST ANNOUNCEMENT



Very



Berry



Christmas

## 2<sup>nd</sup> Training School

### Nutrigenetics & Nutrigenomics, 2017

(more information about dates and programme will be available later)

## SCIENTIFIC EXPERT'S OPINION

Conducting a human intervention study is time consuming, costly and risky, especially if the trial lasts for months and requires large numbers of volunteers. Most of us involved in these trials have experienced some disappointing results at some point in our careers! A few years ago, we conducted a study over 3 months on 50 volunteers, taking many skin biopsies and using sophisticated measurements of skin health, but despite some promising results in a small study (1), numerous published animal studies and a plausible *in vitro* mechanism, the results showed no effect of a high dose of green tea supplements against UV damage (2). This could have been for several reasons, but one of the main limitations of studies on humans can be the variability in response between individuals. On closer analysis of the data, we could see that some volunteers exhibited a response, whereas others did not. Is this just experimental noise, or can we somehow separate the volunteers into subgroups and explain why they did or did not show an effect? The challenge here is to find a plausible mechanistic reason for allocating sub-groups, and not just separate the volunteers for our convenience. Sometimes we just need to accept that our beautiful theory really has been destroyed by ugly facts!

**Professor GARY WILLIAMSON**  
**School of Food Science**  
**& Nutrition**  
**University of Leeds, UK**



## A personal view on the significance of inter-individual variability in studies on food bioactives

The variation between individuals can arise from numerous factors, such as gene polymorphisms, dietary history, gut microbiota composition and metabolic status. What is not known for bioactives is whether any inter-individual variability in response is correlated to an individual's bioavailability profile. In my experience, the extent of absorption of bioactives between subjects almost always varies by ~10-fold, however it is assessed. Logically we can then ask if the best absorbers of the active component exhibit the greatest biomarker response. One of the problems with food bioactives is that any biological response may be derived from several mechanisms from multiple active constituents.

It is also important to ask if a high responder or absorber is always high. We conducted a study where we assessed absorption and metabolism of phenolics from coffee, with a view to ranking 39 individuals in a

continuum from high to low absorbers, thinking that we might then correlate this with health biomarkers. However, defining high and low absorbers was much more complex than we first envisaged. Chlorogenic acids from coffee give rise to numerous measurable metabolites and conjugates, as a result of metabolism by the small intestine, gut secretions, liver and gut microbiota. It was difficult to decide which metabolite (or sum of all?) to use to define a "good" absorber. Each participant was assessed by consuming the same amount of coffee in an identical procedure on 3 separate visits. We found that not only was there the expected inter-individual differences, but there was also a large intra-individual variation in the concentration of all metabolites excreted in the urine. This meant that we had to average the data from 3 visits in order to properly rank the participants. Most studies do not (or cannot) consider intra-

## SCIENTIFIC EXPERT'S OPINION

Sometimes with a robust effect, all or almost all of the individuals will respond. We can then consider how to exploit high and low responders. One of the earliest examples for bioactives was the suggestion that soy isoflavones would have a greater effect in those individuals who were able to make more equol (3). When we conducted an acute study examining the effect of a fruit paste on post-prandial blood glucose from bread, all 16 volunteers responded, and we were pleased to get an overall  $p$ -value of  $<0.001$  for a human study (4)! However, even in this case, the response varied between individuals by  $\sim 2.5$ -fold. We are now designing further studies to see if these differences can help us to get mechanistic information *in vivo*.

So, how can we exploit inter-individual variation? Working on pre-characterised sub-groups with a particular response is one solution, for example on subjects with metabolic syndrome, well-defined polymorphisms, with an impaired response, or with at risk groups. Sometimes this is difficult if the active component is not known, if the effects are small or if the factors affecting the biomarker of interest are not well understood. We can also exploit data retrospectively if we can show that a particular effect is higher in certain types of individuals (bearing in mind the caveat above). If the study was not initially powered to show a significant effect in a sub-group, then this can be used to set the parameters for an appropriately powered second intervention study. One of the challenges for projects like POSITIVE is to work out additional ways to exploit data on individual varia-

tion, and in this way help to keep the costs of intervention studies manageable.

### References

1. Rhodes LE, Darby G, Massey KA et al. Oral green tea catechin metabolites are incorporated into human skin and protect against UV radiation-induced cutaneous inflammation in association with reduced production of pro-inflammatory eicosanoid 12-hydroxyeicosatetraenoic acid. *Br J Nutr* 2013;110:891-900.
2. Farrar MD, Nicolaou A, Clarke KA et al. A randomized controlled trial of green tea catechins in protection against ultraviolet radiation-induced cutaneous inflammation. *Am J Clin Nutr* 2015;102:608-15.
3. Setchell KD, Brown NM, Lydeking-Olsen E. The clinical importance of the metabolite equol—a clue to the effectiveness of soy and its isoflavones. *J Nutr* 2002;132:3577-84.
4. Nyambe-Silavwe H, Williamson G. Polyphenol- and fibre-rich dried fruits with green tea attenuate starch-derived postprandial blood glucose and insulin: a randomised, controlled, single-blind, cross-over intervention. *Br J Nutr* 2016;116:443-50.



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## RESEARCH DISSEMINATION

## PUBLICATIONS

Mol. Nutr. Food Res. 2016, 00, 1–16

DOI 10.1002/mnfr.201600557

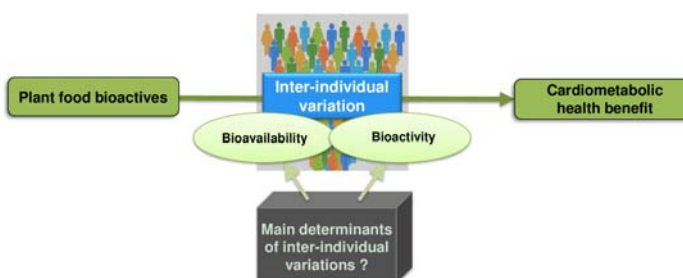
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## REVIEW

## Addressing the inter-individual variation in response to consumption of plant food bioactives: Towards a better understanding of their role in healthy aging and cardiometabolic risk reduction

Claudine Manach<sup>1\*</sup>, Dragan Milenkovic<sup>1\*</sup>, Tom Van de Wiele<sup>2</sup>, Ana Rodriguez-Mateos<sup>3</sup>, Baukje de Roos<sup>4</sup>, Maria Teresa Garcia-Conesa<sup>5</sup>, Rikard Landberg<sup>6,7</sup>, Eileen R. Gibney<sup>8</sup>, Marina Heinonen<sup>9</sup>, Francisco Tomás-Barberán<sup>5</sup> and Christine Morand<sup>1</sup>

Publication in *Molecular Nutrition and Food Research* of the first collaborative position paper addressing the objectives of POSITIVE. The paper examines the main factors likely to influence the individual responses to consumption of plant food bioactives, including those affecting bioavailability or bioactivity related to cardiometabolic health, and presents a range of perspectives for the future assessment and consideration of the human inter-individual variability.



**RESEARCH DISSEMINATION**
**PUBLICATIONS**

AJCN. First published ahead of print November 23, 2016 as doi: 10.3945/ajcn.116.136051.




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**Narrative Review**


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The role of metabolism (and the microbiome) in defining the clinical efficacy of dietary flavonoids<sup>1</sup>

*Aedin Cassidy\* and Anne-Marie Minihane*

Department of Nutrition and Preventive Medicine, Norwich Medical School, University of East Anglia, Norwich, United Kingdom

This recent review paper by Cassidy & Minihane (Am J Clin Nutr, 2016) is from POSITIVE partners: Dept of Nutrition & Preventive Medicine, Norwich Medical School, University of East Anglia (UK). It reviewed the current knowledge for the main subclasses of flavonoids, including anthocyanins, flavonols, flavan-3-ols, and flavanones, and concluded that current knowledge of the aetiology of the variability in flavonoid metabolism and how this affects health outcomes is limited. The key areas that were thought to require further research were:

- ⇒ To conduct adequately powered, longer term, clinical studies to determine the impact of age, sex, habitual diet, genotype, drug interactions, and the microbiome on flavonoid metabolism
- ⇒ To conduct trials to understand the bidirectional relationship between flavonoid metabolism and the microbiome; prospectively recruit participants to clinical trials on the basis of the extent of absorption and metabolism to establish dose-response relationships
- ⇒ To identify and validate a panel of robust biomarkers of flavonoid intake and subsequent metabolism that can be used to examine associations of bioavailable flavonoids with health outcomes in future prospective cohort studies
- ⇒ To further develop metabolomic data sets to assist in the development of biomarkers

⇒ To conduct hypothesis-driven research to investigate the impact of specific genotypes on flavonoid metabolism with a particular focus

on variants in LPH,  $\beta$ -glucosidases, phase I metabolism, and phase II metabolism, with prospective recruitment by genotype for associations established with the use of the retrospective genotype approaches

⇒ To conduct intervention studies to determine how food composition and flavonoid source affect bioavailability

⇒ To conduct trials in which metabolism and health outcomes are addressed simultaneously

Addressing these research gaps would provide the basis for the development of targeted dietary advice for subgroups who are likely to be most responsive and help us work toward the development of specific dietary guidelines for several dietary flavonoid subclasses.



**AEDIN CASSIDY &  
ANNE MARIE MINIHANE**

**RESEARCH DISSEMINATION**
**PUBLICATIONS**
**Interindividual variability in the interactions between wine polyphenols and gut microbiome**

**BEGOÑA BARTOLOMÉ & M<sup>a</sup> VICTORIA MORENO-ARRIBAS**

A current key issue regarding the health implications of polyphenols is their interaction with the microbiota, which has become a hot topic in order to improve nutritional strategies with potentially important health implications. Wine polyphenols comprising several classes of phenolic structures might be a good exponent of this potentiality. Recent scientific evidence suggests that wine polyphenols exert their effects through interactions with the gut microbiota, as they seem to modulate microbiota and, at the same time, are metabolized by intestinal bacteria into specific bioavailable metabolites. Microbial metabolites are better absorbed than their precursors and may be responsible for positive health activities in the digestive system (local effects) and, after being absorbed, in tissues and organs (systemic effects). Differences in gut microbiota composition and functionality among individuals can affect polyphenol activity and therefore their health effects. There is a great inter-individual variation in the profile and/or content of phenolic metabolites in physiological fluids (urine, plasma, faeces) after a controlled intake of phenolic-rich foods. Analysis of the fecal composition not only provides valuable information regarding microbial produced metabolites and unabsorbed dietary components, but also clarifies whether the functional stability of the gut ecosystem could undergo modifications after dietary interventions.

Within the general objective of deepening the effects of moderate wine consumption on gastrointestinal health, Muñoz-González *et al.* (*J. Agric Food*

*Chem.* 2013., 61, 9470-9479) evaluated changes in phenolic metabolites in human feces, after moderate and regular consumption of red wine in healthy volunteers. A controlled and randomized trial study involving 41 healthy volunteers (33 intervention and 8 control subjects) was performed in order to establish changes in the microbial-derived phenolic metabolite profile of feces after moderate consumption of red wine (250 mL/day, 4 weeks). Out of the 35 phenolic metabolites identified, 10 compounds (mainly benzoic and 4-hydroxyvaleric acids) showed statistically significant increases ( $P < 0.05$ ) after the wine intake. Also, the total phenolic metabolites content was significantly ( $P < 0.05$ ) higher in the samples after the wine intake ( $625 \pm 380 \mu\text{g/g}$  feces) in comparison to the samples before ( $358 \pm 270 \mu\text{g/g}$  feces). Most interestingly, and despite the great inter-individual variability observed, a tentative distribution of the individuals into 3 groups according to the levels of metabolites in the faeces: low, medium and high metabolizers ( $<500$ ,  $500-1000$ , and  $>1000 \mu\text{g/g}$  feces, respectively) by their capacity to metabolize wine polyphenols has been established. These results suggest different human phenotypes in relation to the ability to metabolize wine polyphenols, as it has been described for polyphenols found in other foods.

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Article  
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**Profiling of Microbial-Derived Phenolic Metabolites in Human Feces after Moderate Red Wine Intake**

Irene Muñoz-González, Ana Jiménez-Girón, Pedro J. Martín-Álvarez, Begoña Bartolomé, and M. Victoria Moreno-Arribas\*

**RESEARCH DISSEMINATION**
**PUBLICATIONS**

In an effort to improve our understanding on the biological effects that phenolic compounds (including red wine polyphenols) exert at the gut level, furthermore different omics studies were undertaken to characterize the metabolome (Jiménez-Girón *et al.*, *J. Proteome Res.* 2015, 14 ,897-905) and the metagenome (Barroso *et al.*, *Mol. Nutr. Food Res.*, 2016, doi 10.1002/mnfr.201600620) of human faeces after moderate consumption of red wine by these healthy subjects for 4 weeks. A non-targeted metabolomic approach based on the use of UHPLC-TOF MS was developed to achieve the maximum metabolite information of 82 human faecal samples. After data processing and statistical analysis, 37 metabolites were related to wine intake from which 20 could be tentatively or completely identified, including: I) wine compounds, II) microbial-derived metabolites of wine polyphenols, and III) endogenous metabolites and/or others derived from other nutrient pathways. After wine consumption, faecal metabolome was fortified in flavan-3-ols metabolites. Also, of relevance was the down regulation of xanthine and bilirubin derived metabolites such as urubilinogen and stercobilin after moderate wine consumption. As far as we know, this is the first study of the faecal

metabolome after wine intake. On the other hand, concerning the metagenomic study, the composition, diversity, and dynamics of fecal microbiota before and after 1 month of wine consumption were analyzed. The 16SrDNA sequencing allowed detection of 2324 phylo-types, of which only 30 were found over the 0.5% of mean relative frequency, representing 84.6% of the total taxonomical assignments. The samples clustered more strongly by individuals than by wine intake or metabolotypes, however an increase in diversity associated to wine intake was observed.

Taking into account the aims of POSITIVE, further studies are now needed to investigate the large inter-individual variations on gut metabolism of wine polyphenols and, most importantly, getting stratification of individuals based on specific gut microbiota functional features to obtain positive polyphenol-mediated health effects.



Journal of  
**proteome**  
 research

Article

[pubs.acs.org/jpr](https://pubs.acs.org/jpr)

## Faecal Metabolomic Fingerprint after Moderate Consumption of Red Wine by Healthy Subjects

Ana Jiménez-Girón, Clara Ibáñez, Alejandro Cifuentes, Carolina Simó, Irene Muñoz-González, Pedro J. Martín-Álvarez, Begoña Bartolomé, and M. Victoria Moreno-Arribas\*

*Mol. Nutr. Food Res.* 2016, 0, 1–9

DOI 10.1002/mnfr.201600620

1

RESEARCH ARTICLE

### Phylogenetic profile of gut microbiota in healthy adults after moderate intake of red wine

Elvira Barroso<sup>1</sup>, Irene Muñoz-González<sup>1</sup>, Esther Jiménez<sup>2,3</sup>, Begoña Bartolomé<sup>1</sup>, M. Victoria Moreno-Arribas<sup>1</sup>, Carmen Peláez<sup>1</sup>, María del Carmen Martínez-Cuesta<sup>1</sup> and Teresa Requena<sup>1</sup>



## RESEARCH DISSEMINATION

### Presenting POSITIVE to the Spanish public: THE WEEK OF SCIENCE at CSIC

The Department of Food Science & Technology at CE-BAS (Murcia) and the Research Institute on Food Science CIAL (Madrid), both part of the Spanish National Research Institution CSIC, participated in the 2016 edition of 'The Science Week' the past November. The events took place in the city gardens of the 'Malecon' near the river in Murcia and, in the CIAL Institute at the University Autónoma, Campus of Cantoblanco in Madrid, respectively.



During the event, members from both Institutions presented the workshop entitled 'The role of Food in Health and the reasons behind the differences between individuals'. During the activities, the researchers talked to the consumers about general aspects of the investigation they carry out: Food & Health, Functional Foods and Nutraceuticals, Cardiometabolic Diseases and the issue of the Interindividual Variability and the POSITIVE project. In addition, and by means of a questionnaire, we asked the participants about their appreciation of a healthy diet and of our response to diet. We also offered the attendees the

possibility of having some cardiometabolic variables (BMI, waist circumference, blood pressure) measured. It was very interesting to chat with many of them and to find out that an increasing number of people, both younger and older, are truly concerned about their metabolic health and are willing to learn more about how to promote health with the diet.



The week of the Science became, once again, an excellent scenario of communication and interaction between the scientific community and the general public.

There is a great opportunity within POSITIVE to prepare informative documents and workshops that will be of great benefit to the general public and their knowledge and practice of a healthy diet.

## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS



**CHRISTOS  
KONTOGIORGIS**

**Democritus University of  
Thrace, GREECE**

#### **What is the focus of your research?**

Our Laboratory of Hygiene & Environmental Protection, Department of Medicine, University of Thrace, Greece, is focused on Epidemiological and Nutritional Studies. We run studies on the Greek Population regarding habits, attitudes and compliance with the Mediterranean diet. We also work on natural products used by the Greek population as a whole product or as an ingredient in oth-

er products and we evaluate their antioxidant and antimicrobial activity.

#### **In what countries/organisations have you studied or worked?**

I graduated in Pharmacy, at the Aristotle University of Thessaloniki, Greece. I continued with my PhD Studies at the same Faculty under the supervision of Professor Dimitra Hadjipavlou-Litina. From 2005 – 2013 I worked as a Postdoctoral Researcher in National and European Calls and as temporary Lecturer. From 6/2016 - 9/2016 I did some postdoctoral studies in Department of Pharmacy in the University of Maryland, U.S.A. on the use of natural products (coumarins) against Alzheimer's disease development under the supervision of Dr Luo Yuan. From 2/2010 – 9/2011, I was a postdoctoral researcher at the Imperial College and the King's College of London, UK.

#### **What has been the greatest achievement in your career?**

My collaboration with many different research groups of different scientific areas. I truly believe that a researcher should continuously adjust to new demands and to keep opened to new challenges and to as many options as possible.

#### **Which is your favourite paper you have written/co-authored and why?**

I am really proud of two of my articles, and not just because of the journals they were published in but mainly because of they meant to me the start of new research areas. The first one is the paper entitled: "Coumarin derivatives protection against ROS production in cellular models of Abeta toxicities. Free Radic Res. 2007 Oct;41 (10):1168-80". This was the first research project I was fully responsible for. I developed and completed the work following my own personal vision. I'm really thankful for this paper to Dr Luo Yuan who gave me the opportunity to carry out the project in his Department of Pharmacy, University of Maryland, U.S.A.. The second most important paper is: "Studies on the antiplatelet and antithrombotic profile of anti-inflammatory coumarin derivatives. J Enzyme Inhib Med Chem. 2015 Dec;30(6):925-33". The relevance of this paper in my career was that I was also entirely responsible for the project and for the organization and schedule of the work in collaboration with many different research groups.

#### **Who is/was your most influential mentor/colleague and why?**

Professor Dimitra Hadjipavlou-Litina is the most important mentor during my career. Not only because of her supervision during my PhD studies but also because of the way she treated me and showed me how to collaborate with other researchers and how to adapt my research background and skills to new projects and research areas.

#### **What is your advice for young scientists?**

The only advice that I can offer is that they should pursue their dreams and follow their own inspiration. There should be no fear for new ideas or new research areas. The way to progress in research is full of sacrifices, disappointments but also success and happiness. Whoever is really prepared to do this will be the one to be distinguished.

#### **Where is your favourite place in the world and why?**

My birth place, Thessaloniki in Greece, is my favourite place for various reasons. It combines unique characteristics like: long history, extremely beautiful Roman and Byzantine sights, a really nice seaside, great energy from the thousands of students and extremely delicious food!

#### **What is your favourite music/book?**

I like listening to Mozart and Verdi while I'm working in my office but when I'm in the lab I'd rather hear something more "energetic" like Greek pop music.

Regarding books, I enjoy reading historical books.

#### **What is your favourite sport(s)?**

I prefer to spend my spare time sailing and playing chess.

## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHERS

#### What is the focus of your research?

My research belongs to the scientific discipline of clinical exercise physiology and environmental physiology. I investigate health aspects that can be improved by exercise training and study how the environment influences the human organism. My research focuses on chronic diseases where I design long-term and short-term exercise training programs and evaluate their effects on health indices under different environmental conditions.

#### In what countries/organisations have you studied or worked in?

I completed all my academic studies at the Aristotle University of Thessaloniki, Greece. Since then, I have worked in many European research programs and have collaborated with many different academic institutes all over the world. For the last four years I have been working at the University of Thessaly, Greece where I completed my post-doctoral research, and now I work at the FAME Lab laboratory as an independent researcher.

#### What has been the greatest achievement in your career?

Until now my greatest achievement is my PhD thesis. Reaching this goal was very stressful and when I defended it I felt really great.

#### Which is your favourite paper you have written/co-authored and why?

I have recently published a research paper in which the impact of inflammation and Autonomic Nervous System imbalance on cognitive impairment in chronic kidney disease patients during a hemodialysis therapy, were investigated. This paper is my favourite because it is unique and also entails the first research that has been conducted until now in this discipline. I believe that with the findings of this paper we can contribute to the better understanding of the pathophysiology and the treatment of the cognitive impairment that hemodialysis patients present.

#### Who is/ was your most influential mentor/colleague and why?

Until now my most inspiring and influential mentor has been Professor Evangelia Kouidi. She is a Professor of Sportmedicine at the Aristotle University of Thessaloniki,

Greece and she was my PhD supervisor. I really admire her work because she was the first in collaboration with Professor Asterios Deligiannis who applied exercise training programs in patients with chronic diseases in Greece. Apart from her research background I admire her personality and her ethical character.

#### Where is your favourite place in the world and why?

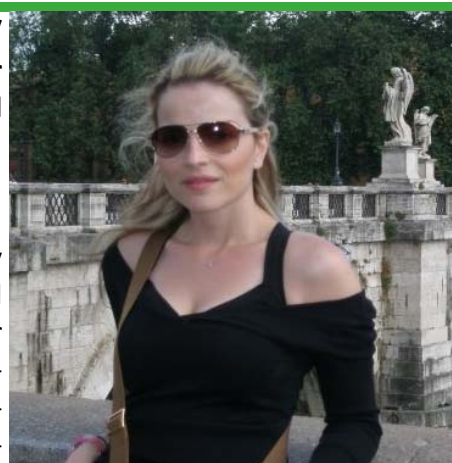
I love Spain. I have visited many different places in Spain and each has a unique character. Also, the music and the food in Spain are perfect and they have perfect sweets. I really love churros.

#### What is your favourite music/book?

I like many different kinds of music depending on the occasion. For example, when I have to concentrate I like to listen to classical music. Generally, I like to collect the soundtracks of movies. My favourite group is Coldplay. Regarding my favourite book, I cannot decide. But my favourite authors are Mario Vargas Llosa and Leonardo Padura.

#### What is your favourite sport(s)?

I love swimming. I used to be an athlete in swimming when I was young. Unfortunately nowadays I do not have time for swimming. Nevertheless, I always try to find a few hours a week to train in the gym. Also, during the last 4 years I've developed an interest for hiking and I try to visit a different location every weekend.



**ANTONIA KALTSATOU**

**University of Thessaly,  
GREECE**

**GET TO KNOW YOUR POSITIVE PARTNER**
**EARLY STAGE RESEARCHERS**

**SOFIA MOCO**
**Nestle Institute, Lausanne,  
 SWITZERLAND**
**What is the focus of your research?**

I work on the metabolism of bioactive small molecules. I am interested in the cellular functions and molecular interplay of bioactives as potential contributors to improved health.

Looking into bioactive foods or mixtures, I am particularly fo-

cused on the concerted effects of bioactives on metabolic pathways in a systematic approach. Since my background revolves around analytical biochemistry, I mainly work with nuclear magnetic resonance (NMR) and mass spectrometry (MS) to study metabolites in biological samples.

**In what countries/organisations have your studied or worked in?**

I studied Chemical Engineering, with a specialisation in Biotechnology, at the Instituto Superior Técnico, part of the Technical University of Lisbon, Portugal. I obtained my PhD at the Laboratory of Biochemistry, Wageningen University in the Netherlands, in the areas of plant biochemistry and metabolomics, with a strong emphasis on big instrumentation (NMR and MS). Subsequently, I joined the Institute of Molecular Systems Biology at the ETH Zurich, in Switzerland. This was just before I joined research at Nestle.

**What has been the greatest achievement in your career?**

So far, it is my PhD thesis. When I started I had little -to-no knowledge on NMR or MS and even less on

plant physiology. I managed to set up methods and strategies to perform analyses on small molecules and obtain one of the first Theses on Plant Metabolomics. These metabolomics strategies were then used by many students that joined the lab after me.

**Which is your favourite paper you have written/co-authored and why?**

I would have to choose my first article (A liquid chromatography-mass spectrometry-based metabolome database for tomato, *Plant Physiology*, 2006). I see that it has quite some citations, so I guess it is perceived as a useful piece of work.

**Who is/was your most influential mentor/colleague and why?**

Jacques Vervoort, one of my PhD advisors. He was probably my most influential mentor. We had a lot of scientific discussions, and I learned a lot about biochemistry of small molecules and proteins. And he gave me a crucial piece of advice: 'You are in the driving seat' (perseverance is the key aspect in research).

**Where is your favourite place in the world and why?**

I have been recently to South Africa, and this place really caught my attention. If I turn to my roots in Portugal, there are a couple of narrow streets in the old city centre of Leiria, where I grew up, that are quite magic.

**What is your favourite music/book?**

Herbie Hancock is one of my favourites. The literature I enjoy the most is written by Portuguese authors, being Fernando Pessoa an absolute favourite.

**What is your favourite sport(s)?**

I like hiking in the Alps, running and swimming.



**CHAIR'S CORNER**

POSITIVE has now reached mid-term which is a perfect moment for a quick assessment of all the work carried out so far and the achievements of the Action that have contributed to promote exchanges and interactions between partners and to progress in the scientific objectives of POSITIVE. Since its effective beginning (March 2015), POSITIVE has held four WG meetings & two scientific workshops, in satellite or as part of 2 large international conferences, Polyphenols & Health (Tours, France 2015) and Bioactive Compounds & Health (Norwich, UK 2016). The Action has also accomplished a very successful Training School on "Metabolomics and Nutrition Research".

At POSITIVE, a special attention is given to support and enhance the capacity building of the community of young scientists working in the area of plant food bioactives and health. This resulted in the creation of the Think-Tank Group constituted by early career investigators (ECIs). This group has proven to be very productive and is currently working in the development of a specific project of high interest for the main topic of the Action. In addition, POSITIVE has funded 13 short term scientific missions (STSMs) which have allowed young scientists within the POSITIVE community to work in different countries and labs of various other POSITIVE partners. The STSMs have resulted very fruitful as shown by the reports elaborated by the students and by the experiences they have shared with us through the newsletters.

Within the POSITIVE network, the dissemination work is also now well underway as illustrated

by the submission and (or) preparation of the first collaborative reviews resulting from the WG activities and by the recent launching of a multiplatform metabolomics test across European laboratories.

The Chair and Co-chair of POSITIVE would like to use this occasion to thank all the members of the Action for all the good work done and their input in the preparation of the mid-term report for COST, which has put together all this work and has been the key for the approval of the budget for the next two years.

**So, thanks a lot to everyone!**

We hope that this POSITIVE dynamics within the network will continue for the next two years and will help in the preparation and launching of future fruitful collaborative research projects! We certainly need to introduce and highlight the relevance of the main topic of POSITIVE, interindividual variability in response to plant food bioactives, so that this is included in future calls of the H2020 European Programme. We all need to work together in this direction.

**The Chair and Co-chair of POSITIVE also would to wish you all**

**CONTACT US**

EUROPEAN COOPERATION IN THE FIELD OF  
SCIENTIFIC AND TECHNICAL RESEARCH

**Contact us:**

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: christne.morand@clermont.inra.fr

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: fatomas@cebas.csic.es

**Webpage:**

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)



POSITIVE

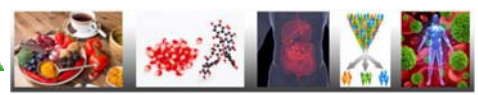
ISSUE 6



# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE V, JUNE 2017

## WELCOME

**S**ummer season is at hand with temperatures almost up to boiling point, yet POSITIVE has not slowed down its pace. We had no sooner met in Olsztyn for the 5<sup>th</sup> Working Group discussions than we started to get ready for the next gathering of POSITIVE partners this coming month of September in Thessaloniki (Greece). This time, the 6<sup>th</sup> WG meetings will be accompanied with the 2<sup>nd</sup> Scientific Workshop and a 2<sup>nd</sup> Training School. Meanwhile, we fulfilled the scheduled Action's work and budget plan for Grand Period 4 which was approved by the Management Committee. So, well done to all members of the POSITIVE family! Thank you for your hard work and commitment.

In this issue of the POSITIVE newsletter you will catch up with some of the recent activities undertaken within the project including the presentation of POSITIVE at VitaFoods Europe, a global nutraceutical event held in Geneva the past May. As usual, we invite you to have a first glance at some recent publications looking at interindividual variability published by POSITIVE members and don't miss the opportunity to read the Scientific Expert's opinion, on this occasion written by our POSITIVE Chair. Take a look at the 'Getting-to-know your POSITIVE partners' section to get familiarized with more senior and young researchers belonging to this COST Action. And, last but not least, save the dates for some of the most important POSITIVE events ahead.

The FG

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## NEWS FROM THE ACTION

**5<sup>th</sup> COST Action POSITIVE Meeting, 21-22 February, 2017**  
**Organized by the Institute of Animal Reproduction and Food Research, Polish Academy of Sciences**  
**Olsztyn, POLAND**



## RESEARCH HIGHLIGHTS

The 5<sup>th</sup> WG meeting was started with a general review by the Chair Dr. Christine Morand who welcomed everyone and presented among other things the work & budget plan for GP4 and associated schedule events for 2017-2018, new application for STSM, articles and reports published, the rules for open access publication, etc. There was also a presentation of the 2<sup>nd</sup> training school on the 'Use of nutrigenetics and nutri(epi)genomics in nutrition'.



### Work Group 1

Leader: **Tom VAN DE WIELE**

Co-leaders: **Claudine MANACH & Rikard LANDBERG**

The WG1 was then initiated by the leaders Tom van De Wiele and Claudine Manach who gave an overview of the tasks and actions carried out. In relation with the Compounds Subgroup, there was a general discussion



about the problems associated with the drawing of the synthetic pathways of the compounds followed by several presentations by Dr- Torsten Bohn, Dr. AnaMarja Aura and Dr. Sofia Moco.

The work will continue by focusing on those most relevant metabolic and absorption steps to try to identify the main proteins involved using a specific template

and PathWhiz. The information will be passed on the microbiome and gene variants subgroups. Other points discussed were related to the comparison with pharmacogenomics studies of drugs metabolism and the use of predictive tools such as Biotransformer (under construction).

Next, Dr. Manach talked to the audience about the free access database Phytohub (<http://phytohub.eu>) to be used in metabolomics. Data curation and biological effects information can be added to this database and may be done by trained POSITIVE partners from WG1 and WG2. More information about PhtoHub and its use was provided in a webinar (11<sup>th</sup> May). On the same date, there was also an additional informative webinar on eBASIS (<http://ebasis.eurofir.org/Default.asp>) by Jenny Plumb from IFR (Norwich, UK). This not-open access database collects information on biological effects of food bioactive and could be linked to PhytoHub.



Within the Metabolomics subgroup, Dr. Maria Bronze presented an update of the metabolomics multi-test. Due to shipping problems there are not yet sufficient results and thus the effectiveness of the test will be seen next. In addition, the analytical subgroup is still working on a template to collect specific analytical features of the bioactive compounds. These data will be made available through PhytoHub.

Finally, there was a presentation of FoodComex, an on-line platform developed by INRA, with the aim of sharing non-commercially available compounds and standards. The tool is open to non-POSITIVE contributors. See a special report on FoodComex by Dr. Claudine Manach on this issue (page 15).



## RESEARCH HIGHLIGHTS

### Work Group 2

**Leader: Ana RODRIGUEZ-MATEOS**

**Co-leaders: Eileen GIBNEY & Dragan MILENKOVIC**

#### *Meta-analysis subgroup*



The 5<sup>th</sup> WG2 meeting (meta-analysis subgroup) was led by Dr. Ana Rodríguez Mateos who as usual presented an overview of the progress of the work carried out and the status of the ongoing meta-analyses. Next, the leaders of each of the different studies presented the progress done. Some of the meta-analyses (flavanols and blood

lipids, flavanols and glucose metabolism, ellagitannins & anthocyanins) are well advanced. In addition to very significant effects found for some of the investigated variables, a number of factors are also emerging as potential modulators and, at least, partially responsible for the inter-individual variability. A future revision of all the analyses will reinforce the relevance of these factors and will greatly contribute to understand the variability in the efficacy of the different bioactive compounds. Other meta-analyses are still at an early stage and need to be pushed forward. A potential collaboration with the COST Action EuroCarotenoid was proposed and will be pursued.

As a novelty, during the meeting in Olsztyn, a joint meeting between WG1 and WG2 was held for the discussion of several common issues such as: data fusion, co-authorship, and the planning and development of a special 'POSITIVE study' which would be carried out between various partners to generate novel data on inter-individual variability for a particular bioactive compound. This study will be given further thoughts *via* a questionnaire sent to all partners.

#### *Cell & Molecular Targets subgroup*

Dr. Dragan Milenkovic (cell and molecular targets subgroup) also summarized the activities done in this subgroup for the main three topics: human, animal and *in vitro* studies. The human studies have all been collected, a template prepared and data extraction initiated. Because the extraction is complex and needs an extra amount of work, a STSM for this task was proposed and a call will be launched. The activities will take place during early summer under the supervision of MGC. The animal and *in vitro* studies continue progressing according to the proposed data extraction procedures and data analyses.

Bioinformatic analyses and docking structure analyses are still pending on the results of these studies and the selection of candidate genes. The objectives are to find and select a number of genes as new targets of the bioactive compounds as well as understanding the biological pathways underneath the beneficial effects of these compounds. Also, a future task in collaboration with the Genetic Variant Group will involve the identification of genetic variants in these genes that may contribute to the inter-individual variability.



## RESEARCH HIGHLIGHTS

### Work Group 3

Leader: Baujke DE ROOS

Co-leaders: Marina HEINONEN

The 3<sup>rd</sup> WG3 meeting of POSITIVE was presented by the group leader Dr. Baujke de Roos *via* teleconference. She first introduced the results of a survey carried out across several European countries to try to identify the main deliverables that are relevant for different stakeholders and end-user groups. The questionnaire was responded by about 100 participants and revealed that most stakeholders and end-users understand the importance of the main objectives of POSITIVE, i.e. to improve the knowledge of the efficacy of plant bioactive compounds to produce better foods and food products so that these can be directed to specific group populations with improved benefits and recommendations. They also perceived the importance of clarifying the metabolism of these compounds and the completion and improvement of databases with information about all these compounds and their beneficial properties.

There are also a number of short videos in progress in which researchers and industrial collaborators will present successful projects and will explain how these projects worked.



The development of an on-line tool for users to search for information about plant bioactives, health effects and interindividuals variability is still in progress with the collaboration of various other POSITIVE partners.

Dr. Baujke has also recently attended the VITAFODDS meeting in Geneve (May the 9<sup>th</sup>) where she presented the COST Action FA1403-POSITIVE aims by delivering a lecture entitled 'Addressing the Inter-Individual Variation in Response to Consumption of Plant Polyphenols: Insights from the COST Action FA1403-POSITIVE' (see on page 19).



### Focus Group

Leader: Mayte GARCÍA-CONESA

Co-leader: Iwona KIEDA

During scientific events, the FG is working on the preparation of a document that collects the responses of a preliminary questionnaire directed to the consumers. The document will summarize the impressions of the participants about metabolic diseases, the role of diet in health and the importance of understanding differences between individuals. Following this first exercise, an improved questionnaire will be prepared and distributed to other partners to investigate and compare the responses of the public in different countries.

Last but not least, the FG co-leader and some of her colleagues in Olsztyn have elaborated a very nice and informative short video featuring POSITIVE that can now be accessed at the POSITIVE website and *via* Facebook and Twitter.

The plenary Focus Group meeting was held the afternoon of February the 21<sup>st</sup>. The FG leader presented a summary of the activities in progress. In addition to the general tasks of keeping up with the POSITIVE website and preparation of the 5<sup>th</sup> edition of the newsletter, the FG has initiated the tasks of communicating the research carried out within POSITIVE to the Food Industry (in collaboration with WG3). Some of the contributions are the publication of a blog in the website of VITAFODDS (see page...) as well as the preparation of a short diffusion article in *The world of Foods Ingredients*.

Further, and following the previous activities where POSITIVE was presented to the general public at local scien-



## RESEARCH HIGHLIGHTS

**Think Thank Group**  
**Leaders: Rocío GARCÍA-VILLALBA & Pedro MENA**

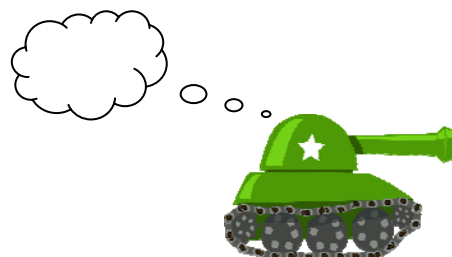
The 3<sup>rd</sup> TTG meeting in Olsztyn was led by Antonio González-Sarrías, as representative of the TTG. The meeting gathered about 15 participants. It started with a short introduction to the new ECI members about the goals reached in the last two year and the progresses that some ECI members have achieved in the TTG project 'How to report interindividual variability in scientific publications'.



During the meeting, it was decided that the new representatives of the TTG for the next year and a half will be: Dr. Rocío García Villalba, from CEBAS-CSIC (Murcia, Spain) and Dr. Pedro Mena Parreño, from the University of Parma (Parma, Italy). Accordingly, they will be responsible for coordinating the activities developed by the TTG up until the end of this Action. Monthly webinars via Google Hangouts will continue to be carried out and will include: i) "Get-to-know sessions" to learn more about the ECI members and their research lines and, ii) further interesting discussions about the progress and next steps of the project "How to Report Inter-individual Variability". At present, the ECIs involved in this project are concluding discussions about which parameters should be included, developing a template for the assessment of a 'quality index', and evaluating a number of manuscripts reporting inter-individual data. These activities promote exchanges between the ECIs and would be very useful in future works.

In addition to the above, a specific committee integrated by various ECIs are in charge of the 3<sup>rd</sup> Scientific Workshop of POSITIVE, that will be held in Thessaloniki (Greece) the 20<sup>th</sup> and 21<sup>st</sup> of September (see further information on page 9 of this issue and on the web <https://www6.inra.fr/cost-positive/Home/News/Upcoming-events-2017>). The title of this year workshop is: "Omics breakthroughs in the health effects of plant food bioactives" and will focus on how all

«Omics» sciences (including Nutrigenetics, Nutri(Epi)genomics, Metabolomics, and Microbiomics) have already contributed to provide new findings on the health effects of plant food bioactives. Several excellent researchers will present their scientific findings resulting from the use of these approaches. For this Workshop, both renowned and promising young researchers have also been invited. We hope you enjoy their talks and discussions.



## RESEARCH HIGHLIGHTS

### SOCIAL EVENTS

The day-long discussions held by all POSITIVE partners attending the meeting were followed by a dinner in a traditional Polish restaurant located in a small village outside Olsztyn. The participants had a chance to taste the typical delicacies of the Warmia & Mazury region cuisine served in interiors reflecting the old Polish land chambers.



Even though Olsztyn welcomed the partners with no snow whatsoever yet very “generous” rain, some of us also decided to take a stroll around the city’s Old Town, visiting the Castle of Warmian Bishops, once inhabited by the famous astronomer Nicolaus Copernicus. The guided tour was then followed by an evening in the Astronomical Observatory, where we enjoyed a “Journey to a Billion Suns”.



## FIRST ANNOUNCEMENT

**7<sup>th</sup> WG meeting in Dubrovnik,  
Croatia,**

**February-March, 2018**



## SAVE THE DATES



**Thessaloniki (GREECE) welcomes you to the**

**JOINT COST Action POSITIVE  
6<sup>th</sup> WG Meeting & 4<sup>th</sup> MC Meetings,  
3<sup>rd</sup> Scientific Workshop & 2nd Training School  
19<sup>th</sup> to 22<sup>nd</sup> of September 2017**

**VENUE:**

**Porto Palace Hotel, 65,  
26th Octovriou Str.,  
Thessaloniki, 546 28**

**ORGANIZERS:**

Dr. Christos Kontogiorgis [ckontogi@med.duth.gr](mailto:ckontogi@med.duth.gr),

Dr. Antonia Kaltsatou [akaltsat@gmail.com](mailto:akaltsat@gmail.com)

Eirini Deligiannidou [deligiannidoueirini@yahoo.gr](mailto:deligiannidoueirini@yahoo.gr)



## SAVE THE DATES



### 3rd Workshop of the POSITIVE COST Action



Thessaloniki, Greece  
September, 20<sup>th</sup> - 21<sup>st</sup>

Dear all,

On behalf of the Scientific and Organizing Committee we would like to invite you to participate in the **3<sup>rd</sup> Scientific Workshop of the POSITIVE COST Action** to be held in **Thessaloniki (Greece)** from the **20<sup>th</sup> to 21<sup>st</sup> of September 2017**.

The POSITIVE COST Action is focused on inter-individual variation in response to consumption of plant food bioactives and determinants involved. The focus of this year workshop, titled "**Omics breakthroughs in the health effects of plant food bioactives**", is on how all «Omics» (including Nutrigenetic, Nutri(Epi)genomics, Metabolomics and Microbiomics) have helped to provide new findings on the health effects of plant food bioactives. Several excellent researchers will show their scientific findings resulting from the use of these approaches. You may see the detailed scientific programme of this workshop and other practical information about abstract submission and registration on the **website: to be announced**.

Please, do not hesitate to contact to us for further details:

[positive.ws2017@gmail.com](mailto:positive.ws2017@gmail.com)

We hope that you will join us for this interesting workshop!

*Thank you for your consideration*

SPECIAL THANKS TO OUR SPONSORS



## SAVE THE DATES

This Training School will combine webinar sessions open to all partners (scheduled between June and September) and a practical session for a limited number of partners.



21<sup>st</sup> to 22<sup>nd</sup> of September 2017

**COST Action POSITIVE 2<sup>nd</sup> Training School**

**Use of Nutrigenetics and Nutri(epi)genomics**

**in Nutrition Research**

**Organized by**

**Dragan MILENKOVIC,**

**Anne-Marie MINIHANNE,**

**Baujke DE ROOS,**

**Wim VAN DEN BERGHE**

**Thessaloniki, Greece**



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## SHORT TERM SCIENTIFIC MISSIONS

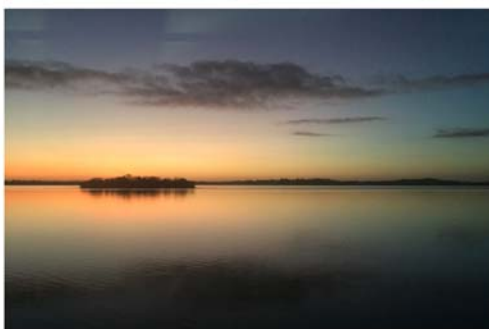
### IRINA UZHOVA from Spain went to UCD, Dublin, IRELAND

I chose to perform my short scientific stay at the UCD Institute of Food and Health which belongs to the University College Dublin and is located in Dublin, Ireland. The project I was working on is the "Fusion" pilot study involving the analysis of individual datasets. The idea was to create a large dataset of raw data from intervention studies conducted in different centres/institutions within COST network, which could be used to specifically understand the factors related to interindividual variation in response to food bioactives. This STSM allowed me to liaise with COST partners in order to identify the available studies within COST, work on the study documentation and plan further analysis, and thus I can affirm that my short stay was very successful in forwarding the project.

The Institute of Food and Health is such a fun place to work. Once you are there you are 100% involved in some of the activities they conduct at the centre, and I loved it. During that period, there was a UCD Healthy Eating Week, which consisted of all kinds of fun food and sport included challenges. Thus, we took a part in the orange eating competition trying to beat the world record by eating 3 x 300g oranges in under 1 minute and 8 seconds. The prize wasn't ours but we had such a great time.

As for the country itself, I could definitely say that Ireland is breathtaking! It is absolutely beautiful! An Emerald island with its rolling hills and vales of green, infinite beaches and mysterious foggy forests I felt in love with it from the first sight. Irish weather is unpredictable and you can't trust the forecast. And, yes, it is raining almost every day. Now I know "there is no bad weather, there are bad clothes".

### STSM Topic: Interindividual variation in response to consumption of plant food bioactives and determinants involved – Analysis of individual datasets





## SHORT TERM SCIENTIFIC MISSIONS

This past April I had the valuable opportunity to visit the Protein chemistry, Proteomics and Epigenetic-signalling (PEPS) lab of the University of Antwerp in Belgium within my Short Term Scientific mission. This mission, focused on the extraction of data from published papers on cellular and molecular targets of plant food bioactives, allowed me to directly contribute to the work of COST Action POSITIVE and achievement of its scientific objectives. Also, it gave me a unique chance to follow the experiments of the investigation about kinase activity using PamGene station in which the host team of Prof. Wim Van den Berghe is an expert. I was able to gain knowledge in a new, state-of-the-art technology and also establish new connections, which will hopefully result in fruitful collaborations and improve my future research. This mission also gave me a chance to meet some great people. The host team was on top of its game, being friendly in and out of the office, showing me the wonderful Antwerp, its social life and guiding me through the tour of famous Belgian chocolates and beers. This STSM was all together a really great experience and I strongly encourage young researchers from the COST POSITIVE network to take the opportunity and apply for their STSM.



**IRENA KRGA from France went to the Protein Chemistry, Proteomics and Epigenetic-signalling (PEPS) lab of the University of Antwerp, BELGIUM**

**STSM Topic: Data extraction from published papers on cellular and molecular targets of plant food bioactives**



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## SHORT TERM SCIENTIFIC MISSIONS

### ANA JELENKOVIC from Serbia went to the School of Medicine, University of Glasgow, SCOTLAND

My STSM lasted from the 3<sup>rd</sup> until the 21<sup>st</sup> of April, and I was hosted by Dr. Emilie Combet Aspray, at the School of Medicine, University of Glasgow. I saw this visit as a unique opportunity to learn a statistical tool I have been eager to for a long time, explore an unknown culture and work with professionals from this field of research.

This STSM was an extension on previous work carried out by WG2 team, and the main objectives were to gain practical knowledge in conducting meta-analysis using the Comprehensive Meta-Analysis software, and apply it in order to explore inter-individual variability in platelets response to the intake of certain polyphenols (flavonols, anthocyanins, ellagitannins). Prior to working with the software itself, there was a need for performing a thorough data review, extraction and categorization. Due to the great variability between studies in terms of platelet outcomes, methods, agonist concentrations – this was a quite challenging work to do. But after hours of concentrated and dedicated effort, and with Dr. Emilie's support, I managed to complete both.



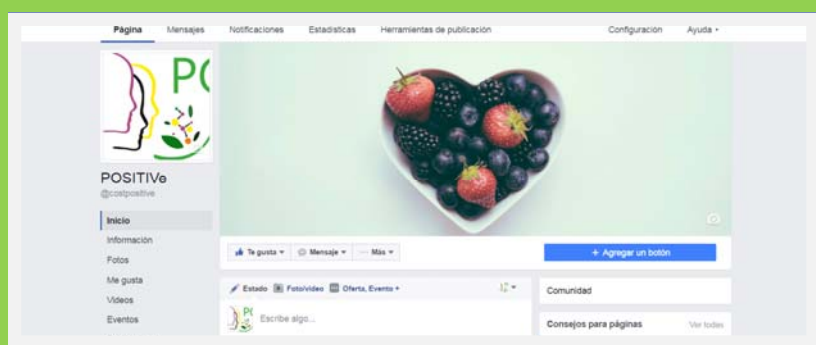
After having the hard work done, I used to stroll around the beautiful city of Glasgow, and seek for Mackintosh's and Alexander Greek Thomson's architectural signatures, or wander through the fairy-tail like Edinburgh, while the stunning Scottish nature left me breathless. I could feel irritated and amused at the same time when all four seasons started changing in one single day, but I always felt enormously happy when I felt the sun warming my face. Scotland is one extraordinary country and Glasgow is one extraordinary city, with vivid music culture and fabulous people. All of this, together with the valuable gained research experience made me have a really unique experience, and I would wholeheartedly recommend to POSITIVE young researchers to apply for STSM grant!

### STSM Topic:

**Meta-analysis training and its application in evaluating polyphenols' effects on cardio-metabolic health**

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## SCIENTIFIC EXPERT'S OPINION

### Dr. Christine MORAND COST POSITIVE Chair

The main physiological functions of the body are known to be developed during the first years of life, reach a peak in early adulthood and then decline. The rate of the decline highly depends on the lifestyle and dietary behaviour. A general consensus raising from a number of population-based and intervention studies is that the most protective diets for human health are those rich in plant foods (Katz & Meller, 2014). A specific feature of these foods is to be the exclusive and abundant dietary sources of a wide range of phytochemicals. This large group of compounds might not be essential throughout life or cause clinically manifested deficiencies, however they are considered "essential" for health and well-being in adulthood and in the elderly population (Holst & Williamson, 2007). Especially, the wide spectrum of their biological activities and associated mechanisms are of interest for the prevention of a diversity of chronic diseases, including cardiometabolic diseases, age-related cognitive decline and some cancers. Thanks to the recent development of databases on phytochemical contents in plant foods, the inverse association between their intake and the incidence of pathologies has been significantly strengthened.

However, to date much of the pleiotropic effects ascribed to dietary phytochemicals are derived from cell studies and animal models and only some of them are backed-up by



## POSITIVE initiatives towards the understanding of interindividual variability and CVD prevention by plant bioactive compounds

human intervention studies. Therefore, the available knowledge is still too limited to establish recommendations for the general population or for populations at risk of specific diseases. In addition, phytochemicals are considered by the body as xenobiotics, underlying a potential risk of toxicity if consumed excessively. For these reasons, research efforts must continue to convince the whole scientific community of nutritionists and physicians about the actual contribution of these non-essential compounds in promoting the health benefits associated to the consumption of plant foods. This is all the more important given that there is no doubt that the real prospects for innovation in the field of nutrition, food and health will come from these plant food bioactive compounds rather than from other macro or micro-nutrients.

We know from clinical research that depending on their physical/genetic make-up individuals respond differently to nutritional challenges, and thereby may experience more or less benefit/risk associated with particular dietary constituents. Even if still poorly explored, this inter-individual variation in responsiveness is of particular relevance for dietary plant bioactives (Manach et al, 2016). Indeed, most of these compounds are absorbed and metabolized through the same polymorphic carriers and enzymatic systems than drugs and other xenobiotics, meaning that the efficiency of their bioavailability is likely to depend on individual genetic background.

In addition, gut microbiota is known to be extensively involved in the metabolism of a number of plant bioactives, especially that of polyphenols. The gut microbiota converts polyphenols into active and bioavailable metabolites; hence variations in its composition and functionality can affect polyphenol bio-efficacy (Tomas-Barberan et al, 2016). Together with genetic background, gut microbiome composition, others factors like age, gender, lifestyle and physio-pathological state could also be responsible for the heterogeneity in responsiveness to plant food bioactives consumption that has often led to inconclusive results in clinical trials aiming to demonstrate the health effects of specific dietary bioactive compounds (Milenkovic et al, 2017).

A clear understanding of why some bioactive plant compounds work effectively in some individuals but not or less in others is crucial for a full consideration of these compounds in future strategies of personalized nutrition to prevent chronic diseases, as well as to underpin the development of new functional and customized foods. Reaching this aim implies first to identify the main determinants of variability and how these different factors interact to influence subject-specific response to the consumption of the main families of plant food bioactives, regarding both their bioavailability and bio-efficacy. This work has been initiated by the European scientific experts involved in the COST Action POSITIVE.

## SCIENTIFIC EXPERT'S OPINION

From the findings of the POSITIVE network and of other complementary initiatives, the relative contribution and possible interactions of the main determinants of inter-individual variability identified should be further validated through dedicated randomized controlled trials and large-scale prospective studies for the different families of plant food bioactives. To show the relative contribution of various factors controlling the bioavailability of the compounds and the individual biological responsiveness to their consumption, as far as possible, these studies will integrate omics approaches for an in-depth characterisation of individuals, including genotyping, gut microbiota analysis, food metabolome profiling, transcriptomic response profile. This information rich datasets will be very useful to establish correlations with health outcomes in both intervention and prospective studies. The power of these studies will also have to be calculated to allow for different 'responsive' subgroups analyses and/or wise targeted recruitments must be performed based on the factors likely to affect the individual response. A major challenge will also be to develop methods and tools to phenotype and stratify individuals based on their ability to respond to the intake of plant food bioactives. Several approaches can be foreseen to develop methods for subjects' stratification, including modelling and challenge tests (Manach et al, 2016). Models may be built from the acquired knowledge to predict the internal exposure of individuals and more complex ones should also be developed to predict biological responsiveness to plant food bioactives intake. To assess the individual's capacity to respond to plant food bioactives intake, the challenge test approach could include the use of standardized supplement containing various bioactives, together with that of standardized postprandial nutritionally challenging conditions defined to induce disturbances impacting health outcomes. This set of approaches will be helpful both to strengthen the scientific knowledge of the determinants of inter-individual variability and to estimate the personal health benefits that an individual can gain from different bioactive compounds.

This research development will undoubtedly lead to innovative applications for these plant food bioactives in the area of personalized nutrition to maintain best health conditions through a balanced and properly administered daily nu-

trition and will offer exciting opportunities for the food and nutraceutical industry to produce healthier and customized foods.

### References:

- Katz D.L., Meller S., 2014. Can we say what diet is best for health? *Annu Rev Public Health*. 35,83-103.
- Holst, B., Williamson, G., 2008, Nutrients and phytochemicals: from bioavailability to bioefficacy beyond antioxidants. *Curr., Opin. Biotechnol.*, 19, 73–82.
- Manach, C., Milenkovic, D., Van de Wiele, T., Rodriguez-Mateos, A., De Roos, B., Garcia-Conesa, M. T., Landberg, R., Gibney, E. R., Heinonen, M., Tomas-Barberan, F., Morand, C. 2016. Addressing the inter-individual variation in response to consumption of plant food bioactives : Towards a better understanding of their role in healthy aging and cardiometabolic risk reduction. *Mol Nutr Food Res*. doi: 10.1002/mnfr.201600557. [Epub ahead of print]
- Tomas-Barberan, F., Selma, M.V., Espin, J.C. 2016. Interactions of gut microbiota with dietary polyphenols and consequences for human health. *Curr Opin Clin Nutr Metab Care*. 19(6):471-476.
- Milenkovic, D., Morand, C., Cassidy, A., Konic-Ristic, A., Tomas-Barberan, F., Ordovas, J. M., Kroon, P., De Caterina, R., Rodriguez-Mateos, A. 2017. Interindividual Variability in Biomarkers of Cardiometabolic Health after Consumption of Major Plant-Food Bioactive Compounds and the Determinants Involved. *Adv Nutr*, 8, 1-13.

## CONTACT US



EUROPEAN COOPERATION IN THE FIELD OF  
SCIENTIFIC AND TECHNICAL RESEARCH

### Contact us:

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: [christne.morand@clermont.inra.fr](mailto:christne.morand@clermont.inra.fr)

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: [fatomas@cebas.csic.es](mailto:fatomas@cebas.csic.es)

### Webpage:

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)

**RESEARCH DISSEMINATION**
**FoodComEx – a chemical library for food compounds and food**

The Food Compound Exchange – FoodComEx (<http://foodcomex.org/>) is a virtual chemical library developed as part of the Food Biomarkers Alliance – FoodBALL project (<http://foodmetabolome.org/>) under the coordination of Claudine Manach (INRA, France), Christoph Weinert (Max Rubner Institute – Germany) and David Wishart (University of Alberta - Canada). The aim of FoodComEx is to maintain an online catalog of food compounds and derived metabolites that are not usually commercially available, but could be shared by academic laboratories.

The lack of standards is a major limitation in nutrition studies, especially when it comes to plant food compounds. Authentic standards are useful for validating identifications of compounds in metabolomics profiles of foods, extracts, and samples obtained in human or animal studies. They can also serve to develop quantification methods. Pure standards are crucial for the investigation of the health effects of bioactive metabolites. Too many *in vitro* studies have been performed so far with non-physiologically relevant compounds, due to the unavailability of standards for the identified circulating metabolites of bioactives such as polyphenols. On the other hand, collections of precious molecules have been isolated or synthesized in academic laboratories all over the world.

The idea behind the collaborative platform FoodComEx is to make these molecules available for new studies and for a wider community. Chemists, food scientists or others that are interested in sharing compounds synthesized, isolated or stored in their laboratories can directly upload their compounds in the FoodComEx platform through a user-friendly interface and guided by a video tutorial. Anyone visiting the website will be able to browse the library and for every compound, obtain a description including the chemical structure, method of production, purity, storage conditions, spectral data and the contact details of the provider. Those interested in obtaining a given compound will be able to contact the group that is offering it and establish a cooperation. Providers can also describe their skills and research interests in the providers' directory, where they can be easily found by others reaching out for collaborations. FoodComEx also features a virtual board where users can add the names/structures of wanted molecules, to stimulate their sharing or synthesis by others. The use of FoodComEx is free of charge and the platform will be sustained over the years thanks to the solid bioinformatics infrastructure of University of Alberta, which already maintains major databases such as HMDB, FoodB, DrugBank and PhenolExplorer.

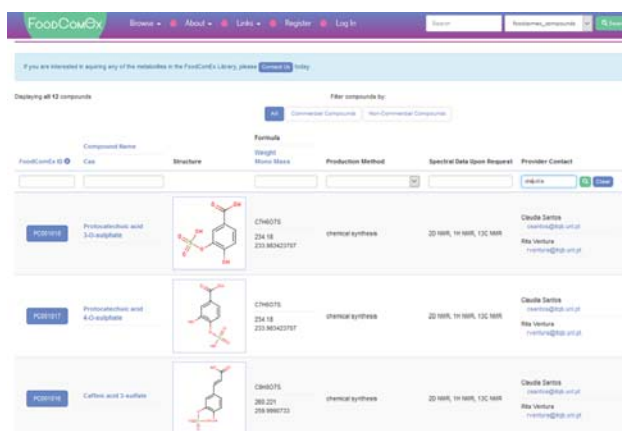
FoodComEx is on its initial development and its success depends on the participation of scientists willing to share their compounds and establish cooperations with other groups. Some of our enthusiastic POSITIVE partners (Claudia

Santos, Pedro Mena, Daniele Del Rio) have already uploaded polyphenol metabolites. Everyone is invited to participate by registering their compounds in the database and forwarding the information on FoodComEx to colleagues likely to be interested in this initiative.

If you have any question, please contact Jarlei Fiamoncini ([jarlei.fiamoncini@inra.fr](mailto:jarlei.fiamoncini@inra.fr)) who is currently leading FoodComEx development



or Claudine Manach ([claudine.manach@inra.fr](mailto:claudine.manach@inra.fr)).

Compound Name	Structure	Weight	Molecular Weight	Production Method	Spectral Data (NMR, IR, MS)	Provider Contact
Protocatechuic acid 3-O-sulfate		234.18	332.36423787	chemical synthesis	2D NMR, 1H NMR, 13C NMR	Claudia Santos <a href="mailto:menap@inra.fr">menap@inra.fr</a> Ray Ventura <a href="mailto:menap@inra.fr">menap@inra.fr</a>
Protocatechuic acid 4-O-sulfate		234.18	332.36423787	chemical synthesis	2D NMR, 1H NMR, 13C NMR	Claudia Santos <a href="mailto:menap@inra.fr">menap@inra.fr</a> Ray Ventura <a href="mailto:menap@inra.fr">menap@inra.fr</a>
Caffeoyl acid 3-sulfate		286.221	384.3867113	chemical synthesis	2D NMR, 1H NMR, 13C NMR	Claudia Santos <a href="mailto:menap@inra.fr">menap@inra.fr</a> Ray Ventura <a href="mailto:menap@inra.fr">menap@inra.fr</a>

## RESEARCH DISSEMINATION

### PUBLICATIONS– WG1

To date, very few human dose-response studies have been conducted looking at (poly)phenol rich foods and health outcomes; such studies are essential to assess cause-effect relationships and to develop dietary recommendations. Health effects of (poly)phenols are considered to be driven by circulating metabolites rather than the native compounds and, up to now, even less work has looked at plasma and urine (poly)phenol metabolite profiles in relation to dose-response intake of (poly)phenol-rich foods.

juices. A total of 14 of all analyzed plasma metabolites (60 compounds) positively correlated with the amount of (poly)phenols ingested in the drink. In contrast, no linear dose-response was found for total urinary excretion over 24 h, however 12 of the 60 (poly)phenol metabolites displayed a positive linear dose-response.

The inter-individual variability expressed as coefficient of variation of area under the curve (AUC) and maximum concentration in plasma (C<sub>max</sub>) was 53% and 51% for total plasma (poly)phenols, respectively. Of the 60 metabolites quantified the lowest variability in C<sub>max</sub> was found for dihydroferulic acid 4-O-sulfate (CV 43%) and highest variability was detected for vanillic acid (CV 216%). The CV for AUC varied be-

### Inter-individual variability in absorption and metabolism of cranberry (poly)phenols

Feliciano et al. (Nutrients 2017) evaluated whether the plasma and urinary levels of phenolic metabolites follow a dose response after consumption of cranberry juice; they also assessed the extent of inter-individual variability of circulating metabolite concentrations. A randomized controlled crossover trial was performed in 10 healthy men, in which blood and urine samples were collected over 24 h after consumption of cranberry juices containing 409, 787, 1238, 1534 and 1910 mg total (poly)phenols.

A linear dose-response increase in total plasma (poly)phenol metabolites was found after intake of the cranberry

between 48% for 4-hydroxybenzaldehyde and 163% for 1-methylpyrogallol-O-sulfate. Despite the homogeneous test population (healthy, young, males) many of the metabolites assessed exhibited a very large inter-individual variability, probably dependent on an individual's ability to generate specific metabolites. The authors identify a number of factors that may influence the metabolism and absorption of (poly)phenols including differences in the gut microbiome, genetic polymorphisms in transporters or metabolizing enzymes and environmental impact.



*nutrients*



Article

## Absorption, Metabolism and Excretion of Cranberry (Poly)phenols in Humans: A Dose Response Study and Assessment of Inter-Individual Variability



Dr. Rodrigo Feliciano



Dr. Charlotte Vills



Geoffrey Istas



Dr. Christian Heiss



Dr. Ana Rodriguez-Mateos

## RESEARCH DISSEMINATION

### PUBLICATIONS-WG2



### An insight into human tissue gene expression interindividual variation in response to supplementation with a pomegranate extract rich in the bioactive compounds ellagitannins

Numerous pre-clinical studies have shown that the beneficial effects attributed to plant bioactive compounds may be mediated, at least partially, by the orchestrated activation in the cells of a range of genes in response to the presence of these compounds. However, how gene expression regulation by plant bioactive compounds may happen *in vivo* remains an unresolved question. An accepted hypothesis is that the compounds that might trigger the gene response in the organism are the metabolites formed in the body and detected in the cells and tissues.

The aim of this human intervention randomized study was to explore some gene expression changes occurring in colon tissues that could be associated with the intake of the bioactive compounds ellagitannins (ETs) or with presence in these tissues of the urolithins, the main gut microbial metabolites derived from ETs. Colon cancer patients consumed a pomegranate extract rich in ETs for several days. We attained colon tissue samples before (baseline biopsies) and after the intervention (post supplementation surgical pieces), extracted the RNA and measured gene expression in comparison with a control group. We also analysed the presence of urolithins in these tissues.

Inter-individual variability in the gene expression response to the intake of bioactive compounds has been scarcely investigated. Gene expression variation is inherent to genes and is influenced by many factors, i.e. disease status, tissue heterogeneity, sampling protocols, etc. Our study corroborated: i) a large inter-individual variability and ii) a considerable impact of the experimental protocol on gene expression. One important issue was that these two aspects were gene- and tissue-specific. Like this, some genes exhibited a lower inter-individual variation (CV=30%) whereas others displayed a

larger one (CV=70%). Equally, some genes were more affected than others by the experimental protocol and some genes resulted induced whereas others were found to be downregulated in the colon samples from the control volunteers. These circumstances, greatly enhanced the difficulty in discerning gene expression changes attributable to the specific supplementation with ETs (expected to be moderate or small changes). Despite all this, we were able to detect some significant and specific gene expression changes in the colon samples from the individuals that consumed the pomegranate extract. These changes suggested a counteracting effect of the consumption of this product to the changes occurring in the control participants. However, these changes could not be associated with the quantity or profile of urolithins in the tissues. Importantly, we were not able to find similarities between the human *in vivo* changes and those previously reported *in vitro* for these metabolites.

Overall, our study shows the feasibility of detecting gene expression changes in human tissues in response to supplementation with bioactive compounds but also points out to various key issues that have yet to be addressed and improved before we can definitively demonstrate these molecular effects *in vivo*: 1) establish an appropriate sample size for these studies, 2) improve designs to reduce protocols impact and enhance samples quality, 3) understand the intrinsic variability in gene expression in human tissues, e.g. factors affecting this variability: epi(genotype), chronobiology, regulation by microRNAs, etc. Gene expression regulation by bioactive compounds is a complex and multifactorial process that will require the implementation of many more complementary *in vitro* and *in vivo* studies before we may be able to reveal the molecular mechanisms underlying the effects of these compounds.

## RESEARCH DISSEMINATION

### INTRODUCING POSITIVE AT:



### Dr. Victoria MORENO ARRIBAS presenting POSITIVE at NUTRACEUTICALS EUROPE (Madrid, SPAIN)

The 1st Edition of the NUTRACEUTICALS Europe Summit & Expo gathered more than 2000 professionals in the sector of the functional and novel ingredients from all over Europe during the past 22<sup>nd</sup> and 23<sup>rd</sup> of February at the Madrid Fair (Madrid, Spain).

With the presentation of more than 50 lectures by national and international leading speakers, Nutraceuticals Europe exposed the latest scientific research, as well as the latest advances in R+D+I of the most relevant companies in the functional and novel ingredients sector.

On this occasion, Dr. Moreno-Arribas from CIAL-CSIC was one of the invited speakers and talked to the audience about: **Wine and Polyphenols, understanding their health benefits through the intestinal microbiome**. After her conference, Dr. Moreno-Arribas also introduced POSITIVE to the attendants using the set of POSITIVE slides prepared by the FG and available to all partners on request.



DETROP, the International Exhibition of Food & Beverage Industry took place at the Exhibition Centre HELEXPO in Thessaloniki (GREECE) during the past 3<sup>rd</sup> to 6<sup>th</sup> of March. DETROP is the a major exhibition in Greece within the food & beverage sector and every year gathers a very high number of exhibitors and visitors. This year, DETROP has been characterized by an extensive international participation from the European Union, Asia and Middle-East, Russia, USA and other places.

Also, a large number of parallel events were organized, including a meeting of the International Observatory of Oxidative Stress, designated: "The anti-oxidant power of the food on our plates". Dr. Christos Kontogiorgis was invited to give a lecture entitled: "**Natural Antioxidants: Truth and myths regarding their role in Public Health**". As part of his presentation, Dr. Kontogiorgis dedicated some time to introduce the aims of the Cost Action POSITIVE using the slides prepared by the FG.



### Dr. Christos KONTOGIORGIS presenting POSITIVE at DETROP (Thessaloniki, GREECE)

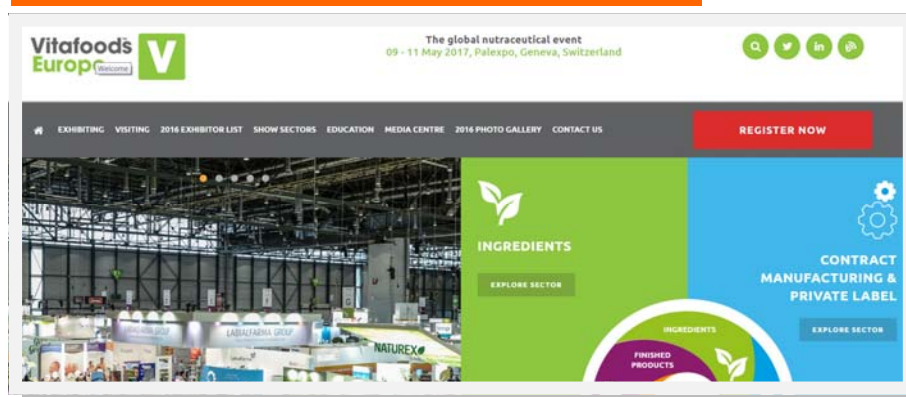
All the attendants recognized the important mission of the Action and the innovative role that plays to impulse the research on the benefits of plant foods for health.



## RESEARCH DISSEMINATION

INTRODUCING POSITIVE AT:  
VITAFOODS

Professor Baukje de Roos  
 Deputy Director, Rowet Institute,  
 University of Aberdeen  
 United Kingdom



between consumption and effects of specific plant bioactives in population subgroups? This would certainly be of interest to the main stakeholder group attending the Vitafoods meeting, which were those involved in producing ingredients for other

On the 9<sup>th</sup> and 10<sup>th</sup> of May (2017) I visited the Vitafoods meeting in Geneva on behalf of the COST Action POSITIVE. This meeting was attended by over 18 thousand stakeholders from all over the world and therefore an ideal platform to present the first results of the POSITIVE consortium. During the Educational Sessions on 'Polyphenols' I had the opportunity to discuss how we can address the concept of inter-individual variation in response to consumption of plant polyphenols within the COST Action. The efficacy by which dietary interventions influence health is currently mainly determined by taking population-based approaches that can favourably shift disease risk factors in the entire population, but many of the large RTCs have effectively demonstrated that only 40% of a cohort responds to dietary interventions. Could we, somehow, overcome and indeed benefit from individual variability in responses to interventions? For example, could we work towards future health claims which would be based on a clear relationship

food businesses.

My presentation outlined examples of inter-individual variation in bioavailability, including absorption, distribution, metabolism and excretion of plant bioactives. It also discussed personal requirements - who needs what? This was illustrated by examples of increased efficacy of specific bioactives in specific subgroups such as the presence of specific polymorphisms, increased efficacy in specific age groups or enhanced efficacy in those that produce beneficial metabolites based on their microbiota. Finally, I presented the outcomes of our stakeholder questionnaire, indicating that stakeholders are specifically interested in producing optimised foods (where processing methods may lead to a higher bioavailability of bioactives); as well as in the availability of databases which provide knowledge on the metabolism of bioactives in the human body. The Phytohub activity within the POSITIVE network is an excellent example of this.

<http://www.vitafoodsinsights.com/blogs/speakers-corner/2017/04/developing-plantbased-foods-that-address-individual-needs.aspx>



BLOG

## Developing Plant-based Foods that Address Individual Needs

by Prof Baukje De Roos · © April 16, 2017

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## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS



**TATJANA RUSKOVSKA**  
 Faculty of Medical Sciences  
 Goce Delcev University  
 REPUBLIC OF MACEDONIA

#### What is the focus of your research?

My research has mostly been related to atherosclerosis risk factors beyond the conventional lipid status measurements in clinical settings. Biomarkers of lipid peroxidation and antioxidant defense, followed by autoantibodies against oxidized LDLs, protein carbonyls and hsCRP were among the key topics of my research.

Recently, my research has been focused on dysfunctional adipose tissue, since its inflammation and oxidative stress in obesity largely contribute to the whole body insulin resistance, which is an important determinant of metabolic syndrome. In this context, the interest of POSITIVE in cardiometabolic outcomes resulting from consumption of plant bioactives is highly complementary to my work, and helped me set my overall research in a new perspective.

#### In what countries/organizations have you studied or worked?

After obtaining the bachelor's degree in life sciences (biochemistry and physiology) at the University "Ss. Cyril and Methodius" in Skopje, Republic of Macedonia, I started working at the Military Hospital in Skopje as a biochemist in the Central Clinical Laboratory. In parallel to my work at the hospital, I completed my master and PhD studies at the same University. After obtaining the PhD degree, I was appointed Head of the Central Clinical Laboratory. In 2009 I was invited to join the Faculty of Medical Sciences at the University "Goce Delcev" in Stip, Republic of Macedonia, as a professor of clinical chemistry and biochemistry. From 2011 till 2014 I served as a Vice-Dean of the Faculty of Medical Sciences.

#### What has been the greatest achievement in your career?

So far, it has definitely been the Fulbright scholarship, awarded by the United States Department of State. This is a highly competitive grant, and as such it means a lot to me. As a Fulbright scholar, I spent the academic 2014/15 at the University of Minnesota, Twin Cities, in the laboratory of Dr. David Bernlohr, where I was working on the pathophysiology of obese white

adipose tissue. It was an exciting time of intense learning, as well as an academic and cultural exchange.

#### Which is your favorite paper you have written/co-authored and why?

I will point out two papers which are my favorites at the moment. The first one is my first paper listed on the PubMed (from my perspective, it looked like an elusive goal for many years). This is the paper entitled "Comparative Analysis of Serum (Anti)oxidative Status Parameters in Healthy Persons", co-authored with Dr. Eugene Jansen from the National Institute for Public Health and the Environment, the Netherlands, with whom I have had an excellent cooperation for many years. The second paper which is also very important to me is the paper "Oxidative stress and protein carbonylation in adipose tissue - implications for insulin resistance and diabetes mellitus", co-authored with Dr. David Bernlohr, and written during the preparation of my Fulbright application.

#### Who is/was your most influential mentor/colleague and why?

There are several colleagues/professors who have had a remarkable influence on my career, which I highly appreciate. I already mentioned the cooperation with Dr. Jansen and Dr. Bernlohr. I will also highlight the role of my mentor Prof. Jordanka Dimovska from the University "Ss. Cyril and Methodius" in Skopje, whose extraordinary guidance was an essential determinant of my early career, as well as the influence of Prof. Helen Griffiths from the United Kingdom, an excellent scientist with a remarkable personality, who was practically my first contact with the European science and higher education.

#### What is your advice for young scientists?

Set your goals, and do your best to accomplish them. Science is exciting, definitely not easy, sometimes even frustrating, but if you like it, it's worth spending your life working on it.

#### Where is your favorite place in the world and why?

I have not decided yet, I still explore the world. It must be a place with a breathtaking nature and kind people. And there must be a lab.

#### What is your favorite music/book?

I listen to modern pop music and every few months I make my own selection of several favorite songs. Some of them attract me with the rhythm, sometimes it is the interpretation, and sometimes the lyrics... it is different for every song. I also like jazz and bossa nova. Regarding the books, it is completely different. For many years now, Coelho's "Alchemist" has been my favorite book. It seems it's all about (bio)chemistry after all.

#### What is your favorite sport(s)?

I am not a fan of sports, and I simply do not keep track of the sports events. For recreation, I like walking/hiking, and from time to time I practice a variation of yoga, for flexibility and relaxation.

## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS

#### What is the focus of your research?

I work in the Nutrition Section of the Food Engineering Department at Ege University, Turkey. It is one of the most important state universities of Turkey, situated in the heart of the Aegean. In this department, I have the pleasure to teach undergraduate and graduate courses. Further, I am supervisor for 3 MsD graduate and 2 PhD students. In addition, a branch laboratory with quite good facilities in scientific research is present. My main scientific approaches are on structuring foods with health benefits, release of bioactive components in the gut and demonstrating health benefits in food systems currently studied, dairy and fruit/vegetable. I took my degree at the department of food engineering. Later on, I made my speciality on food science and nutrition. After my undergraduate and graduate programs, being well informed on the subject of food and knowing the food processes well has been a great advantage for me in nutrition studies. I am currently studying topics such as *in vitro* static digestion of food and *in vitro* amylase and lipase inhibition in fat and carbohydrate digestions.

#### In what countries/organisations have you studied or worked?

I have not worked in any other countries, but I have partner projects with many countries. The newest is the European Union project named Pathway27 which is still going on.

#### What has been the greatest achievement in your career?

For me, my greatest achievement was my transition to academia after a professional career. Since then every day comes and feels as an achievement. For me greatest attainment is waking up every day and still having that zeal and enthusiasm to go to work like it's your first day. Therefore I would like to count my enthusiasm and love of 35 years in academia as my greatest achievement.

#### Which is your favourite paper you have written/co-authored and why?

My favourite one would have to be "El S. N., Simsek S. Food Technological Applications for Optimal Nutrition: An Overview of Opportunities for the Food Industry. 2012. Comprehensive Reviews in Food Science and Food Safety. Vol 11, 2-12."

That year, (2012) I had the chance to give inspiration to many young researchers on the subject of food and nutrition including my graduates in choosing the subject of their thesis. The years that followed, this paper and it's subject conceived many publications. I would like to think I had a good foresight.

#### Who is/was your most influential mentor/colleague and why?

That would be my colleague and friend Dr. Sibel Kara Kaya.

Our friendship started on our youthful first days at the university, and still goes on in the academic platform. We have been working on the same discipline for 30 years. This always gave us a good synergy and together we did fruitful studies and brought up students.



**SEDEF NEHIR EL**  
**EGE UNIVERSITY,**  
**Food Engineering Dept.,**  
**Nutrition Section,**  
**Izmir, TURKEY**

#### What is your advice for young scientists?

To young scientist, I would suggest them to always have a deadline for whatever their heart desires to study or research and to keep their deadlines. Yes, over time they may be more anxious, alert or even sometimes impatient when racing time. This is not something to worry, for these are all beneficial for the passion when one follows the path of science.

#### Where is your favourite place in the world and why?:

My favorite place in the world is my home. It embraces all the places I've had the chance to visit, where I walked, what I ate, how I lived. All these experiences come together in beautiful harmony that energies and reflects, reminds me.

#### What is your favourite music/book?:

There is one song that always holds the special place in my heart ever since my earlier years; it is called 'Living Next Door to Alice' by Smokie. I am attaching the youtube link for you to listen; <https://www.youtube.com/watch?v=Z6qnRS36EgEU>

Among the sea of books, it is very hard to pick one. But I can encourage everyone to read Momo by Michael Ende.

#### What is your favourite sport(s)?:

I am ashamed to say that I am not the athletic type therefore I do not have any favorite sports. But I have always taken pleasure from watching artistic skate championships and never miss to do so.

## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHERS

#### What is the focus of your research?

In the Laboratory of Vascular Biology and Nutrigenomics of the CNR Institute of Clinical Physiology (CNR-IFC)-Lecce (Italy) we studied the effect and related mechanisms of food and dietary ingredients, mainly of the Mediterranean dietary pattern, on the pathophysiology and clinic of cardiometabolic diseases. To this aim, we use relevant *in vitro* model systems including human endothelial cells, monocytes/macrophages, and adipocytes to perform cellular and molecular studies. Furthermore, we perform human studies to evaluate changes in health indices or discover new biomarkers of exposure/effect in response to diet or dietary constituents. We are particularly interested in the health effect of polyphenols (from olive oil, red wine, etc.) and fatty acids (mono- and poly-unsaturated fatty acids).

#### In what countries/organisations have you studied or worked in?

I completed all my academic studies in Italy. I graduated in Biology at the University of Salento, Lecce, and received my PhD in Innovative Strategies in Biomedical Research at the Sant'Anna School of Advanced Studies, Pisa. During my PhD studies and then as a Postdoctoral Researcher I conducted my research activities at the CNR-IFC, Lecce, Laboratory of Vascular Biology and Nutrigenomics. Now I work at the CNR-IFC Lab as a permanent researcher.

#### What has been the greatest achievement in your career?

The greatest achievement in my career is the joint collaboration and networking with other researchers to exchange scientific ideas, doubts, research projects and results. This has helped to open my mind to the critical thinking, to adopt a multidisciplinary approach to the research and to be prone to discussion with my peers as a step for my personal and scientific growth.

#### Which is your favourite paper you have written/co-authored and why?

My favourite paper relates to the important effect of two extra virgin olive oil compounds, the monounsaturated fatty acid oleic acid and the polyphenol hydroxytyrosol, on the regulation of adiponectin, an adipokine with beneficial properties against cardiometabolic diseases (Additive regulation of adiponectin expression by the mediterranean diet olive oil components oleic Acid and hydroxytyrosol in human adipocytes. *PLoS One*. 2015 Jun 1;10(6):e0128218. doi: 10.1371/journal.pone.0128218. eCollection 2015). After a years-long and hard research activity, this publication represents an important personal milestone and also would contribute to the advancement in the understanding of the Mediterranean diet health benefits.



**EGERIA SCODITTI**

**CNR - Institute of Clinical Physiology  
Lecce, ITALY**

#### Who is/was your most influential mentor/colleague and why?

Professor Raffaele De Caterina is the most important mentor during my career. Besides being my PhD thesis supervisor, he introduced me to the research field inspiring ideas and projects, and importantly encouraging me to be self-confident and independent.

#### Where is your favourite place in the world and why?

My favourite place in the world is Sicily in Italy, because of its history, art and archeology all around the island, sunny places, breath-taking scenery, and unforgettable Mediterranean food.

#### What is your favourite music/book

I love reading Isabel Allende, but also crime novels. Regarding music, I like listening to pop music.

#### What is your favourite sport(s)?

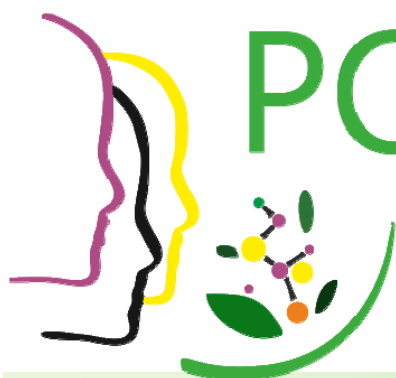
I like walking in the countryside with my 14-years old husky Jack.





POSITIVE

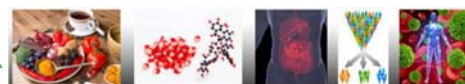
ISSUE 7



# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE VI, DECEMBER 2017

## WELCOME

**D**ear partners, we are now approaching the end of 2017 and entering the last term of our COST Action POSITIVE. Once more, this December issue brings together summaries and snapshots of all the past year activities including meetings, workshops, training school, STSM, publications and various presentations as well as our regular expert opinion and collection of surveys from amid the POSITIVE participants.

Thus far, the FG has tried firmly to cover all the aspects dealt with during the past years and to reflect the efforts and the good work done by all the working groups. We have been very keen on including as many pictures as possible that clearly show all the many nice people from the different countries that have intervened in the different research tasks. The get-to-know-each-other section continues highlighting the story of POSITIVE partners so that we will end up the Action with as many friends and colleagues as possible. We honestly hope to continue fulfilling our dissemination job up until the very end of the Action by September 2018. We still have one more year to go and from the members of this FG we wish you all a wonderful and successful 2018.

**Merry Christmas (the Focus Group)**



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## NEWS FROM THE ACTION

### 6<sup>th</sup> COST Action POSITIVE Meeting, 2017

Organized by **Dr. Kristos Kontogiorgis** and **Dr. Antonia Kaltsatou**,  
Thessaloniki, GREECE

During September 19-23, 2017 Thessaloniki, Greece hosted major events crucial to a successful implementation of COST POSITIVE. The 6<sup>th</sup> Working Group and 4<sup>th</sup> Management Committee meetings allowed Action partners to network and share the results of activities performed so far as well as plan further tasks to progress towards implementation of POSITIVE final objectives. The WGs and MC meeting was accompanied with the 3<sup>rd</sup> Scientific Workshop attended by both renowned and promising young researchers who discussed their most recent findings on omics-based evidence of the health effects of plant food bioactives.

The events took place in a pleasant atmosphere built by a heartfelt hosting of our Greek partners with a sunny and warm weather in the background. Participants of the meetings had a chance to get advantage of very fruitful discussions and enjoy evening strolls around the city of Thessaloniki and the delicious Greek cuisine.



## RESEARCH HIGHLIGHTS

### Work Group 1

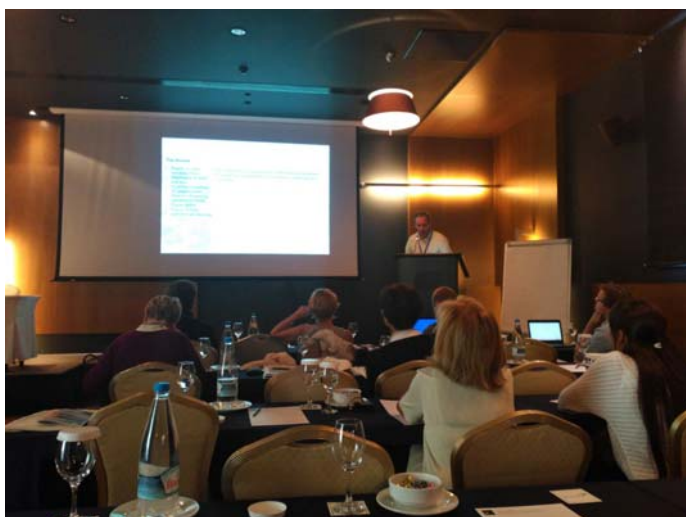
Leader: Tom VAN DE WIELE

Co-leaders: Claudine MANACH & Rikard LANDBERG

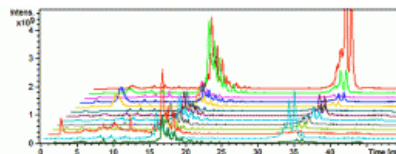
The WG1 meeting was started off by Rikard Landberg who divided the initial session into one session dedicated to the Gene Variant group and the second one to the different subgroups looking at specific bioactive compounds. An important aspect to discuss was the current state of the work on the metabolic pathways for the various compounds investigated.



There were some presentations by Dr Torsten Bohn on the research about ADME pathways of carotenoids which is well advanced and almost ready for publication and also by Wiktor Jurkowski on the different web resources that can be used for modelling and visualization of metabolic pathways, where Pathwhiz and Minerva may be applicable for the objectives of the WG1.



The different subgroups need to complete and hand a template prepared for the purpose of getting the information needed for the drawing of the metabolic pathways of the different compounds.



The session about metabolomics and the compounds subgroups was led by Dr. Claudine Manach. Some tasks such as the compilation of key analytical issues needed for metabolomics analyses and identification of compounds and metabolites were reopened. Further work is guaranteed through web meetings and collaborative efforts. Presentation by Dr. Maria Bronze updated the progress of the multiplatform test analyses and the status of a new article due in December. Due to the various difficulties and problems in this area, further work is needed in order to reach consensus on how to perform wide coverage and accurate analyses and identification of metabolites. Issues such as the use of standards with different polarity, tools to predict retention times or stability of the mixed compounds were also discussed. More partners may join the platform and more web meetings and STSM will be organized to continue with this work.



On the second day of the WG1 meeting, the work focused on the status of the reviews about the different compounds subgroups: papers selection, data extraction and analysis, publications, etc. Changes and needs in the different subgroups were also discussed by different partners. An important number of papers have been published, submitted or will be completed in the next few months.

## RESEARCH HIGHLIGHTS

### Work Group 2

Leader: Ana RODRIGUEZ-MATEOS

Co-leaders: Eileen GIBNEY &  
Dragan MILENKOVIC

#### *Meta-analysis subgroup*

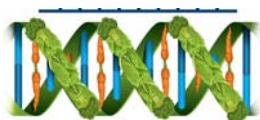
The WG2 meeting was led by Eileen Gibney who started the session by updating the current status of the meta-analyses published and in preparation. A general discussion followed about some critical issues on the results interpretation, especially in view of the data limitation and lack of significance of the subgroup analyses. Next, Paula Pinto presented all the work carried out on the flavanols meta-analysis looking at blood pressure (BP) and flow mediated dilation (FMD). Some of the problems found during this analysis were exposed so that future studies should include and consider important aspects such as better description of the methodology, clearer setup of the subgroups, and more research on the relationship dose-response. Her presentation was followed by others given by: Antonio González-Sarrías on the meta-analysis on ellagitannins and anthocyanins, Pedro Mena on hydroxycinnamic acids, Eileen Gibney (on behalf of Antonia Katsaltou and Christos Kontogiorgis) on the systematic review about the interaction between polyphenols and exercise and, Emilie Combet on the metanalysis of flavanols and glycemic function. Several important issues on these analyses were



commented and the need of a summary of the key findings was proposed.

There was also a presentation by Eileen Gibney on the current status of dataset analyses and on the potential POSITIVE study. After examining the responses to the questionnaire previously sent around, it was found that problems such as funding, ethics, specific compound or product to investigate, and study design were of concern and that further discussion and consideration should be given to the planning of the study. Another key aspect was the importance of including the bioavailability as a factor affecting variability in the response. Overall, the idea needs to be further settled in order to prepare a feasible and valuable study.

#### *Cell & Molecular Targets subgroup*



The activities carried out in this subgroup were introduced by Laurent Monfoulet. During the meeting, Mayte García-Conesa also presented the work carried out by Biljana Pokimica during a STSM in Spain in her lab at CEBAS-CSIC (June 2017). A full and updated revision and selection of articles about gene expression effects of bioactive compounds in human clinical trials as well as data extraction has

been completed and a draft article is being prepared. Further work on the results presentation and general discussion is on its way. The article may be published before the summer 2018.

Regarding other nutrigenomic studies in cell and animal models, although an important amount of work has been done, there is some concern about the completion of some of the tasks initially proposed and the collaboration of more people was requested. There was a general discussion as to how to tackle the work that still need to be done and more STSM were considered but not finalized.





## RESEARCH HIGHLIGHTS

### Work Group 3

Leader: Baujke DE ROOS

Co-leader: Marina HEINONEN

A WG3 plenary meeting gathered most of the Thessaloniki meeting attendants. During this session, the WG3 leader Baukje de Roos presented the results of a questionnaire distributed to Portuguese consumers that evidenced a considerable interest and knowledge on plant bioactive compounds as well as the importance of improving the knowledge about their efficacy for preparing new products applicable to specific populations. Other tasks proposed within the group such as the development of movies and webinars were a bit delayed but a short video with Zohar Kerem about a successful collaboration between academia and industry was filmed during the meeting. Other videos are in preparation. The presentation at VitaFoods in Geneva was also commented, as well as the development of a decision-tree style on-line tool and a final roadmap. The roadmap is essential to summarize the work done as part of POSITIVE to evidence the complexity of the aspects involved in inter-individual variability in response to the bioactive compounds. It is also very important to establish the gaps in knowledge and the needs for future research in the area.



The plenary Focus Group meeting was opened by the FG leader Mayte Garcia-Conesa who presented the past and ongoing communication activities within the Action, and invited attendees to consider future application of a preliminary questionnaire on food & health introduced to consumers at local science events in Spain. Partners discussed the possibilities of producing an improved version of the questionnaire by investigating participants' knowledge about: metabolic diseases, the role of diet in health, the importance of understanding differences between individuals, as well as identifying challenges that may show up when we try to apply it to other groups across COST partners in Europe for a larger survey.

Furthermore, new means of disseminating POSITIVE impacts and achievements were considered. FG intends to work on a 'template document' that will collect the most relevant information obtained from the WGs activities and publications. This information will then be exploited to design a brochure with the most relevant messages to be conveyed to different target groups, i.e. science community, food industry and general public. In addition, several FG members agreed to continue working on short videos with interviews to academic and

### Focus Group

Leader: Mayte GARCÍA-CONESA

Co-leader: Iwona KIEDA



industrial partners of the Action to introduce successful collaborations between research and industry, further distributed on the POSITIVE web page and social media channels.

Finally, upcoming events for informal presentation of POSITIVE were highlighted (POSITIVE workshop for school children during the European Researchers' Night in Poland, see page 19 for a summary of the activity).

## 3rd POSITIVE Workshop

### Think Thank Group

Leaders: **Rocío GARCÍA-VILLALBA & Pedro MENA**

The 3<sup>rd</sup> Scientific Workshop of the COST Action POSITIVE entitled "Omics breakthroughs in the health effects of plant food bioactives" was carried out in Thessaloniki (Greece) the 20<sup>th</sup> and 21<sup>st</sup> of September, 2017. The workshop was focused on how Omics-based disciplines (including Nutrigenetics, Nutri (Epi)genomics, Metabolomics and Microbiomics) contribute to provide new findings on the health effects of plant food bioactives. The scientific programme was elaborated by members of the Think-Tank Group, the group constituted by Early-Career Investigators of the Action.



The workshop was organized in four sessions: one session about Metabolomics, two sessions on Nutrigenetics, Nutrigenomics and Nutriepigenomics, and one session on Microbiomics. Both renowned and promising young researchers presented the highest quality and most interesting recent findings resulting from the use of these approaches.

Each session consisted of three presentations delivered by recognized scientists from inside and outside the COST Action. The metabolomics session was opened by **Dr. Albert Koulman** (Cambridge University, UK). He presented a lipidomics approach to study the lipid metabolism of infants,

validating key features of the lipid profiles as nutritional biomarkers. **Dra. Mireia Urpi Sarda** (University of Barcelona, Spain) showed the application of metabolomics approaches to study biomarkers of Mediterranean diet adherence and polyphenol-rich food intake (Nutrimetabolomics). **Dra. Marynka Ulaszewska** (Fondazione Edmund Mach, Italy), focused on nutrigenetics studies where the aim was to identify the metabolic products of apple polyphenols using an untargeted metabolomics approach and to evaluate their relation to individual members of the gut microbiota.



In the first Nutrigenetics, Nutrigenomics and Nutriepigenomics session, **Dr. George Patrinos** (University of Patras, Greece) discussed the difficulties to integrate Nutrigenomics into the everyday lives of consumers. He presented a recent study of 38 genes included in commercially available nutrigenomics tests and commented on the need for ethical considerations when approaching nutrigenomics. **Geoffrey Istaq** (King's College London, UK) discussed the results of a study that investigated the impact of chronic blueberry consumption on both gene and miRNA expression in peripheral blood mononuclear cell (PBMC) using integrated nutrigenomic analysis.



### 3rd POSITIVE Workshop (cont.)

During the second session of Nutrigenetics, Nutrigenomics and Nutriepigenomics, **Dr. Clarissa Gerhäuser** (German Cancer Research Center, Heidelberg, Germany) gave a presentation of the PATHWAY-27 project, whose objective is to understand the role and mechanism of action of bioactive-enriched foods on risk factors of the metabolic syndrome combining advanced omics techniques (transcriptomics, metabolomics, epigenomics and microbiomics). **Dr. Dylan Mackay** (University of Manitoba, Canada) discussed an association between the variability in the LDL cholesterol in response to plant sterol consumption and genetic variations. The final presentation in this session, given by **Dr. Ken Decker** (University of Antwerp, Belgium), focused on the integration of transcriptomics, epigenomics and kinomics to characterize the immunomodulatory properties of an *Echinacea* extract in monocyte cells.



The last session of the workshop was focussed on Microbiomics. In this session, **Dr. Kieran Tuohy** (Fondazione Edmund Mach, Italy) discussed several methodological approaches to study how the diet:microbe interactions contribute to the functioning of the gastrointestinal tract and health promoting diets and foods. **Dr. Alan Walker** (University of Aberdeen, UK) presented a recent work identifying diet-responsive microbes as drivers of inter-individual variation in response to consumption of plant food bioactives. The aim is to consider the importance of microbiota composition/activities in personalized nutrition-based strategies. Finally, **Dr. David Berry** (University of Vienna, Austria) discussed how individual variation in the gut microbiota can impact the metabolism of polyphenols using the example of the microbial degradation of rutin.

To conclude the workshop, some of the organizers and participants in the workshop: **Dr. Pedro Mena, Dr. Noemí Tejera, Dr. Albert Koulamn, Dr. Dylan Mackay, and Dr. María Teresa García Conesa** gathered to debate about the current status of the omics disciplines as well as about some of the main features presented during the workshop. Overall, the



omics technologies have provided new and interesting insights into the health effects of dietary compounds and nutrients and have opened new research areas that warrant further investigation with promising POSITIVE results. The omics are here to stay and future research should adapt to the complex designs needed to obtain the best results of these disciplines.



The workshop was finalised with the handing of an honorary prize to the best poster presentation by **Irena Krga** (University of Belgrade, Serbia) and to the best flash-poster presentation by **Dr. Wim Vanden Berghe** (University of Antwerp, Belgium). The Scientific Committee of the Workshop thanked the Organising Committee (**Dr. Christos Kontogiorgis, Dr. Antonia Kaltsatou, and Dr. Eirini Deligiannidou**) and the audience for their help and participation.

Overall, the workshop was great!.



## RESEARCH HIGHLIGHTS

### SOCIAL EVENTS

During the meeting in Thessaloniki it was the privilege of the organizing committee to indulge the participants of the "Omics breakthroughs in the health effects of plant food bioactive" conference as well as all the attending POSITIVE partners into a city tour on foot. We took off from the city's landmark, the White Tower, and reached the historic district of Ladadika, enjoying a brief presentation of the city's long history delivered by the local organisers - Dr. Christos Kontogiorgis, Dr. Antonia Kaltsatou and Eirini Deligiannidou.



A dinner gala was held in the eastern part of the city in a traditional tavern with a vast variety of sea food combined with Greek "ouzo" for the braver of us as well as dancing initiated by professional dancers of a local school, who volunteered for our entertainment. Laughter and joy under the sounds of "sirtaki" lead most of the attendants to dare a spin on the dance floor, proving the open and welcoming spirit of the Action in general.

Living up to our nation's reputation, all the attendants were invited to try on some of the delicious foods that Thessaloniki has to offer. And this was done in more than one occasion throughout the meeting! Towards the end of the second day, after an educating set of presentations and with lots of ideas in our brains, all parties had the opportunity to enjoy a nice relaxing dinner in the heart of the city followed by a nice evening stroll by the seaside.

That was a meeting to remember for sure!



## TRAINING SCHOOL

Attending the training school on "Use of Nutrigenetics & Nutri(epi)genomics in nutrition" has been an outstanding experience. It was my first time attending a Training School of this kind and I had great expectations of the results. All the topics covered in the course were stimulating and all the teachers were very knowledgeable of their subject, and explained step by step everything they presented. They also encouraged us to maintain an open dialog rather than just giving their presentations without interacting.



## Use of Nutrigenetics & Nutri(epi)genomics in nutrition



Regarding the subjects imparted, that about Clinical trials in Nutrigenetics presented by Dylan S. MacKay, PhD of the University of Manitoba, offered me a much clear understanding of the requirements to properly perform a clinical trial on Nutrigenetics. This helped me get started on designing my own proposal. There was a general talk considering all the steps required for such a project, from picking the genetic variant(s) to designing the trial and taking under consideration the aspects that might affect it in terms of reliability. What was even more helpful was the tasks we had to do in groups in which we had to draft and present our own design to the class and discuss its feasibility as well as its strengths and limitations.

There were three main outcomes for which I consider that attending this training school was very beneficial for my research and future work. First, I had the chance to work in groups with the other participants and this forced me to explore my own knowledge and capabilities as well as to learn from all the colleagues attending the school. Second, I was introduced to interesting yet occasionally complex subjects

such as: i) bioinformatic analyses, presented by Ken Declerck of the Department of Biomedical Sciences – University Antwerp and, ii) DNA sequencing, presented by Sarah Bastkowski of the Earlham Institute, in a very amenable way. Last, but not least, I got to keep in touch with both the teachers and the other attendants for future collaborations. Overall, it has been an amazing event that both met my needs and exceeded my expectations.



By Eirini Deligiannidou

The training also included some webinars that can be seen at:

<https://www6.inra.fr/cost-positive/Trainings-Webinars>



SAVE THE DATES



**COST Action POSITIVE**

**7<sup>th</sup> WG Meeting, 6<sup>th</sup> and 7<sup>th</sup> March 2018**

**VENUE: VALAMAR LACROMA DUBROVNIK HOTEL**

**ORGANIZERS: Dr. Nada Knezevic, Director of Regulatory Affairs Department & Dr. Suzana Rimac Brncic, University of Zagreb**

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<https://www.facebook.com/costpositive/>

**Final COST Action POSITIVE  
WG Meeting and Final Conference,  
24<sup>th</sup> - 27<sup>th</sup> September 2018**

**VENUE: OEIRAS (PORTUGAL)**

**ORGANIZERS: Dr. Claudia Do Santos**

**iBET - Instituto de Biologia Experimental e Tecnológica**



## SHORT TERM SCIENTIFIC MISSIONS

**BILJANA POKIMICA from Serbia went to CEBAS-CSIC, Murcia, SPAIN**

Thanks to the COST Action POSITIVE and to Dr Mayte Garcia Conesa, I spent the most useful and pleasant time during the past month of June 2017, being a STSM intern at the CEBAS-CSIC in Murcia (SPAIN). There, I learnt how to prepare and write a Review Article on 'Human gene expression regulated by plant bioactives'.

I had to read and revise a total of 63 articles all looking at the influence of the supplementation with a range of bioactive compounds and products (foods, extracts, mixtures) from diverse plant origin on the expression of a number of genes in different human tissues. All the articles were based on RT-PCR analysis. Once I read the articles, my main assignment was to carefully extract detailed information about different sections of the research (study design, quality of the gene expression studies, results, etc) into template Excel and Word tables. Dr Mayte García-Conesa helped me through the whole procedure, double-checked the work I had done, and explained to me what was the best way to do it and what was the most important details that we need to obtain for the purpose of the Review. Thanks to her I have learnt a lot regarding quality of studies and articles, gene expression regulation and review preparation. Therefore, the knowledge I have attained during this STSM is very useful for my PhD thesis, that I am currently writing, as well as for my future work in general.



Murcia is a fabulous University town where I met a lot of nice students from different countries, and I made lifetime friendship with two students from Turkey and Russia. I enjoyed being in Murcia also because of its wonderful landscapes. I walked near beautiful trees, cactuses, flowers and lemon trees every day on my way from University dorms to CEBAS-CSIC, both located at the University Espinardo Campus.

## STSM Topic: Gene expression regulation in human trials following intervention with bioactive compounds: a literature survey

Dr Mayte García-Conesa was both my supervisor and a sincere friend. Every working day we had lunch and coffee together, she showed me around the city and introduced me to her friends and colleagues, who were all very nice to me.



During the weekends, I visited amazing sandy beaches near Murcia, located in Cabo de Palos, Torrevieja, Alicante and La Manga, where I enjoyed swimming.

Also, I had a great time sightseeing Cartagena from the boat.

This STSM made me richer in both scientific knowledge and friendships, and enabled me to spend one month in the beautiful country of Spain.



## SHORT TERM SCIENTIFIC MISSIONS

Gut microbiota plays a key role in the metabolism of many plant bioactives, such as certain polyphenols. Gut microbiome is not uniform among individuals, which suggests that different individuals or groups of individuals might respond differently to the intake of plant polyphenols. An STSM was initiated in December 2016 by COST POSITIVE to address this question. In the framework of the STSM entitled studying the relationship between microbiome genetic variation and polyphenol metabolic conversions, Ditta Kolimár a postgraduate researcher of the Szent István University, Faculty of Food Science (Budapest, Hungary) spent three months at the group of Dr David Berry, at the University of Vienna, Division of Microbial Ecology between Jan-March 2017. The actual goal of this research was to increase the level of understanding of the effect of interindividual variation of human gut microbiome on the metabolism of rutin (quercetin-3-O-rutinoside), one of the most abundant flavonol conjugates present in widely consumed plant foods. *In vitro* modelling of gut microbial fermentation of rutin was carried out utilising the microbial consortium of human faecal samples of 10 healthy volunteers. The microbial response to acute rutin treatment was followed

**DITTA KOLIMÁR** from Hungary went to the university of Vienna (AUSTRIA)

with a specific fluorescent staining technique called BONCAT, which enables the selective detection and quantification of metabolically active members of the highly complex microbial community at the single-cell level. After completing some basic training and gaining hands-on experience in the experimental work, Ditta carried out the planned incubations and fluorescent imaging under the supervision of Dr Alessandra Riva, a post-doc of the Vienna group. Due to the focussed work plan, this short-term stay provided valuable experimental results and the hypothesised inter-individual variability in microbial activity could be experimentally confirmed.

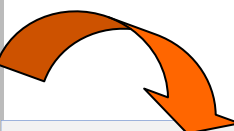
In addition to the gained actual scientific output, this STSM moved one step further. It has contributed to the fundamental aim of the COST action, namely to initiate or foster further collaborations between COST members. In particular, after closing the STSM stay, results from the STSM were completed with metabolomic profiling at the host institute of the applicant in Budapest under the supervision of Dr László Abrankó. Combined results of this collaborative research were

**STSM Topic: Studying the relationship between microbiome genetic variation and polyphenol metabolic conversions**



recently presented as an oral talk at the XIX EurFoodChem conference, held between the 4 and 6 of October (2017) in Budapest.

This is still not the end of this successful story. Results of the STSM were used as a proof of concept in a proposal to the call of a bilateral Austrian-Hungarian science foundation. The idea got granted and, at present, this collaborative research on interindividual variability of gut microbial polyphenol metabolism keeps going on between Dr Abrankó and Dr Berry. Finally, it should be proudly noted that this successful collaboration was initiated by an STSM grant of COST POSITIVE. And no doubt, the initial momentum gained during the STSM was absolutely essential for this evolution process, and enabled to go beyond the original scope.





## SHORT TERM SCIENTIFIC MISSIONS

### Kateřina Valentov from CZECH REPUBLIC went to ITQB-UNL/IBET, Oeiras, PORTUGAL

The past July 2017, I had the opportunity to spend one week at the Disease & Stress Biology Laboratory, ITQB-UNL/IBET in Oeiras, which is located in the Lisbon Metropolitan Area, Portugal. My visit was one of the STSM funded by the COST Action POSITIVE and gave me the opportunity of working with Dr. Cludia Nunes dos Santos. The aim of this STMS was to finalize our review on the Inter-individual variability of quercetin ADME in humans. We had been working on the review together with other POSITIVE WG1 members: A. Filipa Almeida, Grethe Iren Borge, Marius Piskula, Adriana Tudose, Liliana Tudoreanu, and Gary Williamson. This work commenced during the first POSITIVE meeting in Belgrade in March 2015. By the time we had the meeting in Olsztyn (February 2017), all the relevant data had been extracted and a number of tables grouping the results were prepared. We had also written by then, the Introduction and Experimental section of the manuscript. We realized that the working hours during the WG meetings were not sufficient and that between meetings, people were busy attending other pieces of work. It was decided that in order to finalize the manuscript as soon as possible, we needed to focus on it and work in close collaboration between, at least, the main authors.



los beach, located at a walking distance from my hotel. I'm looking forward to visiting the place again during the last POSITIVE meeting September 2018!

### STSM Topic: Inter-individual variability of quercetin ADME in humans

Indeed, during the STSM, I worked very hard together with Claudia and A. Filipa Almeida and had regular consultations with Dr Gary Williamson by Skype. The concentrated effort on the manuscript allowed us to finalize all the sections of the manuscript: tables and results, discussion, conclusion and the full list of references. The complete draft was then circulated among the remaining authors for final remarks and the paper was submitted to the *Comprehensive Reviews in Food Science and Food Safety* in September 2017.

Overall, my stay was a really nice experience, the host team was great and I am especially grateful to Cludia for the wonderful welcome dinner in family on the amazing Carcave-



## CONTACT US



EUROPEAN COOPERATION IN THE FIELD OF  
SCIENTIFIC AND TECHNICAL RESEARCH

### Contact us:

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: [christne.morand@clermont.inra.fr](mailto:christne.morand@clermont.inra.fr)

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: [fatomas@cebas.csic.es](mailto:fatomas@cebas.csic.es)

### Webpage:

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)

## SCIENTIFIC EXPERT'S OPINION



Dr. David BERRY  
Associate Professor,  
University of Vienna, AUSTRIA

phyla including *Actinobacteria*, *Verrucomicrobia*, and *Proteobacteria*), capacity of the microbiota to degrade and transform dietary compounds, increased abundance of vitamin biosynthesis pathways, and higher numbers of butyrate-producing bacteria (Yatsunenکو *et al.*, 2012). Generally, the composition of the gut microbiota is known to be shaped by diet, health state, host genetics, and environmental/lifestyle factors (Clemente *et al.*, 2012). From studies of the gut microbiota in healthy individuals it has become clear that adults have a relatively stable microbiota, the composition of which is person-specific, which raises the question: what are the implications of the inter-individual variation in gut microbiota?

A well-studied example for inter-individual variability in plant bioactives is the polyphenol equol, which is an agonist of

## Individuality in the gut microbiota: State of Knowledge and Future Directions

Each of us is home to a diverse and complex community of microorganisms – including *Bacteria*, *Archaea*, and *Fungi* – collectively termed the human microbiome. The intestinal tract is an especially rich microbial environment, with hundreds of species totaling an estimated  $10^{14}$  cells that together form a highly dense and diverse ecosystem. The intestinal microbiome has drawn widespread attention as it has become clear that it plays important roles in human health, affecting nutrition, immunity, metabolism, and susceptibility to enteropathogenic infection (Subramanian *et al.*, 2015). Technological progress in the field of next-generation sequencing technology has advanced our understanding of both the genetic diversity of the microbiome as well as the physiological and pathological processes that are influenced by the commensal microbiota. A clearer picture is now emerging of the composition of the human microbiota in healthy individuals and the diverse factors affecting its variability (Yatsunenکو *et al.*, 2012).

The gut is initially colonized at birth - though there are reports that even the fetus is not sterile - by taxa such as *Bifidobacterium*, *Lactobacillus*, *Staphylococcus*, and *Enterobacteriaceae*, and pioneer colonizers are derived in part from the mother's vaginal microbiota, skin and fecal microbiota of parents and siblings, breast milk, and other infants. In the first three years of life, the gut microbiota develops into a "mature microbiota" with increased species richness, predominance of the bacterial phyla *Bacteroidetes* and *Firmicutes* (with lesser

the estrogen receptor  $\beta$  and exerts manifold effects, including anti-inflammatory and anti-cancer activities (Duda-Chodak *et al.*, 2015). Equol is formed in the intestine by the bacterially-mediated transformation of the soy isoflavone daidzein. Only a small number of bacteria have been identified to be able to form equol from daidzein, such as *Eggerthella* spp., *Slackia* spp. and *Adlercreutzia equolifaciens*. The variability in abundances in equol-producing bacteria is thought to be an important factor explaining that the prevalence of equol producers is approximately 30–50% of the population. While equol has been the subject of much study, little is known about the metabolism of many other plant bioactives and interactions between plant bioactives and the gut microbiota. One of the aims of the COST Action POSITIVE is to identify for which plant bioactives the microbiome is an underlying factor of variability for ADME processes. In order to gain deeper insights into the molecular mechanisms of this variability, it is essential to move forward and identify critical metabolic steps and microbial enzymes for the transport and metabolism of these compounds. With this information in hand, it will be possible to screen large metagenomic datasets generated by major microbiome sequencing projects such as the Human Microbiome Project and the MetaHIT project to evaluate the variability in the abundances of these key genes across the human population.

## SCIENTIFIC EXPERT'S OPINION

How can we use microbiome information to inform therapeutic practice or dietary recommendations? There are interesting examples from nutrition research suggesting that microbiome composition can be a useful diagnostic marker. Cotillard et al. (2013) conducted diet-induced weight-loss and weight-stabilization interventions in obese and overweight individuals. They found that individuals with reduced microbial gene richness had increased metabolic dysfunction and low-grade inflammation. Interestingly, though the dietary intervention was able to improve low gene richness and clinical phenotypes, it was less efficient for inflammation parameters in individuals with lower gene richness. Therefore, low gene richness may be a useful diagnostic parameter to stratify individuals and predict the efficacy of an intervention. Another recent example was a crossover trial of the effect of industrial white or artisanal sourdough bread consumption on glycemic response based on an oral glucose tolerance test (Korem et al., 2017). They found that there was high inter-individual variability in the cohort and that neither bread type elicited a better glycemic response. However, looking into the microbiome of the participants, they were able to predict whether an individual would have a better glycemic response to industrial white bread or artisanal sourdough bread based on distinctive signatures in the microbiome. As the glycemic response to bread type was person-specific and microbiome-associated, this study suggests that it may be possible to use microbiome information for personalized nutrition.

The other possibility in the future is to “improve” microbiomes by adding bacteria that perform desired metabolisms, which have been termed functional probiotics (Bolca et al., 2013). Probiotics have had a variable track record, in some cases producing positive short-term clinical responses, yet rarely leading to the stable establishment of a beneficial bacterium in the intestinal ecosystem (Walker & Lawley, 2013). However, by using gut-derived probiotic bacterium and screening of microbiomes to identify missing microbial components, it was possible to engraft an exogenous *Bifidobacterium* species in the human gut (Maldonado-Gómez et al., 2016). The time may be coming when microbiome monitoring and modification is a routine part of personalized nutrition and medicine. While it will likely be a long road before this is standard practice, identifying the microbial factors driving inter-individual variation in plant bioactives ADME processes is an important challenge that we must address in order to be able to consider diagnostic and therapeutic applications.

### References

- Bolca S, Van de Wiele T, Possemiers S. (2013). Gut metabolotypes govern health effects of dietary polyphenols. *Curr Opin Biotechnol* **24**:220–225.
- Clemente JC, Ursell LK, Parfrey LW, Knight R. (2012). The impact of the gut microbiota on human health: an integrative view. *Cell* **148**:1258–1270.
- Cotillard A, Kennedy SP, Kong LC, Prifti E, Pons N, Le Chatelier E, Almeida M, Quinquis B, Levenez F, Galleron N, Gougis S, Rizkalla S, Batto J-M, Renault P, consortium AM, Dore J, Zucker J-D, Clément K, Ehrlich SD, members AMC. (2013). Dietary intervention impact on gut microbial gene richness. *Nature* **500**:585–588.
- Duda-Chodak A, Tarko T, Satora P, Sroka P. (2015). Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: a review. *Eur J Nutr*. doi:10.1007/s00394-015-0852-y.
- Korem T, Zeevi D, Zmora N, Weissbrod O, Bar N, Lotan-Pompan M, Avnit-Sagi T, Kosower N, Malka G, Rein M, Suez J, Goldberg BZ, Weinberger A, Levy AA, Elinav E, Segal E. (2017). Bread Affects Clinical Parameters and Induces Gut Microbiome-Associated Personal Glycemic Responses. *Cell Metabolism* **25**:1243–1253.e5.
- Maldonado-Gómez MX, Martínez I, Bottacini F, O'Callaghan A, Ventura M, van Sinderen D, Hillmann B, Vangay P, Knights D, Hutkins RW, Walter J. (2016). Stable Engraftment of *Bifidobacterium longum* AH1206 in the Human Gut Depends on Individualized Features of the Resident Microbiome. *Cell Host Microbe* **20**:515–526.
- Subramanian S, Blanton LV, Frese SA, Charbonneau M, Mills DA, Gordon JI. (2015). Cultivating Healthy Growth and Nutrition through the Gut Microbiota. *Cell* **161**:36–48.
- Walker AW, Lawley TD. (2013). Therapeutic modulation of intestinal dysbiosis. *Pharmacol Res* **69**:75–86.
- Yatsunenkov T, Rey FE, Manary MJ, Trehan I, Dominguez-Bello MG, Contreras M, Magris M, Hidalgo G, Baldassano RN, Anokhin AP, Heath AC, Warner B, Reeder J, Kuczynski J, Caporaso JG, Lozupone CA, Lauber C, Clemente JC, Knights D, Knight R, Gordon JI. (2012). Human gut microbiome viewed across age and geography. *Nature* **486**:222–227.

**Dr. David Berry, member of POSITIVE Working Group 1 received  
CITY OF VIENNA PROMOTION AWARD!**

The City of Vienna Awards are awarded annually to individuals who have made major achievements in areas ranging from architecture, literature and art to humanities and natural sciences. David Berry received the City of Vienna Promotion Award 2017 (Förderungspreis der Stadt Wien) in the category Natural Sciences.



## RESEARCH DISSEMINATION



'Microbial metabolism of polyphenols, inter-individual response' by Dr. F. Tomás-Barberán; 'Polyphenols on modulation of gut microbiota in vitro' by Dr. T. van de Wiele; 'The frailty phenotype and polyphenol exposure towards healthy aging' by Dr. C. Andrés La Cueva; 'Polyphenols modulation of miRNA' by Dr. D. Milenkovic. In addition, several other oral shorter presentations by POSITIVE members were included in the different sections of the conference such as: 'Gut metabolism of quinic acid' by Dr. S. Mocco; 'Bioavailability of cranberry polyphenols' by Dr. A. Rodríguez-Mateos; 'Bacterial enzymes as a tool to prepare polyphenol metabolites' by Dr. K. Valentová; 'Phytohub online platform' by Dr. C. Manach; 'Interindividual variability in the nutrigenomic response to

### Significant and extensive participation of the members of the COST Action POSITIVE at the 8<sup>th</sup> edition of the 'International Conference of Polyphenols and Health' in Quebec (Canada)

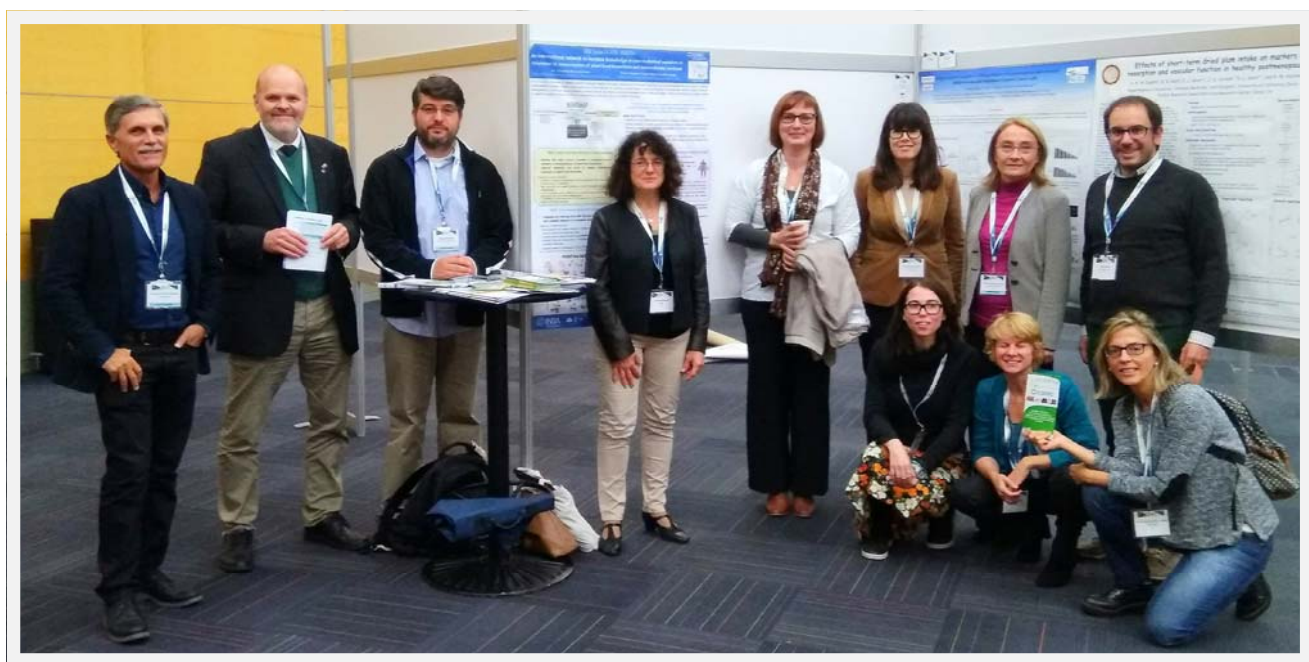
The 8<sup>th</sup> edition of the 'International Conference of Polyphenols and Health' was successfully held at Quebec (Canada) the past 3<sup>rd</sup> to 6<sup>th</sup> of October, 2017. With the participation of more than 500 researchers from all over the world, the conference gathered a number of oral presentations given by members of the COST Action POSITIVE (FA1403) covering several research areas of polyphenols and health i.e., bioavailability and metabolism, role of bacteria, health effects of polyphenols (cardiovascular effects, aging, epigenetic and nutrigenomic effects), new databases available, and all of these under the common frame of the 'Inter-individual variability in response to the consumption of these bioactive compounds'.

Some of the keynotes and plenary lectures introduced by POSITIVE members were: 'Epigenetic control of cardiovascular health by polyphenols' by Dr. W. van der Berghe;

curcumin' by Dr.C. Morand or 'Contrasting in vitro vs. in vivo molecular effects of the ellagitannins metabolites urolithins' by Dr. M.T. García-Conesa. All these talks covered the main objectives and research carried out within the WG1 and WG2 of the Action.

To strengthen the presence of POSITIVE in the conference, a poster with the main objectives and tasks developed by the Action was put up, and the tryptic and newsletters about POSITIVE were distributed during the poster sessions.

The principal objective and message of POSITIVE has been definitively widely spread to the scientific community in the field during the conference.



**RESEARCH DISSEMINATION**
**PUBLICATIONS– WG1**


Elucidating the colonic microbial metabolism of phenolic acids: an essential step towards the understanding of interindividual variability in the response to dietary polyphenols

JOURNAL OF  
**AGRICULTURAL AND  
 FOOD CHEMISTRY**

Article

[pubs.acs.org/JAFC](https://pubs.acs.org/JAFC)

## Effect of Bioprocessing on the *In Vitro* Colonic Microbial Metabolism of Phenolic Acids from Rye Bran Fortified Breads

Ville M. Koistinen,<sup>†,‡</sup> Emilia Nordlund,<sup>‡</sup> Kati Katina,<sup>‡,§</sup> Ismo Mattila,<sup>‡,||</sup> Kaisa Poutanen,<sup>‡</sup> Kati Hanhineva,<sup>†</sup> and Anna-Marja Aura<sup>\*,‡</sup>

COST-Positive partners from UEF and VTT Ltd (Finland) have published this collaborative article combining techniques of cereal bioprocessing, an *in vitro* colon model and state-of-the-art metabolite analyses using targeted and non-targeted mass spectrometry.

The current article compared phenolic acid metabolism of native and bioprocessed rye bran fortified wheat breads and elucidated the microbial metabolic route of ferulic acid from food matrix. The breads were first subjected to a simulated upper intestinal *in vitro* digestion and the digested samples were inoculated with faecal microbiota in an *in vitro* colon model. In this study, the faecal inoculum was pooled from several donors to eliminate the possible variability, as we focused on the metabolic routes themselves.

The time course of the metabolite formation was followed using mass spectrometry (GCxGC-TOFMS and UPLC-QTOF). While original cereal phenolic acids were released more extensively from the bioprocessed bran bread and ferulic acid had consistently higher concentrations in the bread type during fermentation, there were only minor differences in the appearance of microbial metabolites. The only difference was that the resilient native rye bran bread showed better the intermediary metabolites of ferulic acid, other hydroxycinnamic acids among them. Therefore, the authors conclude that the microbial metabolites formed by the faecal

microbiota are common for all hydroxycinnamic acids, namely hydroxylated phenylpropionic acids, phenylacetic acids and benzoic acids, which can be connected to many flavonoids and polymeric flavanols. When metabolites are scattered to different small phenolic and organic acids, their detection may be challenging. Moreover, when the source is a complex dietary fibre matrix, such as whole grain cereals, the release and conversion is slow and may not be distinguished from other sources.

The best sample for human intervention for detection of microbial metabolites is 24-hour urine, which gives a history of metabolites circulating in the body during the past 24 hours. The metabolites have a long residence time in the body fluids, and they are gradually excreted to urine. Therefore, the health benefits of microbial metabolites may come *via* synergistic effects from several sources and the correct approach would be a comparison of whole diets instead of individual foods. It is not well known how interindividual differences in the ecology of colonic microbes or metabolite-related genes affect the metabolism of phenolic acids and more research is thus warranted on the metabolizing capabilities of individual microbial strains or individual communities.

## RESEARCH DISSEMINATION




















## PUBLICATIONS– WG2

Access to all dissemination products:  
<https://www6.inra.fr/cost-positive/Dissemination>

*Nutrients* 2017, 9(7), 746; doi:10.3390/nu9070746

Open Access Review

## A Systematic Review and Meta-Analysis of the Effects of Flavanol-Containing Tea, Cocoa and Apple Products on Body Composition and Blood Lipids: Exploring the Factors Responsible for Variability in Their Efficacy

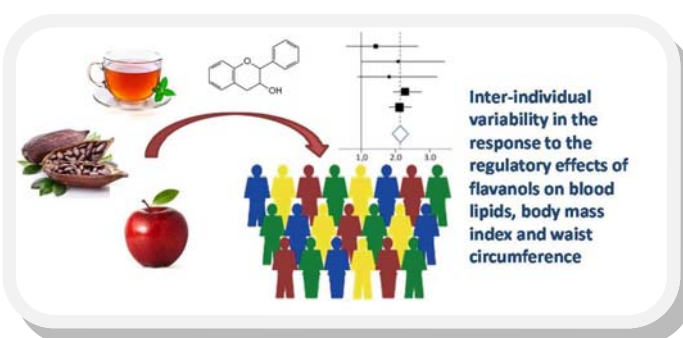
Antonio González-Sarrias<sup>1,\*</sup>  , Emilie Combet<sup>2</sup>  , Paula Pinto<sup>3</sup> , Pedro Mena<sup>4</sup>  , Margherita Dall'Asta<sup>4</sup> , Mar Garcia-Aloy<sup>5,6</sup>  , Ana Rodríguez-Mateos<sup>7</sup> , Eileen R. Gibney<sup>8</sup>  , Julie Dumont<sup>9</sup> , Marika Massaro<sup>10</sup> , Julio Sánchez-Meca<sup>11</sup> , Christine Morand<sup>12</sup>  and María-Teresa García-Conesa<sup>1,\*</sup>  

**Flavanols against cardiometabolic risk factors: accumulated evidence of their efficacy supports their beneficial effects and the relevance of population stratification**

This is the second published article of a series of meta-analyses that the members of POSITIVE are conducting as part of the activities planned within the WG2 of the Action. With the collaboration of partners from different research institutions from Spain, UK, Portugal, Italy, & France, we have collected and critically revised a total of 120 randomized controlled clinical trials (RCTs) in the search for the current evidence of the efficacy of flavanol-containing tea, cocoa and apples, on body mass index (BMI), waist circumference (WC) and blood levels of cholesterol and triglycerides (TAGs). In addition, various factors considered to have an influence on the response to the consumption of these type of compounds have been explored.

A number of important issues have come out of this analysis. First of all, the heterogeneity of the trials is very high and thus, a considerable number of the studies need to be pooled in order to achieve significant results. Indeed, when all the studies were pooled together the overall evidence of the reduction of BMI, WC, total and LDL-cholesterol, and TAGs and of the increase in HDL-cholesterol was very significant. These effects were quantitatively comparable to those produced by some drugs, life-style changes or other natural products.

On the other hand, grouping the studies taking into account factors such as the baseline-BMI, sex, or health status of the participants, or the source and form of administration of the compounds, or the country where the study was conducted gave us some preliminary indication of the potential influence of these factors on some of the outcomes. The results suggested that the flavanols may be more effective in specific subpopulations such as in overweight/obese people or when administered as part of tea drinks or tea extracts. Nevertheless and given the still high heterogeneity of the studies and the reduced number of them per subgroup the



significance of these results is very limited.

It is important to remark that, so far, the description of the participants in the different human studies has not always been very thorough and thus, important features such as the ethnicity, sex, age, menopausal stage, smoking or disease condition have not been properly described. Often, the intervention has been conducted in mixed populations making difficult the extraction of data useful for the study of the factors affecting interindividual variability in the response to these compounds. Further, other important factors such as life-style habits (sport practising, alcohol intake, etc) have not been usually considered.

In the future, these and other critical factors such as intestinal microbiota composition or genetic make-up will have to be incorporated into the human intervention studies. Also, full characterization of the products used in the intervention is required so that proper doses and metabolism of the flavanols (or other bioactive compounds) can be estimated. Improved design of future studies taking into account all these will definitively enhance our understanding of interindividual variability in response to bioactive compounds and of their efficacy against cardiovascular and metabolic diseases.

## RESEARCH DISSEMINATION

## PUBLICATIONS– WG3

**The NATCONSERV Project: persuading the food industry to use berry extracts as a natural source of bioactive antioxidants for the meat industry: A successful story of the POSITIVE Romanian partners in collaboration with the Romanian Food Industry stakeholders.**

Following public concern about the use of synthetic food antioxidants, there is an increasing demand for the application of mixed or purified natural alternatives to maintain the quality of meat and meat products during storage. Moreover the texture, flavour and mouthfeel arising from the intake of foods are critical to consumer choice and acceptability.

The rules to design food structure for existing meat products have been well established although not necessarily completely and scientifically described and understood. Currently, there is a strong drive to produce healthy consumer acceptable meat products, pushing products into a formulation space whereby some of the well-known rules no longer apply. On the other hand, the costs of developing formulation production replacing the so called traditional additives are of concern to many producers.

Members of the POSITIVE's Romanian group (Prof. Camellia Papuc and Prof. Liliana Tudoreanu) in collaboration with other colleagues from the Faculty of Veterinary Medicine of Bucharest (Dr. Corina Nicoleta

Predescu, Dr.Valentin Nicorescu and Dr. Iuliana Gâjaila) conducted a research project to find the most suitable natural bioactives as antioxidants in the formulation of several minced meat products. The project NATCONSERV- Natural food preservatives for functional safe and healthy foods ended in August of 2017. The Romanian food company involved was Group ANGST Romania ([www.angst.ro](http://www.angst.ro)) which is a Romanian-Swiss company specialized in meat products. The project was funded by the Executive Agency for Higher Education, Research, Development and Innovation Funding (<https://www.uefiscdi.ro/>) and by the Group ANGST (Romania).

The main objective of the project was to develop new meat products reducing the use of synthetic food antioxidants and applying instead, natural bioactive compounds from hawthorn berries and fermented juices. The results so far have been excellent and the natural extracts rich in bioactive compounds tested were more effective antioxidants than the synthetic counterpart butylated hydroxyanisole (BHA) in minced meat products (see article below).

As a result of this project, two patents have been submitted to the Romanian office for patents OSIM (<http://www.osim.ro/>) for natural antioxidants to be used by the meat industry and two new products developed (frankfurters). One of the main outcomes is that the good quality of the products obtained with the natural antioxidants persuaded Group Angst Romania to start designing a new formulation of products based on natural antioxidants.

Journal of the  
Science of  
Food and Agriculture

Research Article

Received: 26 October 2016    Revised: 24 June 2017    Accepted article published: 7 August 2017    Published online in Wiley Online Library:  
(wileyonlinelibrary.com) DOI 10.1002/jsfa.8599

**Comparative study of the influence of hawthorn (*Crataegus monogyna*) berry ethanolic extract and butylated hydroxyanisole (BHA) on lipid peroxidation, myoglobin oxidation, consistency and firmness of minced pork during refrigeration**

Camellia Papuc,<sup>†</sup> Corina Nicoleta Predescu,<sup>†</sup> Liliana Tudoreanu,<sup>\*,‡</sup> Valentin Nicorescu and Iuliana Gâjailă



## RESEARCH DISSEMINATION

### INTRODUCING POSITIVE TO THE GENERAL AUDIENCE

On September 29, 2017, POSITIVE Partner, Institute of Animal Reproduction and Food Research PAS organized in Olsztyn (Poland) one of the largest science celebration events in Europe – Researchers' Night. Through a vast array of experiments, science shows and workshops researchers advocated a crucial role of science in our everyday life, dispelling negative stereotypes around research work, and building mutual trust with the society at large. Everyone could find first-hand answers to the questions concerning health, nutrition, technology or engineering. Institute invited Night's guests to visit usually inaccessible laboratories offering experiments with antioxidants, workshops on microbiology and methods of assessing the prohealth value of everyday food products.

Institute's researchers prepared a presentation introducing school children, their teachers and parents to the mission of COST POSITIVE, pro-health values of plant food bioactives and the phenomenon of inter-individual variability. During workshops "Build your health", young students learnt what is the new food pyramid, how it is built, what are the factors affecting its composition (age, sex, lifestyle), and how did it change over the last decades. Kids and youngsters built a proper, up-to-date pyramid using magnets representing different food products, paying a special attention to those containing plant-based bioactive compounds. Then, participants were challenged to differentiate products as to their beneficial and potentially harmful effects on a human body. Here they were familiarized with the aspects of interindividual variability and other determinants affecting the response of our organism to biologically active compounds. During the entire event, children acquired a new knowledge concerning informed nutritional choices and importance of physical activity.

### EUROPEAN RESEARCHER'S NIGHT IN POLAND





## GET TO KNOW YOUR POSITIVE PARTNER

facility at the Czech University of Life Sciences.

### EARLY STAGE RESEARCHERS

#### What is the focus of your research?

My research is focused on the bioactivity of natural products. It is quite broad, driven by the interest to get an insight into the related areas. In my early career I investigated the antimicrobial activities of essential oils chemistry and their effect on food pathogens. Later, I focused on phenolics and other classes of natural compounds, studying their inhibitory properties against enzymes, as well as the cytotoxic and antimicrobial activity they exhibit. In the meantime, together with my research group, we have discovered honey bees as an interesting model to study antimicrobial interactions between food and natural product supplements and mi-



### JAROSLAV HAVLIK

Czech University of Life Sciences,

Czech Republic

crobiota. Invertebrates as a model can overcome many obstacles associated with ethics and health safety measures. To better understand our model, we had to get a better understanding of the insect-associated microorganisms. Two years ago I joined the team of Christine Edwards and Emilie Combet at the University of Glasgow as a postdoc working on a BBSRC project. We studied the mutual interactions of human microbiota, food-derived polyphenols and dietary fibres. After finishing my postdoc, I returned to the Czech Republic and now continue studying human catabolism of polyphenols, especially stilbenoids, and some aspects of foodomics.

#### In what countries/organisations have you studied or worked in?

After obtaining my degree in life sciences at the Czech University of Life Sciences, I started working at the same university as a postdoc, then as a lecturer, and finally as a senior lecturer in agricultural chemistry and nutrition. Having returned from Scotland, I now work as a researcher and senior lecturer in a metabolomics

#### What has been the greatest achievement in your career?

Fundamental research does not always lead to something that can be practically useful. However, when it happens, you feel great satisfaction. We are now trying to commercialise the plant-based antimicrobial substituents for honey bees and some other things, running a spin-off company. It is very different from the lab work we have been used to.

#### Which is your favourite paper you have written/co-authored and why?

With Christine Edwards, Emilie Combet and other scientists from Glasgow University, we are now finishing a manuscript on the influence of dietary fibre on the large intestinal catabolism of polyphenols, also focusing on the interindividual differences. Different kinds of dietary fibre are certainly interacting with bacterial groups, facilitating their growth and changing their metabolic activities. The profile, latency and quantities of metabolites change in the presence of certain fermentable fibres. Usually, polyphenol metabolism is studied apart from the food matrix, therefore our novel approach will provide very interesting data to be available in the paper that will be published early next year.

#### Who is/was your most influential mentor/colleague and why?

In my early career, it was my PhD. supervisor, Prof. Ladislav Kokoska. He has a wonderful ability to motivate his students to not give up hope, especially when our first experimental do not confirm the hypothesis. In my recent career it was Prof. Christine Edwards, who I value for her leadership skills.

#### Where is your favourite place in the world and why?

Somewhere in the South-East Asia. I have travelled to Indonesia, Thailand, Cambodia, Malaysia, but spent the longest time in central Vietnam with the Czech Aid project, and later shortly at the Food Technology Department in Saigon. Only in Vietnam you can sit at the table, eat a snake and discuss whether a dog tastes better than a cat. Despite cultural differences many people have a western-like way of thinking. In Indonesia, Java, Bali and Lombok, the hospitality of local people is like nowhere else in the world. As a student-backpacker, I was invited to the families to stay overnight, and these were very memorable moments of my journey.

#### What is your favourite music/book?

I enjoy Electronic rock, Teddybears, Chemical Brothers, Pendulum, electroswing or experimental music like Einsturzende Neubauten. My favourite writer is Haruki Murakami. His *Hard-Boiled Wonderland and the End of the World* or *Kafka on the Shore* magic realism novels really captivate imagination.

#### What is your favourite sport(s)?

I enjoy running marathons. In Istanbul, when thousands of runners run over the Bosphorus Bridge connecting Asia and Europe, you can feel the bridge shaking. In Vienna or Prague, it is really touching when you hear waltz or The Moldau melodies when crossing the finishing line. Besides, I enjoy swimming, cycling and hiking. Scotland was a perfect place for this.

## GET TO KNOW YOUR POSITIVE

### EARLY STAGE RESEARCHERS

#### What is the focus of your research?

The focus of my research is development, validation and application of analytical methods for the quantification of food bioactive compounds. Besides, we investigate the bioavailability, biological activity and metabolism of phytochemicals by means of cellular models, animal and human studies for the prevention and treatment of diseases.

#### In what countries/organisations have you studied or worked in?

I graduated from Istanbul University Department of Biology. Then I got my MSc and PhD degrees at the Istanbul Technical University, Department of Food Engineering. During my PhD I got a scholarship from the government and joined the research group of Prof. Gerald Rimbach at the Christian Albrechts University (Kiel, Germany), Institute of Human Nutrition and Food Science, to perform the practical part of my thesis, and stayed there for 3.5 years. During my PhD I had chance to work at the University of Hohenheim (Stuttgart, Germany), Department of Biofunctionality and Safety of Food, for 2 months. After I completed my PhD thesis, I started to work again with Prof. Rimbach as a postdoc for 14 months. When I came back to Turkey, I got a position at the TUBITAK Food Institute. As a senior researcher, under an EU Project, I visited the Institute of Food Research (Norwich, UK) for 6 months.

#### What has been the greatest achievement in your career?

The greatest achievement in my career is to get the scholarship from the government and go to Germany for the PhD studies. This was a great experience for me and it allowed me to improve myself personally and scientifically.

#### Which is your favourite paper you have written/co-authored and why?

My paper demonstrating the results of my *in vivo* study entitled "A diet rich in olive oil phenolics reduces oxidative stress in the heart of SAMP8 mice by induction of Nrf2-dependent gene expression" (*Rejuvenation Research*, 2012, 15: 71-81) is my favourite. It was the first paper to use my scientific skills in and it has the highest citation number among all my papers. Besides, the paper entitled "A validated method for the determination of selected phenolics in olive oil using high-performance liquid chromatography with coulometric electrochemical detection and a fused-core column" (*Food Chemistry*, 2014, 138: 1663-1669) is also important to me, because I published it after I faced many technical problems.

#### Who is/was your most influential mentor/colleague and why?

The most influential mentors in my life are Prof. Gerald Rimbach and Prof. Jan Frank. Prof. Rimbach, who was the supervisor of my thesis and I worked in his lab for 4.5 years. He is a very experienced scientist with a profound knowledge. He always encouraged me and taught many scientific skills that I needed to progress in my research career such as accurate scientific writing.



**BANU BAYRAM**

University of Health Sciences,  
Turkey

Prof. Frank was a post-doc in Kiel while I was doing my PhD, now he is a professor at the University of Hohenheim. He is a very good friend of mine, a great personality and a very successful excellent scientist. I learned all about analytical techniques from him. Both mentors strongly supported me during my PhD and I learned almost everything what I know in the scientific world from them.

#### Where is your favourite place in the world and why?

The magnificent city of Istanbul is my favourite place in the world. It is an exciting, living city where I was born and still live in. Istanbul is one of the most important historical and cultural centres in the world and I am in love with the view of Bosphorus.

#### What is your favourite music/ book

I like listening to R&B, Latin and Greek music. Ricky Martin, Shakira, Rihanna, Pitbull, Enrique Iglesias, and Keti Garbi are my favourite singers. I like reading books of Carlos Ruiz Zafon, and Dan Brown.

#### What is your favourite sport(s)?

Unfortunately, I am not actively involved in any sport, but I go to matches of basketball, volleyball, football and tennis very often. Besides, I go to the gym a few times in a week.

## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS

#### What is the focus of your research?

I have been working in the field of biology and biotechnology of animal reproduction for about 20 years. Since 2006 EU and many other countries banned antibiotics as feed additives and synthetic hormones as growth promoters in animal husbandry, based on their negative consequences for animal health and food safety. These restrictions accelerated the process of searching possible substitutes. Herbs and herbal extracts, by-products of fruits and vegetables processing proved as a valuable alternative, being useful as growth promoters and therapeutic agents. We started to analyse the effect of new phyto-genic feed additives on the reproductive system of animals (plant extract from *Tribulus terrestris*, micro algae *Spirulina platensis*). Ovulation rate and oocyte quality are important determinants of reproductive efficiency in females. The processes of follicular growth are closely regulated by endocrine and paracrine factors, including the gonadotrophins, metabolic factors and several local growth factors. Nutritional manipulations, especially supplementation of plant bioactive substances, can affect fertility. **Focus of my research is on understanding how they do that or how they can regulate the follicular growth leading to ovulation.** There are many questions to be clarified, e.g. whether bioactives (and which ones) can affect hormonal level or local growth factors (GDF9, BMP15), or whether they can affect the epigenetic reprogramming of developing oocytes? Inter-individual variation in response to bioactives from the reproductive system is also a very interesting topic, and we have started to pay more attention to this fact in our research.

#### In what countries/organisations have you studied or worked?

I finished my PhD at the Research Institute of Children and Adolescence Physiology in Moscow, Russia. Although my main scientific work is related to the area of reproduction, my PhD thesis was related to the cardiovascular system. I investigated the micro vascularization of rat's mesentery during the sexual maturation period. Having taken part in COST Action MITO-FOOD, I was able to participate in the STSMs programme and perform research activities in the Institute of Physiology of the Czech Academy of Science in Prague. Under the leadership of Prof. Josef Houstek, we analysed the activity of mitochondrial enzymes in the ovaries of mouse treated with *Spirulina platensis* and organic selenium-selenopyran. My another valuable scientific visit took place in China, in the State Key Laboratory of Reproductive Biology, Chinese Academy of Science, headed by professor Qing-Yuan Sun, where I investigated mitochondria in oocytes with the methods of confocal microscopy. In Italy, Milano, in the lab of professor F.Gandolfi, I had the opportunity to perform studies related to the *in vitro* fertilisation. All in all, these scientific missions allowed me to get



### ELENA KISTANOVA

Bulgarian Academy of Sciences,  
Bulgaria

familiarized with different cultures, various approaches to research work, and to be part of a useful transfer of knowledge.

#### What has been the greatest achievement in your career?

There are many achievements in my career I consider important. They are all related to different parts of my work. I was the scientific expert in a significant FP7 – ReProForce project (<http://reproforce.ibir.bas.bg/en>), worked as a deputy director of our Institute (till 2014), and initiated a broad international collaboration while working in the COST Actions, bi- and multilateral projects.

However, my most important achievement is the education of future generations of scientists– the people, who I have transferred my knowledge and passion for science to. I am proud that my daughter caught “the bug for science” (she is a PhD student now) and that my two my PhD students (Desislava Abadjieva and Vanya Mladenova- members of POSITIVE) are now holding research positions in our Institute. I believe that they will continue our investigations and keep developing their scientific careers. They give me a hope that my scientific legacy will be continued.

## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS

#### Which is your favourite paper you have written/co-authored and why?

It is Abadjieva D., Kistanova E. (2016) *Tribulus terrestris Alters the Expression of Growth Differentiation Factor 9 and Bone Morphogenetic Protein 15 in Rabbit Ovaries of Mothers and F1 Female Offspring*. *PLoS ONE 11(2): e0150400. doi:10.1371/journal.pone.0150400*. There are two reasons for choosing this paper as my favourite: a) we published interesting results proving the transgenerational effect of the aphrodisiac plant on the reproductive performance; b) the article was accepted and published in a recognized peer-review journal. It is no secret how difficult it is to publish articles from eastern European countries in peer-review journals with the IF. That is why we consider having our article published a great success.

#### Who is/was your most influential mentor/and why?

It was my PhD mentor Prof. V.I Kozlov, DSc. Now he is the head of the Anatomy Department at the Medical Faculty of Peoples' Friendship University of Russia. He was a pioneer in the area of investigating blood microcirculation by bio(vital) microcopy. Our group included 6 PhD students who investigated the micro vascularization in different organs. He taught us to be creative, to work together, and to be ready to help each other. The basic knowledge and skills obtained during my PhD studies have helped me throughout my whole scientific life and allowed me to adapt to different scientific environments. The friendship between all of us is maintained until now.

#### What is your advice for young scientists?

Maybe these are more than enough, but I believe everyone can choose the right ones for themselves:

- Respect ethical code in career development and remember that you are a human first.
- Do not put success in a competition or in a career above friendship.
- Be creative and dispel stereotypes.
- Don't use the already known pathways – try to find your own.
- Don't feel discouraged if something goes wrong - you are

young and have the time to keep trying.

- Be open to mobility;
- Respect your colleagues and get inspired by their experience.

Only through working together and having a common contribution to science challenges we can achieve significant results and discoveries.

#### Where is your favorite place in the world and why?

I've travelled a lot, but not everywhere. It may be I've not reached this place yet. However, my heart belongs to two magnificent places: the white birch grove of Russia and the mountains of Bulgaria.

#### What is your favorite music/book?

It may sound old fashioned but I prefer classical music. Its harmony is the best relaxing tool in our competitive life. Also classical and modern ballet has not stopped to amaze me all my life. I am happy that I had the occasion to see the best performances in the most famous theatres – as in Bolshoi in Moscow, in Covent Garden in London, in Albert Hall in London, in Mariinsky in Saint-Petersburg. Among chansons, my favourite song is "Dance me to the end of love" of a Canadian singer-songwriter Leonard Cohen. I was pretty surprised to find out that I share the same favourite book with the colleague from Serbia – "The Alchemist" of P.Coelho. Sofia theatre "199" produced an amazing performance based on this novel. It is unbelievable how Coelho described in a few simple words the depth of feelings, people's relationships, and the necessity to follow a Personal Legend (something like our purpose in life). I read all of his subsequent books, but none of them moved me so deep like "The Alchemist."

#### What is your favorite sport(s)?

I'm not really a sport kind of a person. I am convinced that the physical and motor activity should serve to strengthen health and not be subject to competition. For me, walking in the forest and mountains is the best way to stay fit. I grew up on the plain. When I moved to Bulgaria and saw the mountains, I fell in love with them. They have this magic that attracts you more and more, they change during the day, during the seasons, however, always remain beautiful and share their positive energy!

## OF INTEREST TO POSITIVE COMMUNITY

### BIOAVAILABILITY 2018

*"Understanding the bioavailability of micronutrients and bioactive compounds for improved public health"*

**DATE: 12-13 September, 2018**

**PLACE: John Innes Conference Centre, Norwich, UK**





POSITIVE

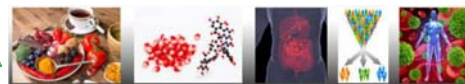
ISSUE 8



# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE VII, JUNE 2018

## WELCOME

Dear All,

Even though the fourth year of our COST Action POSITIVE is getting to an end and the final meeting is just around the corner, we are neither thinking about the finish line nor slowing down the pace. We celebrated a very successful 7th Working Group meeting the past March in Dubrovnik, and are now getting ready for the Final POSITIVE Conference in September in Lisbon. The Action is in a high gear, with the partners strongly engaged in networking, research dissemination activities and effective implementation of short-term scientific missions, either hosting early stage researchers in their labs or undertaking the training themselves. The word “final” will probably be tossed around the coming months, however we should keep in mind that it is not the end. It is, indeed, the commence of new collaborations and projects that will allow us to continue working together and getting to know each other.

This time, more than ever, we wish to thank all contributors who devoted their time and efforts to make this issue as well as all the previous newsletters happen.

Hope to meet you all in Lisbon for a final meeting (and party!)

THE FG

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## NEWS FROM THE ACTION

### 7<sup>th</sup> COST Action POSITIVE Meeting, 2018 6<sup>th</sup> – 7<sup>th</sup> March Dubrovnik, CROATIA

The POSITIVE partners continue working hard towards the achievement of their respective objectives and met once more in March 2018, this time, in the beautiful surroundings of the city of Dubrovnik (Croatia). The meeting was held at the Valamar Lacroma Dubrovnik Hotel and it was kindly organized by **Dr. Nada Knezevic**, Director of the Regulatory Affairs Department and by **Dr. Suzana Rimac Brncic** from the University of Zagreb.

We take this opportunity to **thank them for the organization** of the meeting and for the great time spent in Dubrovnik!



## RESEARCH HIGHLIGHTS

### Work Group 1

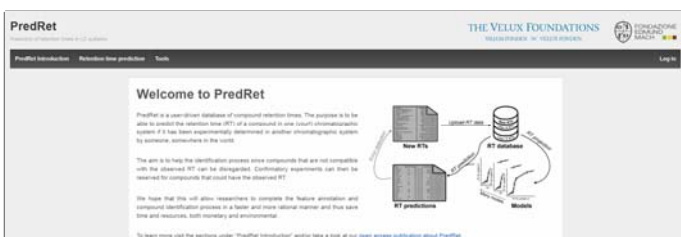
Leader: Tom VAN DE WIELE

Co-leaders: Claudine MANACH & Rikard LANDBERG

The members of the WG1 gathered in Dubrovnik to continue working and discussing about the different tasks they still need to complete. They first talked about the **Data-base** that is under construction and will collect as many **Plant Bioactive Metabolites** as possible reported in urine and plasma samples, together with their known health benefits and analytical needs.

There were also further discussions in the area dedicated to **Metabolomics**. A few important issues still need to be done for the completion of the manuscript regarding the multiplatform coverage test such as the normalization of the retention times (RT) of the compounds analysed in the different platforms, and the preparation of some general guidelines for a reference method applied to untargeted analysis. A few journals are under consideration for this publication, after which, a few other activities will follow: validation of this method, preparation of combined spectra and comparison of sample preparation and extraction protocols provided by different partners.

Another interesting issue commented during the meeting was the utility of applying RT predictive tools such as the database **PredRet** (<http://predret.org/>) for the analysis of metabolites derived from plant food bioactive compounds. INRA will be testing this database with known compounds.



Progress on the work of the **Microbiome and Gene Variants** was also further discussed. Efforts are still directed towards the identification of key molecules (genes & proteins), both of human and microbial origin, and pathways involved in the metabolism and absorption of the plant bioactive compounds as well as for the related and relevance genomic information: polymorphisms, presence in different microbial groups, etc. Enhancing knowledge in this area remains essential for the understanding of the bioavailability of plant bioactive compounds and the variability in humans to metabolize and absorb these compounds. The need to reinforce the workflow in this area by improving means of sharing knowledge between subgroups was highlighted.

Last, but not least, a number of **Knowledge gaps and Research needs** for the specific types of plant bioactive compounds were revised and discussed. There are still many unclear aspects that need further and thorough investigation. Finding the key factors, i.e. most relevant microbial and human enzymatic activities, major metabolites derived from this activity, main transporters across the intestinal barrier, will allow for a better understanding of the interindividual variability in the bioavailability of the plant bioactive compounds and their link to variability in the cardiometabolic responses. A more integrated approach is needed bearing in mind the general idea that different compounds and metabolites from different diets may have the same benefits!



## RESEARCH HIGHLIGHTS

### Work Group 2

Leader: Ana RODRIGUEZ-MATEOS

Co-leaders: Eileen GIBNEY &  
Dragan MILENKOVIC

#### Meta-analysis subgroup

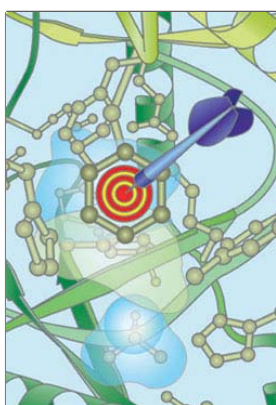
The activities programmed within this subgroup have progressed well and a number of meta-analyses have been now completed and published whereas a few others should be finished within this last period of the COST Action, covering like this the cardiometabolic effects of a variety of plant bioactive compounds and a thorough examination of the factors that may influence the responses and were identified and available in the published RCTs collected. In addition to a combined revision of all these publications to have a general overview of the current situation and the issues that still need to be further investigated, the collaboration with the WG1 to explore the feasibility of adding together bioavailability studies and cardiometabolic effects was considered and taken on board by some partners of both groups. Awareness of the importance of other key factors not yet incorporated into the analysis of the cardiometabolic effects such as microbiome and the host genetic variants were remarked. Potential reviews of publications related to these areas were proposed and will be discussed with the WG1 members.



In terms of future proposals, a working sub-group was organised with the aim of preparing some grant applications for future studies incorporating many of the recommendations and best practices that will emerge at the end of the Action from all the outcomes of the WG1 and WG2.



#### Cell & Molecular Targets subgroup



The meeting of the cell and molecular target subgroup was led by Dr. Tatjana Ruskovska who presented an overview of the progress done on the revision of pre-clinical evidences. The strategy employed was a combination of literature search, bioinformatics tools and docking studies to identify genes, transcription factors and pathways that may be implicated in the response to the bioactive compounds in relation with cardiometabolic endpoints.

The work done in animal models was well advanced for some groups of compounds (flavanols) with several genes and pathways identified. Further studies with those data were proposed such as finding out relevant information about those genes in humans and exploring the interindividual variability. After this study is completed, other bioactive compounds should follow. Regarding the revision of *in vitro* studies, the work on flavanols and phytosterols is still in progress, with data extraction completed and the bioinformatics analysis just started. The main aims are the same as in animal studies, i.e. finding key regulated genes and pathways in human cells exposed to these compounds.

Work on human clinical trials looking at gene expression regulation by plant bioactive compounds is now further reinforced with the organization of a new subgroup led by Dr. Vauzour. A considerable number of nutrigenomic studies using microarrays was collected and are ready for data extraction.



In the final gathering of WG2 a few other tasks were proposed such as the collaboration with the Gene Variant group to progress on the understanding of gene variants with an effect on cardiometabolic responses to plant bioactives. Other various discussion as to how to complete data analyses and presentation of the meta-analyses took also place during the meetings.



## RESEARCH HIGHLIGHTS

### Work Group 3

Leader: Baujke DE ROOS

Co-leader: Marina HEINONEN



The WG3 meeting was moderated in place by Professor Tomás Barberan and was focused mostly on the development of a **Roadmap** with all the Action outputs and specifically directed to stakeholders and Brussels. It was

proposed the preparation of several white papers that will include the main results of the work done in the Action and that will contribute to increase awareness of the complexity of the human interindividual variability in response to the intake of bioactive compounds. These articles will translate the main results of the Action into practical applications and what are the things that remain to be done in future research plans with a focus on 1) stakeholders, 2) policymakers and 3) scientist working in the field. Regarding the scientific community, the work will be published in the form of reviews in a relevant journal.



During the Working Group meetings in Dubrovnik the upcoming activities of the Focus Group have been revised. It was decided that members of the FG will be actively involved in the elaboration of the POSITIVE Research Roadmap and will contribute to the production of the dissemination material dedicated to stakeholders. In addition to the regular actions connected with reporting on ongoing progress of the Action, research papers published and scientific missions completed, the Focus Group will commit to further dissemination of POSITIVE outputs during events dedicated to general public and industrial stakeholders. Additionally, potential ways of leveraging the ECI-oriented networking base developed by the Think Thank group (Getting to know initiative) were discussed.

### Focus Group

Leader: Mayte GARCÍA-CONESA

Co-leader: Iwona KIEDA



## RESEARCH HIGHLIGHTS

## Think Thank Group

Leaders: Rocío GARCÍA-VILLALBA &amp; Pedro MENA



The 5<sup>th</sup> Think Tank Group (TTG) meeting in Dubrovnik was scheduled as an ordinary meeting of the Early Career Investigators (ECIs). The meeting was open to the whole ECI community since online participation was available. This helped to increase the numbers of attendees, being a good way to continue building the network of young scientist in plant bioactives and inter-individual variability. The meeting gathered 11 participants: Rocío García Villalba, Geoffrey Istas, Banu Bayram, Viktorija Maksimova, Eirini Deligiannidou, Paul Young Tie Yang, Dorrain Low, Mar García-Aloy, Teresa Serra, Maria Rosa Tumulo, and Pedro Mena. Three of them were introduced as new members, which showed the interest of the ECIs to be involved in the Action activities, even if it is finishing. The meeting started with a short introduction to the new ECI members about the goals reached in the last three years and the progresses that some ECI members have achieved in: 1) the TTG project 'How to report interindividual

variability in scientific publications', and 2) writing a perspective article as a result of the Workshop in Thessaloniki (September 2017). Three important issues were discussed throughout the meeting:

**New steps for a perspective paper related to the 3rd Sci. WS.** This project had been somehow inactive during the last 5 months. The strategy to finish the paper was discussed and now there is a final manuscript ready to be reviewed by all the authors and sent to the POSITIVE leaders for comments and approval.

**New steps within the 'How to Report Interindividual Variability in Publications' project.** This project needs to be finished quite soon since it could be part of a Special Issue with the main conclusions of the Action. Moreover, the project will be presented by Dr. Aleksandra Konic-Ristic at the last Sci. Workshop (to be held in Lisbon, September 25-26, 2018). In order to finish this project, a Short Term Short Mission will be carried out by Marina Nikolić, from the Center of Research Excellence in Nutrition and Metabolism, Institute for Medical Research, University of Belgrade (Serbia), in the research group of Dr. Pedro Mena and Prof. Daniele Del Rio at the University of Parma (Italy) during June 2018. Dr. Konic-Ristic will also take active part in this collaboration.

**Ideas for the coming online meetings and the "Get to Know" sessions.** All the attendees agreed on the need for new activities favouring the participation of all the ECIs in the monthly online meetings. After discussion, it was decided that the new ECIs will introduce themselves and that a new, quick round of presentations will be carried out. The new round will be focused on presenting the current situation of each ECI and the possibilities to collaborate in the future. Following these ideas, a successful meeting was carried out in April. Up to 12 ECIs attended the online conference. We had 3 very nice presentations and subsequent discussions with Margherita Dall'Asta, Viktorija Maksimova, and Paul Young. A new meeting has been scheduled for June.



## RESEARCH HIGHLIGHTS

### SOCIAL EVENTS

Thanks to the great hospitality of the local organizers, POSITIVE partners were offered the opportunity to experience the wonderful culture, heritage and cuisine of Dubrovnik. During a guided tour we had a chance to trace the mighty city walls, explore the shooting scenes from Game of Thrones, and admire incredible sea views. After a day-long discussions the partners were also invited to a **traditional Croatian dinner**, where they could taste local specialties and carry on networking in a pleasant and relaxing atmosphere.



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<https://www.facebook.com/costpositive/>



## SAVE THE DATES

### Lisbon welcomes you to the ...

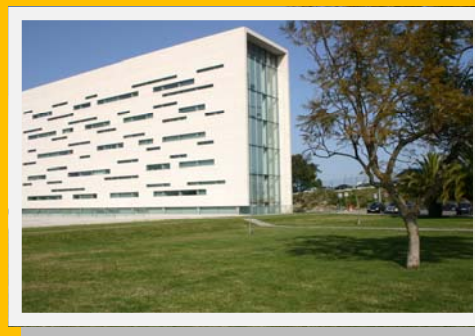
**COST Action POSITIVE  
JOINT WG & MC Meetings**



**VENUE:**

Vip Executive Art's Hotel  
Avenida D. Joao II, n°47  
1998-028 Lisboa

**Final POSITIVE Conference  
25-26<sup>th</sup> September 2018**



**VENUE:**

NOVA University rectory building  
Campus de Campolide, Lisboa

### LOCAL ORGANIZERS:

Dr. Claudia Nunes-dos Santos ([csantos@ibet.pt](mailto:csantos@ibet.pt)) (iBET, Oeiras, Portugal)  
Dr. Maria Bronze (FFU Lisboa, Portugal)  
Dr. Paula Pinto (IPS-ESA, Santarem, Portugal)

## JOIN US ON TWITTER



**#Cost\_POSITIVE**

**@Cost\_POSITIVE**

**[www.twitter.com](http://www.twitter.com)**

## SAVE THE DATES

And Lisbon also welcomes you to the...

2<sup>ND</sup> CONFERENCE ON

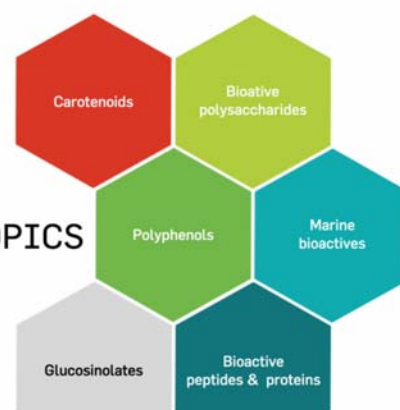
# FOOD BIOACTIVES & HEALTH



26-28 SEPTEMBER 2018 LISBON PT



### MAIN TOPICS



**T**he conference will gather experts on different types of food bioactive compounds and will cover a wide range of aspects of the research in this area: metabolism, effects & mechanisms, functionalisation, characterisation, bio-transformation, interactions, novel compounds.

If you need further information please contact:

**FBHC 2018 Organizing Committee**  
**2<sup>nd</sup> International Conference on Food Bioactives and Health 2018**

E-mai: [fbhc2018@itqb.unl.pt](mailto:fbhc2018@itqb.unl.pt) or visit the website at: <http://www.itqb.unl.pt/fbhc2018>

## SHORT TERM SCIENTIFIC MISSIONS

### EIRINI Deligiannidou from Greece went to the UEA, Norwich, UK

Winter in the UK can be rather bad, however, in this Action we share the belief that there is enough sun for everyone, so I packed a bit of the Greek sunshine and started my journey to the beautiful city of Norwich. From January the 8<sup>th</sup> till March the 15<sup>th</sup> I was privileged to work in two well respected institutions: The Norwich Medical School of the University of East Anglia and The Earlham Institute in Norwich, UK, under the joined supervising of Prof. Anne Marie Minihane (MED) and Dr. Wiktor Jurkowski (EI) on the subject of "Data integration to study flavonoid metabolism".



Madrid to Mumbai.

Both my supervisors have been with me every step of this mission, providing guidance and support and encouraging me to do more and aim higher, which I find priceless. Never have I missed a smile from them, which made Norwich feel like home even more and professional business aside, we had great fun!



On a non-scientific point of view, I have experienced living abroad which was life changing, visited the beautiful Leeds Castle in Canterbury and also picked up the habit of drinking my tea with milk! Regarding the city, long walks, is something

## STSM Topic: Data integration to study flavonoid metabolism



During this mission I was located at The Bob Champion Research and Education Building, working closely with both my supervisors on finding the best possible way to put the knowledge of published papers on flavonoid

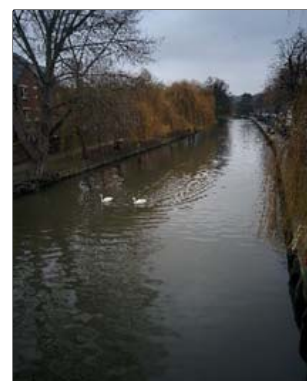
metabolism, into an illustration that would be publicly available to the research community to further investigate, amend and improve. My task was to extract information from older and new literature, regarding the metabolic fate of flavan-3-ols and use illustrating tools such as PathWhiz and PathVisio to visualize the pathway. Using existing knowledge from the POSITIVE members as well as databases such as PhytoHub and PubChem, I have gathered information on the metabolites involved in this pathway which led to its illustration via PathVisio and publication on WikiPathways.

Through this mission I have gained knowledge on the use of metabolic pathway illustrating tools, the importance of keeping track of your work via (sometimes endless) spreadsheets and also created a picture that was actually a thousand words (or rather reactions!). Furthermore, I have learned how an open office works, participated in the monthly meetings of the department of Medicine learning even more about ongoing research projects and have met amazing people from

to do in Norwich, which is a lovely small city with warm people to make up for the cold weather and also England's first UNESCO City of Literature!

The University of East Anglia is a huge institute with a beautiful campus that I can only describe as a "condensed version of the world". Surely this mission had widened my horizons personally and professionally and for this I am thankful to this Action and especially to the STSM coordinator Dr. Aleksandra Konic Ristic, who helped to every step of my application and to my mentor Dr. Christos Kontogiorgis who introduced me to POSITIVE.

Lesson learned: **"Amazing things happen, if you just stay POSITIVE!"**



## SHORT TERM SCIENTIFIC MISSIONS

Our STSM took place at King's College of London under the supervision of Dr. Ana Rodríguez Mateos. Casually, our STSM coincided at the same time of the year and we were able to work together enriching more the STSM experience. Our mission was focused in the analysis of phenolic compounds in plasma and urine of high cardiovascular risk patients after beer and non-alcoholic beer ingestion (Víctor's job) and measurement of anthocyanin-derived metabolites after consumption of capsules enriched with anthocyanins (Michele's task). For these purposes we used a solid phase extraction (SPE) protocol and the samples were analysed using an Orbitrap mass spectrometer. These new approaches are needed to enhance the knowledge of how the ingestion of food with high amount of polyphenols could affect and modulate health.

## Víctor Micó Moreno & Michele Tassotti visited King's College London, UK



### STSM Topics:

**Michele Tassotti: Measurement of anthocyanin-derived metabolites in plasma using LC-MS.**

**Víctor Micó Moreno: Measurement of beer's polyphenol levels in urine of an interventional study with beer in high cardiovascular risk patients.**

For us, the realization of this STSM was a great opportunity to know other laboratories and other ways of working different from our respective laboratories.

We would like to thank Dr. Ana Rodríguez Mateos' group the great welcome to both of us and all the help and support provided to carry out the STSM. In addition to this, the possibility to know other researchers will have a great impact in our career and it could open future opportunities and collaborations among our groups.

But, The STSM means more things. It was a great personal experience. To us, this STSM was also the chance to meet with the lab group after work, visit beautiful places in London, take a lovely lunch by the Thames riverside enjoying the sun (yes! Sun exists in London!) and meet new people. To conclude, we want to thank the POSITIVE COST Action the opportunity given to us by these STSM and we would like to highly recommend them to other researchers due to the **great experience both professionally and personally.**



**Michele Tassotti**

**Víctor Micó Moreno**

## SHORT TERM SCIENTIFIC MISSIONS

### Ralph Rühl from Hungary visited University of Vigo, Spain

As the plan was to stay for two months, I had the fantastic idea to drive my car across the whole of Europe. Well, it's just 3200 km and 31 h of driving without a break. Sounds easy, so let's go ! Vamos a la playa ! Car was checked and all packed. A short stop at my family's in Germany and the Atlantic coast in France went all smoothly, till we drove passed the sign '50 km to Vigo' at the highway. At this exact point my car



started making very strange noises. Lucky enough Vigo was reached and we got to our apartment by the harbor. Just when the car made extremely loud not-normal noises. It's better not to mention which car brand.

The next day we initiated intercultural relationships with some local car-repair guys, Diego and Carmen, manager and sister, respectively. And quickly we learned that there are small differences between the German way of organization and the Spanish one. Especially measures of time were handled slightly in a different way. Diego and Carmen tried to teach us Spanish, starting with the most famous Spanish word 'mañana'. Diego and Carmen learned also, like all young Spanish people, the language of their autonomous region at school. In this case the 'autonomous region of Galicia', so, Galego. We even learned this language: "mañá". English, German, French or Hungarian were not so well distributed in Galicia as I experienced, but thank God at the University we could communicate well. After 2-weeks, the car was finally repaired, immediately

Research went very well and all in time, till we had a gigantic wood fire coming from Portugal and entering Vigo. The whole University surrounding was under fire and the University closed down for a couple of days. The apartment in the top floors of the building was filled completely with black smoke. This night was spent at the harbor, near the water, while the air was like cigar smoke till the next morning.



With a small delay, our project was finalized like planned. We found for our novel identified lipid hormone, new unique nutritional precursors present in food as well as in the human organism. Usually nutritional precursors of hormones were named Vitamins and **together with our Vigo cooperators, we patented and will publish ours and named it: Vitamin A5.**

**PATENTED**

### STSM Topic: Identification of the new lipid hormone 9-cis-13,14-dihydro-retinoic acid (9CDHRA) after supplementation of nutritional

broken again at the same place and so on. Thank God, we had a guy named "Jesus" as our colleague in our labs and he thought us devotion and patience.

In the lab, we started quickly our projects and all went like expected, more complicated and slowly like planned. But, nevertheless, the nice food in Galicia (and in general in Spain), and especially some of the Spanish wines (Rioja) diluted all troubles quickly. As Vigo is the second biggest fishery harbor in the world, after Tokio, all what the sea contained was eaten, like crabs and 'calamares' and mostly the local specialty 'percebes'. They look like aliens, but it is an animal which is attached to the ground and filters plankton out of the sea water. The only thing which we didn't eat, were our new friends in the bay: the five dolphin families.



The way back from lovely Vigo by car went very well and the 45 bottle of excellent Spanish/Portuguese wine arrived also in well shape back to Hungary. Thanks to the COST "POSITIVE" and to Vigo and all it's people, except two. Hasta la vista, hasta luego, Vigo, I'll be back ! **Ralph Rühl**



## SHORT TERM SCIENTIFIC MISSIONS

My STSM took place between the 5<sup>th</sup> of December 2017 and the 15<sup>th</sup> of December 2017. I was hosted by Dr. Cláudia Santos at the Molecular Nutrition and Health research from ITQB, Universidade Nova de Lisboa, Portugal. The aim of my mission, as part of the WG2, was to update an ongoing meta-analysis exploring inter-individual variability after consumption of flavanols from cocoa, apple and tea on the cardiovascular system. During this short stay, under the supervision of Dr. Paula Pinto, I learned how to perform a meta-analysis using the Comprehensive Meta-Analysis software to assess the overall effect of flavanol consumption. In addition, I familiarized with subgroup analyses by studying how flavanol consumption is affected by individual variables such BMI or gender. With Paula's great help, I managed to extract and patch the required papers in an intensive short period of time.

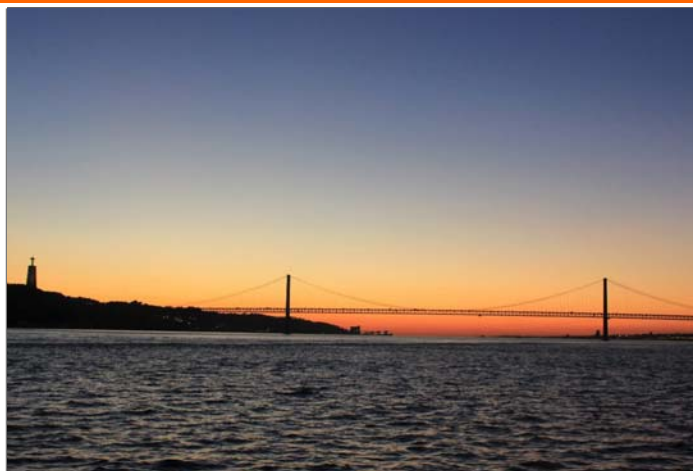
## Paul Young Tie Yang from UK visited ITQB Nova, Portugal



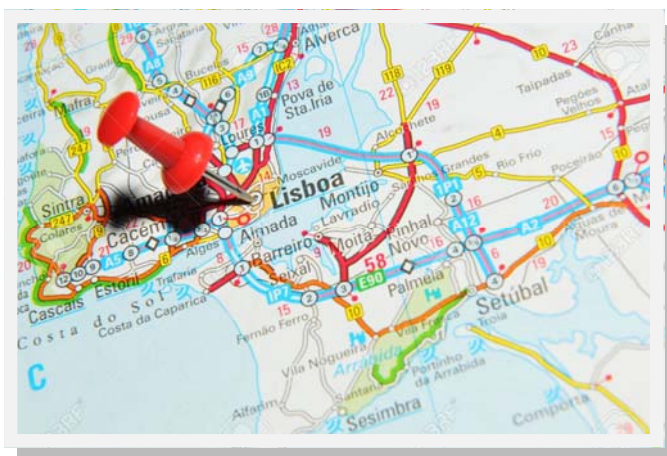
## STSM Topic: Inter-individual variability on the effects flavanols on the cardiovascular system: systematic review and meta-analysis

Aside of learning about meta-analysis, this STSM has been an opportunity for me to meet young researchers, attend a PhD Viva and meet other members of the COST action. From the touristic point of view, Lisboa has a lot to offer, wonderful historic places, sunny terraces, great food and a very positive atmosphere. All this contributed to make my STSM a great experience.

Once again, I would like to thank everyone from Cláudia's lab for such a great and warm welcome from the very first day and I am definitely looking forward to meet the group again for the final COST POSITIVE meeting in Lisboa.



Paul Young



## SCIENTIFIC EXPERT'S OPINION

**Dr. ANNE-MARIE MINIHAHE**  
 Nutrition and Preventive Medicine,  
 Norwich Medical School, UEA, Norwich, UK



**T**he health benefits of plants foods and plant bioactives are widely recognised, which is the basis for typical recommendations to consume at least two servings of fruits and three servings of vegetables per day. Low intake of fruit and vegetables is among the top 10 risk factors for mortality worldwide. In the global *PURE* cohort, up to a 40% reduction in the risk of chronic diseases was evident in high versus low consumers of fruit, vegetables and legumes [1]. Although popula-

tion effects-sizes have been widely reported, our understanding of how an individual will respond to increased intakes is

[NCT01922869?term=COB&cntry=GB&rank=1](https://doi.org/10.1093/ajcn/88.5.1171) ).

Prospective cohort and genome wide analysis studies, where power allows, should investigate response to treatment in population subgroups (e.g. males vs. females, old vs. young). A greater use of individual participant data meta-analyses will allow data from smaller investigations to contribute collectively to a more comprehensive understanding. Models may be built from the acquired knowledge, which will be improved as new data and knowledge are generated.

Given the large effect of plant bioactives on health, and the fact that <25% of global populations meet current recommendations, **the identification of key determinants of metabolism and bio-efficacy is a worthy journey**. Such knowledge will inform refinement of current dietary guidelines (dose and plant foods), and the targeting of products and recommendations towards consumers who are likely to be most responsive and gain most health benefits. Developments in pharmacogenetics, and increasingly bespoke approaches to prescribing, should provide us with encouragement.

1. Miller, V, et al., *Lancet*, 2017. 390:2037-2049;
2. Cassidy, A and Minihane, AM. *Am J Clin Nutr*, 2017, 105:10-22.
3. Manach, C, et al., *Mol Nutr Food Res*, 2017, 61:1600557-1600573.



## UNRAVELLING THE SOURCES OF INTER-INDIVIDUAL VARIABILITY IN RESPONSE TO PLANT BIOACTIVES: A long way to go, but worth the 'journey'

almost entirely lacking.

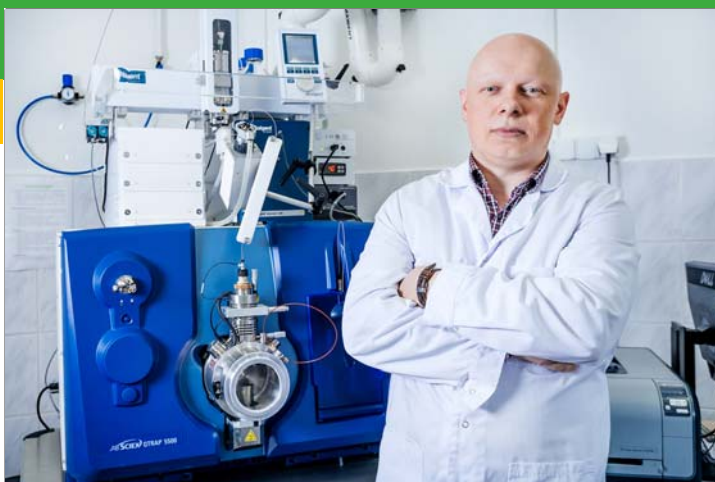
The aetiology of the large heterogeneity in response is likely to be an inter-play between (epi) genetic profile, physiological status (e.g. sex, microbiome speciation and metabolism, and menopausal status) and behavioural attributes (e.g. prescribed medications, and habitual diet) [2, 3]. Such variables affect bioactive bioavailability, metabolism and bio-efficacy. Many argue that gaining an understanding of determinants of response is a mammoth task, with the picture likely to be too complex, and the impact of individual variables too small to allow a meaningful predictive framework to be derived. This is a pessimistic view. *'Rome was not built in a day'*. We need to be patient. Although a comprehensive understanding is lacking, and research is somewhat fragmented, investigating the impact of one factor at a time, a growing number of studies are beginning to describe potential sources of variability. Unravelling factor\*plant bioactive effects on health is best approached using prospective recruitment methodologies on the basis of the variable(s) of interest in adequately powered studies, such as the approach taken in the ongoing COB trial (<https://clinicaltrials.gov/ct2/show/>



## RESEARCH DISSEMINATION

## PUBLICATIONS- WG1

The research on a natural colorants is an important part of current science regarding food technology and nutrition. In this context, betalains - water-soluble natural pigments - are an interesting and important group of phytochemicals which chemical structure is based on the skeleton of betalamic acid linked with a cyclo-3,4-dihydroxyphenylalanine residue in case of betacyanins or with different amino acid in case of betaxanthins. Betalains are pigments responsible for **red-purple (betacyanins)** and yellow-orange color (betaxanthins) present only in plants belonging to Caryophyllales and in some species of higher fungi.



Food Research International 108 (2018) 530-538



Contents lists available at ScienceDirect

Food Research International

journal homepage: [www.elsevier.com/locate/foodres](http://www.elsevier.com/locate/foodres)

## The impact of the matrix of red beet products and interindividual variability on betacyanins bioavailability in humans

 Wieslaw Wiczowski<sup>a,\*</sup>, Ewa Romaszko<sup>b</sup>, Dorota Szawara-Nowak<sup>a</sup>, Mariusz K. Piskula<sup>a</sup>
<sup>a</sup> Institute of Animal Reproduction and Food Research, Polish Academy of Sciences in Olsztyn, Tuwima 10 Str., 10-748 Olsztyn, Poland

<sup>b</sup> NZOZ Atarax, 1 Maja 3 Str., 10-117 Olsztyn, Poland

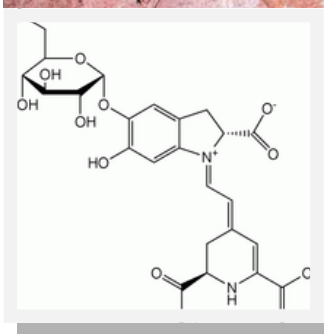

Due to their relative stability and their very interesting color, betalains are widely used in the food industry for the coloring of a wide range of food products. The human body is very often exposed to these natural compounds. In addition, there are evidences that betalains display strong biological activities. In spite of the above facts, the fate of betalains in the human organism has not been well recognized yet. To exhibit positive effects of betalains in the human organism, these compounds have to first enter the human systemic circulation. Since consumption of food rich in these pigments does not have to imply at the same time its good bioavailability, adequate estimation of betalains bioavailability from different foods is a prerequisite for further consideration of their involvement in the physiological processes. In addition, in the course of bioavailability studies, apart from the analysis of which compounds were absorbed and metabolized, it is also necessary to track the impact of the food matrix on bioavailability as well as the effect of interindividual variability. With regards to the food matrix influence, the bioavailability of phytochemicals from liquid matrix will be different from that from the solid matrix. Equally, it will be different from a raw matrix than from the macerated/softened matrix.

In relation with the interindividual variability influence, bioactive compounds considered bioavailable for one individual may not behave in the same way for another. A significant role in these processes may be imputed to factors addressed as genetics, sex, age and disease states. Genetic variation of enzymes involved in the absorption and metabolism of phytochemicals may result in a complete absence or enhanced expression of a functional enzyme. Up- and down-regulation of gene expression in response to an altered cellular environment may achieve the same range of metabolic function, but often in a less reliable, predictable and time-dependent manner. Hence, these important issues are under consideration of the POSITIVE Action.

Overall, there was no data on the differences in betalains bioavailability for various food matrices and comprehensive studies in relation to interindividual differences as far as the absorption and biotransformation of betalains. In Poland, and also in Europe and worldwide, betalains are known mainly as the pigments of a red beetroot - a vegetable which is very often eaten in a cooked form as a salad, fresh juice, soup or as a fermented product.

## RESEARCH DISSEMINATION

### PUBLICATIONS– WG1



Red beetroot is a very rich source of betalains, and because betalains are potent antioxidants resulting from the structure of their molecules, therefore, among other, red

beet is placed among the ten vegetables characterized by the strongest antioxidant properties.

The analysis of the red beet products matrix and interindividual variability impact on **betacyanins bioavailability** in humans presented in the recent article of Wiczowski et al. (Food Research International, 2018, 108, 530-538) showed that betacyanins bioavailability from juice and crunchy slices is similar, with the matrix of products consumed having an impact on betacyanins excretion profile, and the phenotype of volunteers affecting betacyanins excretion rate. Briefly characterizing this work, it should be pointed out that except for the difference in the matrix, red beet products, namely juice and crunchy slices, used in that study contained betanin and isobetanin but in different ratio of these pigments, i.e. 9 : 1 and 6 : 4, respectively. Further, urine samples examined by HPLC-DAD-MS method after the consumption of both products contained not only native betacyanins but also their aglycones. In the case of juice, the highest betacyanins urine excretion rate was observed within the first 2 hours, while in case of crunchy slices within the period of 2-4 h. As the Authors suggested, this phenomenon may result from a more easier absorption of betacyanins from juice than from the matrix of crunchy slices which had to undergo softening under the influence of the digestive process to allow the release of betacyanins from this matrix.

Further, among volunteers, a high interindividual variability in the average total betacyanins excretion rate and in the fraction of betacyanins dose eliminated in urine was found. However, it should be emphasised that the same volunteers were characterized with the highest and the lowest value of these parameters. The Authors indicate that two

reasons for the variability observed may occur, namely the activity of intestinal bacteria, and the genetic variation which may influence the degree of absorption, metabolism, and excretion of betacyanins.

Taking into account the aims of POSITIVE, further studies are now needed to discover the gut metabolism of red beet betacyanins as well as how the paths of absorption and metabolism of betacyanins in regard to this process are exactly shaped.

**Genetic variation of enzymes involved in the absorption and metabolism of phytochemicals may result in the complete absence or enhanced expression of a functional enzyme. Up- and down-regulation of gene expression in response to an altered cellular environment may achieve the same range of metabolic function, but often in a less reliable, predictable and time-dependent manner.**

This article is available at.

<https://reader.elsevier.com/reader/sd/90504A54036B5A147BCBD04A3D82508E1E09AA200E6EB5CCAC0785FD6871BAF47E8FC100EC7D4F883BB7E22CF22C77BE>



## RESEARCH DISSEMINATION

## PUBLICATIONS– WG2



In the Protein chemistry, Proteome analysis and Epigenetic signaling (PPES) lab, PhD candidate Ken Declerck's and Prof. Wim Vanden Berghe's research is focusing on identifying molecular inflammaging mechanisms that drive epigenetic clock progression.

Full article available at: <https://www.sciencedirect.com/science/article/pii/S0047637417302476>

Videocast of interest: <https://videocast.nih.gov/summary.asp?Live=19257&bhcp=1>

Mechanisms of Ageing and Development xxx (xxxx) xxx–xxx



Contents lists available at ScienceDirect

## Mechanisms of Ageing and Development

journal homepage: [www.elsevier.com/locate/mechagedev](http://www.elsevier.com/locate/mechagedev)



### Back to the future: Epigenetic clock plasticity towards healthy aging

Ken Declerck, Wim Vanden Berghe\*

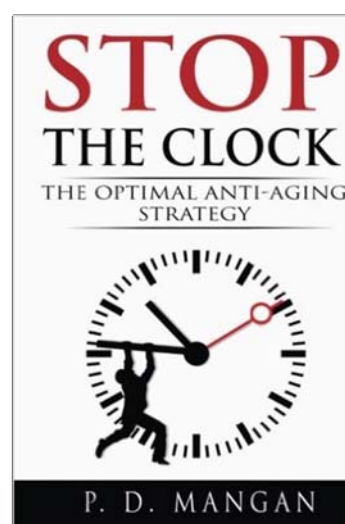
*Laboratory of Protein Chemistry, Proteomics and Epigenetic Signaling (PPES), Department of Biomedical Sciences, University of Antwerp (UA), Belgium*

A deeper understanding of the epigenetic mechanisms that might be implicated in aging can be applied in therapeutic nutritional or pharmaceutical rejuvenating interventions to promote healthy aging, or to prevent inflammatory-related disorders such as cancer, cardio-metabolic and neurodegenerative aging diseases.

Approximately 100 years ago, Albert Einstein proposed that time is a relative concept. Einstein's theory of relativity states that time and space are not as constant as everyday life would suggest. He suggested that the only true constant, the speed of light, meant that time can run faster or slower depending on gravity in space, and how fast you are travelling. Today, we face another paradigm of nonlinear dynamic time scale in biological aging. In contrast to your chronological aging since birth, biological aging is more variable and flexible in response to the environment.

Variable speed of biological aging can be determined by measuring DNA methylation intensities of your epigenetic clock. Remarkably, different lifestyle factors (smoking, stress, high caloric food, pollution) can speed up biological aging relative to your chronological age, whereas other factors (healthy diet, exercise) make you younger. For example, healthy centenarians with a Mediterranean diet may have a biological age of 80, but a chronological age of 100. Reciprocally, heavy smokers may have a biological age of 100, but a

chronological age of 80, with advanced disease/mortality risk. As such, **the epigenetic clock signature could be used as a lifestyle management tool to monitor healthy aging, to evaluate preventive interventions against chronic aging disorders and to extend healthy lifespan.** In addition, the epigenetic DNA methylation clock signature is increasingly used as a biomarker to estimate aging-related disease susceptibility and mortality risk.



## RESEARCH DISSEMINATION

## PUBLICATIONS– WG2










Overall analyses corroborate the benefits of Anthocyanins and Ellagitannins but factors influencing these effects remain poorly understood: Further research in the area is needed.



International Journal of  
Molecular Sciences

Review

## Meta-Analysis of the Effects of Foods and Derived Products Containing Ellagitannins and Anthocyanins on Cardiometabolic Biomarkers: Analysis of Factors Influencing Variability of the Individual Responses

María-Teresa García-Conesa <sup>1,\*</sup> , Karen Chambers <sup>2</sup>, Emilie Combet <sup>3</sup> , Paula Pinto <sup>4,5</sup> ,  
 Mar Garcia-Aloy <sup>6,7</sup> , Cristina Andrés-Lacueva <sup>6,7</sup>, Sonia de Pascual-Teresa <sup>8</sup> , Pedro Mena <sup>9</sup> ,  
 Aleksandra Konic Ristic <sup>10,11</sup>, Wendy J. Hollands <sup>2</sup>, Paul A. Kroon <sup>2</sup>, Ana Rodríguez-Mateos <sup>12</sup>,  
 Geoffrey Istaş <sup>12</sup>, Christos A. Kontogiorgis <sup>13</sup>, Dilip K. Rai <sup>14</sup> , Eileen R. Gibney <sup>15</sup> ,  
 Christine Morand <sup>16</sup>, Juan Carlos Espín <sup>1</sup> and Antonio González-Sarrías <sup>1,\*</sup> 

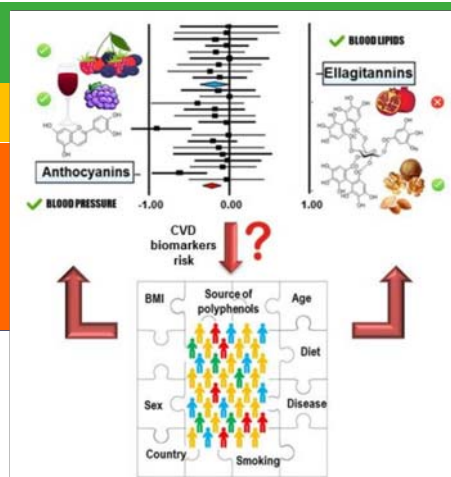
Following the main aims of POSITIVE, and, in particular, the objectives of the WG2, i.e. understanding the interindividual variation in the responsiveness to plant bioactive compounds regarding cardiometabolic endpoints, we have now completed and published a 3<sup>rd</sup> meta-analysis in which we have compiled the effects of berries, grapes, nuts and pomegranate containing as the major bioactives, ellagitannins and (or) anthocyanins, on a number of cardiometabolic markers. The results corroborated that, globally, these products have a benefit on some lipid markers (waist circumference, WC, total-cholesterol, HDL-cholesterol), blood pressure or flow mediated dilation (FMD). The size of these effects is small to moderate but continued intake of these products may contribute to reduce or maintain lower levels of these biomarkers. We detected some differences between products with: i) berries and grapes being more effective at reducing blood pressure, ii) nuts and pomegranate resulted better regulators of LDL-cholesterol, triglycerides (TAGs) or glucose. But these differences cannot be yet solely attributed to differences in ellagitannins or anthocyanins composition.

Nevertheless, and as already stated in our previous meta-analyses, the analysis of the influence of various factors (baseline BMI, sex, age, health status, smoking, country where the study was carried out) on the effects of these foods and

food products is limited and inconclusive mostly due to the small number of studies carried out with specific subpopulations e.g., only women or men, or people with normal BMI (<25 Kg/m<sup>2</sup>), or patients with a specific condition, etc. Also, and, very importantly, the studies carried out so far did not describe thoroughly some of these characteristics in the investigated subpopulation and have missed out other important ones such as the ethnic group, dietary habits, lifestyle, etc... It is thus not yet possible to come up with any conclusion as to any particular condition or subpopulation that could benefit from the intake of these products better than others. More and better studies are surely needed in this direction.

Equally important is to understand whether the benefits of the intake of bioactive compounds are specific of each type of product and compound or whether we are looking at some common benefits of a wide range of these dietary bioactive compounds, perhaps acting through common mechanisms *via* the intestine? Doses and duration of the interventions still remain poorly understood and should also be further investigated.

Although we are still a long way to reaching specific recommendations of these products/compounds for specific groups of consumers, **the way forward is now more clearly set up: Research in the area should continue to decipher inter-individual variability in response to all bioactive compounds.**



## RESEARCH DISSEMINATION

**PUBLICATIONS– FG:**  
The views of the consumers



**Research Open**

Nutrition Research and Food Science Journal

Volume 1 Issue 1

Research Article

## Spanish Consumers' General Understanding of Metabolic Diseases and how they may be Influenced by Diet and Novel Foods: a Preliminary Survey

Laura Laguna<sup>1</sup>, Begoña Bartolomé<sup>1</sup>, Victoria Moreno-Arribas<sup>1</sup>, María-Teresa García-Conesa<sup>2\*</sup>

<sup>1</sup>Institute of Food Science Research (CIAL), CSIC-UAM, C/Nicolás Cabrera 9, 28049 Madrid, Spain

<sup>2</sup>Research Group on Quality, Safety and Bioactivity of Plant Foods, CEBAS-CSIC, P.O. Box 164, 30100 Campus de Espinardo, Murcia, Spain



**SCIENTISTS IN DIRECT CONTACT WITH COSUMERS: The need to improve the communication and translation of our understanding of the binomial 'HEALTH-DIET' to the general public**

**T**his article collects the results of a simple preliminary survey distributed to a Spanish random population sample constituted by casual visitors to a general public Science event. Researchers from the Spanish Research Institution CSIC (CIAL & CEBAS) were interested in finding out how much the general public was aware of their metabolic health status and how much they knew about some very basic concepts related with metabolic disorders such as hypercholesterolemia or diabetes and about the influence of diet and lifestyle on their health. The survey also included some very simple questions about novel healthy products such as 'Functional Foods' and 'Nutraceuticals' and one final question regarding the understanding of the consumers about the potential differences of the effects of diet in different people.

The analyses of the results showed that despite a general concern about maintaining a good health status and some notions about the importance of eating well and keeping good life habits, the participants had a very limited knowledge of chronic disorders and manifested little familiarity and understanding of novel foods or nutraceuticals. The concept of inter-individual variability in response to diet was poorly understood by most participants.

Despite the limitations of this preliminary study, the results support the importance and need to continue providing more and updated information to the general population about metabolic diseases and how to prevent them. **New products, such as foods or tablets enriched in beneficial constituents and, new concepts, such as the relevance of the interindividual variability in response to diet and personalized nutrition should be clearly translated and explained to the consumers.**

**GET TO KNOW YOUR POSITIVE**
**SENIOR RESEARCHERS**
**What is the focus of your research?**

I am a pediatric gastroenterologist. I joined the School of Nutritional Sciences at the Hebrew university with the vision of carrying out research that would serve as a bridge between clinical and basic sciences regarding issues relevant to malnutrition. Specifically, I have devoted the majority of my career to investigating vitamin A and vitamin A deficiency. My research work on vitamin A encompasses three spheres: *nutrition, inflammation and growth*, and their inter-relationships. Because my academic training began in the area of Paediatric Gastroenterology, the impetus for my first research projects was based on clinical observations; from there my focus moved to identifying animal and in-vitro models that characterized specific phenomena of interest and then my work expanded to intensive investigation dedicated to unravelling underlying mechanisms of action. Recently I founded a start-up where we have an IP protected technology to produce high quality isolate of chickpea protein which is as an excellent source of plant protein, non-allergenic with negligible amounts of phytoestrogens, non-GMO and of course lactose and gluten free. This is a result of longstanding research on enhancement of the nutritional qualities and more than 15 years of work in the developing world to alleviate malnutrition.

**In what countries/organizations have you studied or worked?**

I went to medical school and did my pediatrics training in Hadassah Medical School at the Hebrew University of Jerusalem. My training in gastroenterology and later nutrition were at the Hospital for sick children in Toronto Canada. I also did a master program in Nutritional biochemistry at the University of Toronto. I spent a year with Prof Crawford in London on omega 3 fatty acids research. Lately I did a master in business administration in Israel as well.

**What has been the greatest achievement in your career?**

I think that we may have contributed to a better understanding of the function of vitamin A especially deficiency of vitamin A and to link it to many phenomena other than vision. We were among the first that used microarray in nutritional research and pointed out that vitamin A deficiency is associated with inflammation and iron deficiency and most of all our humble contribution to find ways to supplement vitamin A in various areas in the developing world.

**Which is your favorite paper you have written/co-authored and why?**

We were among the first to link nutritional work to in collaboration with colleagues in Wageningen. We were able to show the expression of relevant genes in the presence and absence of vitamin A but our recent reviews on both vitamin A deficiency and chickpea summarizes our work over the last 20 years. As a head of nutrition in our university I also had a chance to influence the curriculum of under and graduate students and possibly to improve their education.



**PROFESSOR RAM REIFEN**  
**HEBREW UNIVERSITY OF JERUSALEM**

**Who is/was your most influential mentor/colleague and why?**

Dr Hagit Hurvitz - an outstanding paediatrician who had an open mind and a unique ability to see beyond symptoms, and many years later Prof Crawford who had a wide angle and a global view on things without neglecting detailed and thorough research. My parents were my role models for life beyond science and medicine. I often ask myself what would my father do or how would my mother react in a certain situation that I am facing.

**What is your advice for young scientists?**

To prepare themselves for a long journey with ups and downs. To use passion in their work. To be attentive to the environment and to keep an open mind, also, to collaborate with people who do different things than they do.

**Where is your favorite place in the world and why?**

By far Jerusalem, our cultural and historical centre which has got beyond history magic and beauty and a unique atmosphere. The second favourite place is Florence full of culture and beauty.

**What is your favorite music/book?**

I am a musician at heart and for a short time I debated whether I should pursue a career as a musician.. I love the seventh symphony of Beethoven and violin concerto of Mendelson. I love listening to Adele and Amy Winehouse and I read almost all the new books by Israeli writers. My favorite one is David Grossman.

**What is your favorite sport(s)?** Swimming and jogging. We have a short winter in Israel and therefore it is easy to do both almost all year round.



## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS



**KIERAN TUOHY**  
**FONDAZIONE EDMUND MACH**

#### What has been the greatest achievement in your career?

This is a difficult question, since most scientific research careers in my experience are built using small, steady but consistent steps over many years. However, if pushed, I'd pick one from the beginning of my career – publishing my first research paper (and realising that the most important thing is to get the papers out and not to procrastinate too long worrying about how they will be received), and one recent highlight, leading my first European project, CABALA\_diet&health (<http://cabalaproject.eu/>).

#### Which is your favourite paper you have written/co-authored and why?

It is probably a review article from a few years ago entitled, "The way to a man's heart is through his gut microbiota" – dietary pro- and prebiotics for the management of cardiovascular risk." Although getting a bit old now, at the time it did serve to concentrate my thinking about how diet as a whole, rather than individual ingredients, can impact on microbiota composition and metabolic output, and consequently influence chronic disease risk. In fact, I would advise young researchers to write review articles on their chosen topics. Regularly. It really does help to advance your thinking, improve your writing skills and give you the confidence to challenge existing dogma. Just reading is not enough, you need to write to really think about of topic, focus your ideas and get your research directions clear in your head.

#### What is the focus of your research?

The focus of my research is diet:microbe interactions in the gut and how they can influence host health and disease risk. To study these interactions we use both in vitro models (gut models and cell lines) and small dietary interventions in people. We collaborate with others for mechanistic studies in laboratory animals. From a technological view point, we use a mix of metagenomics and metabolomics, as it is becoming apparent that it is not sufficient to know your microbiome by name, you must understand how they contribute to the human system at a molecular level through both metabolic and immune interactions.

#### In what countries/organisations have you studied or worked?

I received my degree (Industrial Microbiology), a long time ago now, from University College Dublin in Ireland, a Masters degree (Environmental Microbiology) from the University of Aberdeen, Scotland, and my PhD, entitled, "Measurement of DNA transfer in the gut using *in vitro* and *in vivo* models", from the University of Surrey in England in 2000. Since then I worked for about 10 years at the University of Reading before moving to Italy in 2010 and joining Fondazione Edmund Mach (FEM). I am now Head of the Department of Food Quality and Nutrition at FEM.

#### Who is/was your most influential mentor/colleague and why?

I was exceptionally lucky in my career to have some fantastic role models, Professors Ian Rowland, Glenn Gibson, Christine Williams and most recently Fulvio Mattivi. All very different characters, all with very different approaches to their science and life as a researcher, but also all fantastic teachers and scientists, always leading from the front, and brave!

#### What is your advice for young scientists?

See above about reviews and writing, and also to help as many people as you can on the way up – makes life a lot easier when your older and pass over the hill!

#### Where is your favourite place in the world and why?

I usually have a favourite place wherever I live – at the moment it's a small outcrop of rock jutting into a local cool mountain stream. Sometimes I fantasise about jumping in – Irish man in hot country syndrome ;)

#### What is your favourite music/book?

The Police, Paul Simon, Beethoven and Placebo, depending on mood, and book, still "In the Name of the Rose".

#### What is your favourite sport(s)?

Rugby and Gaelic Football – Up Mayo!

## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHERS

**What is the focus of your research?** My main research interests are orientated to the medicinal plants closely related to the antioxidative activity due to different phytochemical compounds. Acting as antioxidants, these molecules are capable to neutralize or scavenge the free radicals, which are responsible for many degenerative processes (cardiovascular diseases, aging), as well as progression of cancer. Therefore, I assume that antioxidative potential of many plant metabolites are in high demand at the current phytotherapy, as well as in nutrition. In this aim, we are using an electrochemical voltammetric method, which has many advantages versus the previous in vitro antioxidants assays. This electrochemical method could be effectively used in revealing the mechanism of oxidation/reduction of plant metabolites, or predicting their interaction with other plant constituents as well as conventional medicines or heavy metals.

**In what countries/organisations have you studied or worked in?**

I have studied pharmacy at the Faculty of pharmacy at Cyril and Methodius University in Skopje, the capital of Republic of Macedonia. On this integrated 5-year study program, I have acquired the degree of master of pharmacy. Then, in 2011, I have continued on the doctoral studies and defended my PhD thesis in 2016 in Stip, at Goce Delcev University, where I have the permanent teaching position (assistant professor), now. During my PhD studies, I have had a few study stays in Leipzig, Germany where I had a chance to work on a cytotoxicity assays and cell cultures and these results were incorporated in my doctoral thesis. During this stay, I have also had a short practical experience in Ca-fluorescence imaging methods, PCR and electrophoresis.

**What has been the greatest achievement in your career?**

As an early career investigator, the publication of the results of my PhD study in a high quality scientific papers, has been the greatest achievement. I am also very proud that as a member of WG2 in our COST Action, I have been included in the meta analyses related to the interindividual variations in the effects of flavonols on cardiovascular risk factors which have been published in a prestige journal.

**Which is your favorite paper you have written/co authored and why?**

Both original scientific papers: Maksimova, Viktorija and Mirceski, Valentin and Gulaboski, Rubin and Koleva Gudeva, Liljana and Arsova-Sarafinovska, Zorica (2016) [Electrochemical Evaluation of the Synergistic Effect of the Antioxidant Activity of Capsaicin and Other Bioactive Compounds in Capsicum sp. Extracts](#). International Journal of Electrochemical Science, 11. pp. 6673-6687. & Maksimova, Viktorija and Koleva Gudeva, Liljana and Gulaboski, Rubin and Nieber, Karen (2016) [Co-extracted bioactive compounds in Capsicum fruit extracts prevents the cytotoxic effects of capsaicin on B104](#)



**VIKTORIJA MAKSIMOVA**  
Univerzitet Goce Delcev, Macedonia

[neuroblastoma cells](#). Revista Brasileira de Farmacognosia. pp. 1-7. published on the results of my doctoral thesis makes me really happy because they are integrating my research interests in a whole picture about a plant fruit (hot pepper) that is very often used in nutrition in my country, as well as world wide. Because of the possible health effects of Capsicum I consider that they are both very important in my career.

**Who is/was your most influential mentor/colleague and why?**

There are many people whose contributions have been very important to my research and to me. Among others, as the most inspiring I will have to emphasize a few of them. Prof. Karen Nieber, prof. Valentin Mirceski and prof. Rubin Gulaboski have influenced a lot in my research and professional upgrade. Their implication on my practical working skills as well as scientific expression style are enormous and I am very grateful to their unselfish advises and suggestions.

**Where is your favorite place in the world and why?** The tallest sand dune in Europe, The Dune of Pilat, located in the Arcachon Bay area, in Bordeaux, France is the most impressive place that I have visited. I had a chance to visit it through one of my short study stays in France and I was impressed by the view of the Atlantic Ocean on one side and an enormous pine forest on the other side of the Arcachon Bay, a sandbank and a peninsula!

**What is your favorite music/book?** As a romantic type, I love to hear the popular rock ballads as well as pop hits. The books of life philosophy and criminal book novels are also interesting to me.

**What is your favorite sport(s)?**

I am not really a sport style girl, but I love to watch figure skating.

## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHERS

#### What is the focus of your research?

I am a PhD student investigating the effects of berry (poly) phenols on cardiovascular health, their bioavailability and potential mechanisms of action in the vascular system. Over the past three years, I have conducted several randomized controlled trials assessing the effects of different berries on vascular function in humans, and also looking at plasma and urinary polyphenol metabolites using liquid chromatography-mass spectrometry. I have used murine models and in vitro approaches to provide mechanistic insights and complement the findings from human trials, together with nutrigenomic analysis to understand the biological pathways affected by (poly)phenol intake in the context of cardiovascular diseases.

#### In what countries/organisations have you studied or worked in?

I studied a Master degree in Biochemistry and Biotechnology at the University of Antwerp (Belgium). As part of an Erasmus program I performed a 6-month research internship in Epigenetics at the Chemoprevention Department in the German Cancer Research Center (Heidelberg, Germany). Under supervision of Dr. Ana Rodriguez-Mateos, I started my PhD at Dusseldorf University (Germany) in 2014. In 2016, our group moved to King's College London, where I am now currently in my last year of PhD.

#### What has been the greatest achievement in your career?

Over the course of my PhD, I developed a network of connections with scientists all over the world, mainly thanks to the COST-POSITIVE action. The relationships I have made are not only helping me throughout my PhD, but will most certainly prove valuable in future endeavors.

#### Which is your favourite paper you have written/co-authored and why?

*Istas et al. Identification of differentially methylated BRCA1 and CRISP2 DNA regions as blood surrogate markers for cardiovascular disease. Scientific Reports. 2017.* Is the paper based on the research I performed during my Master project and it is my first "first author" paper. The aim was to compare the epigenome of healthy individuals and atherosclerotic patients and to identify potential biomarkers of cardiovascular disease. Our analysis shows that *BRCA1* and *CRISP2* promoter methylation status in blood leukocytes might predict development of atherosclerosis.

#### Who is/was your most influential mentor/colleague and why?

Ana Rodriguez-Mateos is my most influential mentor. She has been very supportive, patient and inspiring over the course of my PhD. Most of my knowledge and skills are thanks to her.



**GEOFFREY ISTAS**  
 King's College London, UK

#### Where is your favourite place in the world and why?

Italy. In my opinion Italy as a holiday destination has everything you need: delicious food, quality wine, good weather, amazing landscapes (beaches, mountains and fields) and nice people!

#### What is your favourite music/book

I am currently reading the "century trilogy" by Ken Follet. It feeds my passion for history and also presents basic knowledge about politics and social structures in an accessible and interesting manner. I love all kinds of music genres including jazz, indie pop, reggae, house and relaxing music.

#### What is your favourite sport(s)?

I am a big fan of Capoeira, a Brazilian martial art that also incorporates dance. As a fervent practitioner for the past 15 years, Capoeira has kept me fit, has provided me with a social network in every country I moved to and embeds me with a warm Latin culture/vibe. I am a strong believer of the quote "a healthy mind in a healthy body" and Capoeira can give me just that!

## Chair's Corner

Dear POSITIVE partners,

The time goes definitely very fast since the Action is entering its fourth and last year! The quality of the collaborative works performed by the WGs since the beginning has already led to the publications of seven open access reviews in good scientific journals, and also several other manuscripts that are either under peer review or being completed. Each of these papers contributes to increasing the state of the art and the knowledge on the interindividual variation in response to plant food bioactives consumption and will provide a cornerstone for elaborating a new and concrete research programme on that topic. The POSITIVE Action has also fostered scientific exchanges within the network, by offering possibilities to more than thirty scientists to perform short-term scientific missions in partner labs.

The next and last major event organized by the Action will be its **Final Scientific Conference** that will be held in **Lisbon (25-26<sup>th</sup> September 2018)**, as a satellite activity of the 2<sup>nd</sup> Food Bioactives & Health Conference. During this two-day POSITIVE Conference (<https://www6.inra.fr/cost-positive/Home/News/Final-Conference>), the main findings of the Action will be presented, and the future of research and concrete applications related to individual response to dietary interventions will be exposed and discussed through the view of international experts and stakeholders. We hope that this event will largely attract scientists from and outside the POSITIVE community and, in any case, the Action will work in that direction by maximizing its efforts to refund the widest possible number of partners for attendance.

**Looking forward to seeing you at the Final Conference of POSITIVE!**

**Christine & Paco**



## CONTACT US



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH

### Contact us:

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: [christne.morand@clermont.inra.fr](mailto:christne.morand@clermont.inra.fr)

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: [fatomas@cebas.csic.es](mailto:fatomas@cebas.csic.es)

### Webpage:

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)



POSITIVE

ISSUE 9

## COST Action FA1403 – POSITIVE Interindividual variation in response to consumption of plant food bioactives and determinants involved

**Final POSITIVE Scientific Conference, September 25-26, 2018**

**Lisbon, Portugal**

<https://www6.inra.fr/cost-positive/Home/News/Final-Conference>



This Final COST Conference is the ideal scenario to present the main findings resulting from the impressive collaborative efforts undertaken by the European scientific experts involved in the POSITIVE network, and further discuss the current unresolved issues and the way to future research in the area of personalized nutrition, as one of the

important tools to combat burden of cardiometabolic diseases. The conference will be also the place to know about recent advances in the field of personalized nutrition and for exchanges between scientists and stakeholders about the integration of plant food bioactives in future strategies of precision nutrition to become healthier.

**You are all very welcome to join us in this exciting and interesting event which will be followed by the 2nd edition of the Food Bioactives and Health Conference!**

Dr. Christine Morand, Action Chair



**Final POSITIVE Scientific Conference  
will be held in satellite to:**



## Scientific Program

**Tuesday, 25<sup>th</sup> September 2018**

**8.00 a.m. – 8.45 a.m. Welcome**

(8.45 a.m. – 17.30 p.m.)

*Main Findings from POSITIVE: Major determinants involved in interindividual variations in plant food bioactives ADME and cardiometabolic responses*

**Morning session 8.45 – 12.25**

8.45 – 9.00	Dr. Christine Morand (INRA-Clermont –Ferrand, France) <b>Introduction of the COST Action POSITIVE – Final Conference</b>
9.00 – 9.35	Dr. Tom van de Wiele (University of Ghent, Belgium) <b>Determinants of interindividual variability in absorption, distribution, metabolism and excretion of plant food bioactives</b>
9.35 – 10.10	Dr. Torsten Bohn (Luxembourg Institute of Health, Strassen, Luxembourg) <b><math>\beta</math>-Carotene in Humans – Metabolic Pathway and Bioactivation - from Digestion to Tissue Distribution and Excretion</b>
10.10 – 10.45	Dr. Anne Marie Minihanne, Univ of East Anglia, UK <b>Key determinants of flavonoids metabolism following mixed dietary flavonoid source – COB Study</b>
<b>BREAK</b>	
11.15 – 11.50	Dr. Claudine Manach (National Institute for Agricultural Research-INRA, Clermont Ferrand, France) <b>Untargeted metabolomics for assessment of true exposure to plant food bioactives</b>
11.50 – 12.25	Dr. Aleksandra Konic-Ristic (University of Belgrade, Serbia - University College Dublin, Ireland) <b>Quality of reporting of clinical trials addressing the inter-individual variation in response to plant bioactives</b>

**LUNCH**

**Afternoon session 13.55 – 17.30**

13.55 – 14.30	Dr. Ana Rodriguez-Mateos (King's College, London, United Kingdom) <b>Investigating variability in cardiometabolic response to plant food bioactives: approaches and main findings from POSITIVE</b>
14.30 – 15.05	Dr. Dragan Milenkovic, National Institute for Agricultural Research (INRA), Clermont Ferrand, France <b>Evaluation of cell and molecular targets of plant food bioactives: implications for inter-individual variability</b>
15.05 – 15.40	Prof. Francisco Tomas-Barberan, CEBAS-CESIC, Murcia, Spain <b>Impact of gut microbial metabolism on cardiometabolic markers</b>
<b>BREAK</b>	
16.10 – 16.45	Dr. Emilie Combet, University of Glasgow, UK <b>Beyond results - lessons learned from POSITIVE meta analyses</b>
16.45 – 17.30	<b>ROUND TABLE “Future of plant food bioactives in precision nutrition”</b> Moderators: Chairs ; Participants : WG leaders, speakers, the audience Introduction: Prof. Baukje de Roos (University of Aberdeen, United Kingdom)  <b>POSITIVE roadmap</b>

## Scientific Program

**Wednesday, 26<sup>th</sup> September 2018**

(9.00 a.m. – 16.30 p.m.)

*Recent advances in research on interindividual variability and interesting perspectives in the field of personalized nutrition*

**Morning session 9.00 – 12.00 a.m.**

9.00 – 9.30

Dr. Eileen Gibney, University College of Dublin, Ireland

***Main findings from Food 4Me - Next steps***

9.30 – 10.00

Dr. Baukje de Roos, University of Aberdeen, UK

***Personalized intervention: a precision approach for the next generation of intervention studies***

10.00 – 10.30

Dr. Kieran Tuohy (Fondazione Edmund Mach, Trento, Italy)

***Microbiome variants in relation to bioavailability of plant food bioactives***

**BREAK**

11.00 – 11.30

Prof. Rikard Landberg, Chalmers University of Technology, Gothenburg, Sweden

***New personalized strategies for optimal metabolic responses to fibre-rich foods***

11.30 – 12.00

Dr. Paul Franks, University of Lund, Sweden

***Lifestyle in the context of precision medicine***

**LUNCH**

**Afternoon session 13.30 – 16.30 p.m.**

13.30 – 14.00

Prof. Wim Verbeke (University of Ghent, Belgium)

***Personal determinants of consumers' healthy and sustainable food choices***

14.00 – 14.15

Dr. Pascale Fanca Berthon (Head of Nutrition & Health Science, Naturex, France)

***From science to market: challenges of personalized nutrition with botanicals***

14.15 – 14.30

Dr. Carlos Javier González Navarro (Director of Innovation, Centre for Nutrition Research, University of Navarra, Spain)

***Food innovation and personalized nutrition: What is (Spanish) industry demanding from scientists and technologists***

14.30 – 14.45

Dr. Marjan van Erk (TNO; program manager public-private consortium on Personalised Nutrition & Health, The Netherlands)

***Technologies and knowledge for tailored, scientifically grounded products and services in personalized nutrition.***

14.45 – 15.00

Dr. Adrian Hodgson (Nutrition Innovation Consultant, SPOON-GURU, United Kingdom-USA)

***Artificial intelligence, machine learning and precision nutrition are transforming the way people eat and drink***

15.00 – 16.00

***Round Table: Debate on personalized nutrition and health with a panel of stakeholders***

(Moderator: Dr. María-Teresa García-Conesa, CEBAS-CSIC, Spain)

16.00 – 16.30

***Closing ceremony and group photos***



## LOCAL ORGANIZERS

**Dr. Maria Bronze, Faculty of Pharmacy, University of Lisbon**

The FFULisboa is a public institution of higher education dedicated to education, research, knowledge transfer and education in the fields of pharmacy, medicine, and pharmaceutical sciences. It provides to the general public a number of specialized services that result from the application of translational research performed in the clinical, instrumental and industrial context



**Dr. Claudia Nunes-dos Santos, IBET—Institute of Experimental Biology and Technology**



# IBET

Instituto de Biologia  
Experimental e Tecnológica

**Dr. Paula Pinto, IPS-ESA Department of Food Technology, Biotechnology and Nutrition (DTABN)**

DTABN mission is to promote education, development and transference of knowledge in the areas of food technology, food safety and food quality, from raw material to the processing of food, its nutritive value and health effects.

iBET is a private not for profit research intensive SME in the area of biotechnology and life sciences. iBET was established in 1989 and bridges university and industry research, by establishing partnerships particularly in the areas related to Health & Pharma and Food &



## SCIENTIFIC COMMITTEE

- Iwona Kieda, Institute of Animal Reproduction and Food Research, PAS, Olsztyn, Poland
- Dr Aleksandra Konic-Ristic, University of Belgrade, Serbia
- Dr María-Teresa Garcia-Conesa, CEBAS-CSIC, Murcia, Spain
- Dr Rocio Garcia Villalba, CEBAS-CSIC, Murcia, Spain
- Dr Eileen Gibney, University College Dublin, Ireland
- Prof Marina Heinonen, University of Helsinki, Finland
- Prof Rikard Landberg, Chalmers University of Technology, Gothenburg, Sweden,
- Dr Claudine Manach, INRA, Clermont Ferrand, France
- Dr Pedro Mena, University of Parma, Italy
- Dr Dragan Milenkovic, INRA, Clermont Ferrand , France
- Dr Christine Morand, INRA, Clermont Ferrand, France
- Dr Ana Rodriguez-Mateos, Kings College London, UK
- Prof Baukje de Roos, University of Aberdeen, United Kingdom
- Prof Francisco Tomas-Barberan, CEBAS-CSIC, Murcia, Spain
- Prof Tom Van de Wiele, Ghent University, Belgium

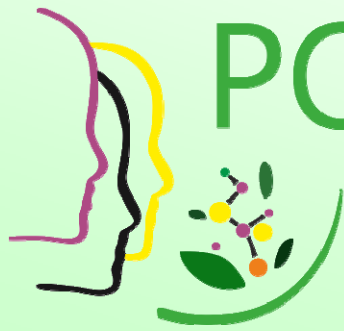


Funded by the Horizon 2020 Framework Programme of the European Union

**PLEASE contact us for further information:**

**Chair:** Dr. Christine MORAND, INRA - France, e-mail: christine.morand@clermont.inra.fr

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain, e-mail: fatomas@cebas.csic.es



# POSITIVE

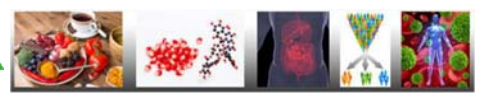
ISSUE 10



# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE VIII, DECEMBER 2018

## FAREWELL MESSAGE

# D

ear friends & colleagues,

It is with some sadness that we are hereby releasing our very last **POSITIVE newsletter**. If we look at the full collection of issues we can clearly see that all together we have done a fantastic amount of work, we have attended great meetings in beautiful countries, we have met many new colleagues and future work partners, we have started new wonderful collaborations, we have discussed and learnt lots of new subjects and concepts and we have produced an important quantity of very informative articles which are of great value to the scientific community working in **Bioactive Compounds & Health** and are also essential for the future development of this research area.

Once more, we also want to thank you all for your patience with us and for your extremely valuable help to build up the information and photos included in these journals. We hope that you have enjoyed reading them as much as we have enjoyed putting them together.

We sincerely hope that you will all look back every now and then to these newsletters and remember good times and moments with all the partners. We certainly will do!

Hope to see you soon Friends!

### The FG



## IN THIS ISSUE:

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## NEWS FROM THE ACTION

## POSITIVE 8<sup>th</sup> WGs Meeting, 24<sup>th</sup> September 2018, Lisbon, PORTUGAL



The last WG and MC meetings of the COST Action POSITIVE took place in Lisbon on the afternoon of Monday, the 21<sup>st</sup> of September, in the rooms of the Vip Executive Art's Hotel.

One more time, the partners gathered first in separate rooms for the final WG1 and WG2 meetings where there was, as usual, an update of the activities done in each group, followed by some presentations on the progress of the on-going meta-analysis and review articles that will be completed and published in the next few months.

In a second part of the meetings a general question was posed to the attendants: 'What had been the main findings and outcomes of the Action? The participants formed different subgroups and

dedicated some time to respond to this question and to communicate their views and opinions about the main results attained during the course of the Action. This was followed by some general and lively discussions. After this, all the responses were shared and a general consensus was summarized by the WG leaders. Overall, there was a clear common message, we need to continue the research promoting and developing improved clinical studies that will allow for confirmation of the influence of all the investigated factors in human interindividual variability in response to food bioactive compounds in relation with the development of cardiometabolic disorders. We all agreed on that the COST Action has identified the scientific gaps that need to be sorted and has outlined the direction to follow in the future research in this area.



## NEWS FROM THE ACTION

### SOCIAL EVENTS

We really want to thank our Portuguese partners for giving us, once more within this COST Action, the opportunity to share a great time and social evening with all our 'POSITIVE friends'.

After a nice stroll in the surroundings of the Hotel area and by the Tagus river bank under a beautiful full moon (all very well prepared by our colleagues Claudia, Paula and the rest of the Portuguese team) we end-up having dinner in a Portuguese typical restaurant where we enjoyed the delicious traditional cod fishes and rice in a pleasant and relaxing atmosphere.



**NEWS FROM THE ACTION**
**FINAL SCIENTIFIC COST POSITIVE Conference,  
 25 - 26<sup>th</sup> September, Lisbon, Portugal**
**Day 1: Main findings from POSITIVE: Major determinants involved in interindividual variations in plant food bioactives ADME and cardiometabolic responses**

As in previous occasions, the Final Scientific Conference of the COST Action POSITIVE –FA1403 was held in satellite with an international conference, the 2<sup>nd</sup> Food Bioactives and Health conference, FBHC-2018, of which a summary follows.

The conference was divided in two main sessions. The first one took place on Tuesday the 25<sup>th</sup> of September and included presentations by some of the WG leaders as well as other partners covering the main findings and results from the research areas of their respective working groups. Following an introduction by the Action chair, Dr. Christine Morand, the speakers talked about diverse aspects of the research in relation with interindividual variability in plant food bioactives absorption and metabolism as well as cardiometabolic responses. The program included talks about general issues of the bioactives ADME, specific insights into the metabolism of carotenes and flavonoids, the application of metabolomics, the impact of gut microbiota, the main lessons learned from the meta-analysis approach or the quality of the reporting in clinical trials.



The presentations were followed by a round table looking at the **'Future of plant food bioactives in precision nutrition'**. The discussions with all the speakers were led by Dr. Baukje de Roos.



## NEWS FROM THE ACTION

### Day 2: Recent advances in research on interindividual variability and interesting perspectives in the field of personalized nutrition

During the second day of the Conference, we had the opportunity to listen to a number of invited speakers, both from the COST Action and external speakers, who are specialised in the area of 'Personalized Nutrition'.

The morning session included several talks looking at the findings of the Food 4Me project, the future approaches for personalized intervention trials or the experience in the context of personalized medicine. The afternoon session was entirely devoted to the area of **consumers** and **stakeholders**. The invited speakers presented the views of consumers as well as of the food industry and market. There were talks about consumer's healthy choices and factors influencing these choices, the interest and problems faced by the natural plant products industry in relation with personalized nutrition, the particular views of the Spanish Federation of Food and Drink Industry, or the application of new technologies to personalized nutrition and food and drink choices.



The presentations were also followed by a round table: **'Debate on personalized nutrition and health with a panel of stakeholders'** led by Dr. María-Teresa García-Conesa and where the speakers debated about the future of personalized nutrition with all the attendants.

## NEWS FROM THE ACTION

## 2<sup>nd</sup> FOOD BIOACTIVES & HEALTH CONFERENCE

26 - 28 September 2018, Lisbon, Portugal



The conference also offered the opportunity to exchange ideas and knowledge with many scientists of the different areas during the breaks in the common room as well as along the posters exhibition.



The 2<sup>nd</sup> FBHC-2018 was successfully held in Lisbon on the 26-28<sup>th</sup> of September right after the Final COST Conference and thus, many POSITIVE partners were able to attend the FBHC and also to present their work in the different topics addressed, i.e. the latest trends in the field of **polyphenols, carotenoids, glucosinolates, marine compounds, polysaccharides, peptides and proteins**, all under the frame of **'food bioactives to improve or maintain our health'**. The opening ceremony was led by Dr. Claudia Nunes Dos Santos and Dr. Rosario Bronze and was followed by the different parallel sessions which included among others subjects: the role of bioactives in neuronal and immune diseases, the mechanisms of action of bioactives and derived metabolites, flash presentations by young researchers, novel applications or dietary interventions.

2<sup>ND</sup> CONFERENCE ON

# FOOD BIOACTIVES & HEALTH



26-28 SEPTEMBER 2018 LISBON PT





## NEWS FROM THE ACTION

## POSITIVE partners in Lisbon at the FBHC-2018



Once again, our kind hosts organized a wonderful conference dinner in a cruiser by the river Tagus from where we were able to admire the coast side of Lisbon at night while having a few drinks on the top deck. We then went to the main dining room of the boat to enjoy a fantastic dinner while listening to some pleasant music.

Overall, it was a great meeting and experience for all. Well done to the Portuguese team who organized everything. Thanks Claudia, Paula, Regina and the rest of the people. We look forward to going back to the beautiful Lisbon.



## POSITIVE on TWITTER



#Cost\_POSITIVE

@Cost\_POSITIVE

[www.twitter.com](http://www.twitter.com)

## RESEARCH DISSEMINATION

## OUR MAIN POSITIVE COLLABORATIVE PUBLICATIONS



Mol. Nutr. Food Res. 2016, 00, 1–16

DOI 10.1002/mnfr.201600557

1

REVIEW

## Addressing the inter-individual variation in response to consumption of plant food bioactives: Towards a better understanding of their role in healthy aging and cardiometabolic risk reduction

Claudine Manach<sup>1\*</sup>, Dragan Milenkovic<sup>1\*</sup>, Tom Van de Wiele<sup>2</sup>, Ana Rodriguez-Mateos<sup>3</sup>, Baukje de Roos<sup>4</sup>, Maria Teresa Garcia-Conesa<sup>5</sup>, Rikard Landberg<sup>6,7</sup>, Eileen R. Gibney<sup>8</sup>, Marina Heinonen<sup>9</sup>, Francisco Tomás-Barberán<sup>5</sup> and Christine Morand<sup>1</sup>



Christine Morand

Mol. Nutr. Food Res. 00, 0, 2017, 1600685

DOI 10.1002/mnfr.201600685

(1 of 37) 1600685

REVIEW

## Host-related factors explaining interindividual variability of carotenoid bioavailability and tissue concentrations in humans



Torsten Bohn<sup>1</sup>, Charles Desmarchelier<sup>2</sup>, Lars O. Dragsted<sup>3</sup>, Charlotte S. Nielsen<sup>3</sup>, Wilhelm Stahl<sup>4</sup>, Ralph Rühl<sup>5,6</sup>, Jaap Keijer<sup>7</sup> and Patrick Borel<sup>2</sup>



Patrick Borel

**Comprehensive  
REVIEWS**  
in Food Science and Food Safety

## Bioavailability of Quercetin in Humans with a Focus on Interindividual Variation

A. Filipa Almeida , Grethe Iren A. Borge, Mariusz Piskula , Adriana Tudose, Liliana Tudoreanu, Kateřina Valentová , Gary Williamson, and Cláudia N. Santos 












Cláudia N Santos

 **metabolites**

 **MDPI**

Article

## Interlaboratory Coverage Test on Plant Food Bioactive Compounds and Their Metabolites by Mass Spectrometry-Based Untargeted Metabolomics

Ville Mikael Koistinen <sup>1,\*</sup> , Andreia Bento da Silva <sup>2</sup>, László Abrankó <sup>3</sup>, Dorrain Low <sup>4</sup> , Rocio Garcia Villalba <sup>5</sup>, Francisco Tomás Barberán <sup>5</sup> , Rikard Landberg <sup>6</sup>, Otto Savolainen <sup>6</sup>, Inmaculada Alvarez-Acero <sup>7</sup> , Sonia de Pascual-Teresa <sup>7</sup>, Christof Van Poucke <sup>8</sup> , Conceição Almeida <sup>2</sup>, Lucie Petrásková <sup>9</sup>, Kateřina Valentová <sup>9</sup> , Stephanie Durand <sup>4</sup>, Wiesław Wiczkowski <sup>10</sup> , Dorota Szawara-Nowak <sup>10</sup>, Raúl González-Domínguez <sup>11,12</sup> , Rafael Llorach <sup>11,12</sup>, Cristina Andrés-Lacueva <sup>11,12</sup>, Anna-Marja Aura <sup>13</sup>, Tuulikki Seppänen-Laakso <sup>13</sup>, Kati Hanhineva <sup>1</sup>, Claudine Manach <sup>4</sup> and Maria Rosário Bronze <sup>2,14,15</sup> 



Rosário Bronze

## RESEARCH DISSEMINATION

## OUR MAIN POSITIVE COLLABORATIVE PUBLICATIONS

ASN REVIEW

Review Journal

## Interindividual Variability in Biomarkers of Cardiometabolic Health after Consumption of Major Plant-Food Bioactive Compounds and the Determinants Involved

Dragan Milenkovic,<sup>1</sup> Christine Morand,<sup>1</sup> Aedin Cassidy,<sup>2</sup> Aleksandra Konic-Ristic,<sup>3</sup> Francisco Tomás-Barberán,<sup>4</sup> José M Ordovas,<sup>5,6</sup> Paul Kroon,<sup>7</sup> Raffaele De Caterina,<sup>8</sup> and Ana Rodríguez-Mateos<sup>9</sup>

WG2



Ana Rodríguez-Mateos

nutrients MDPI

Review

## Impact of Flavonols on Cardiometabolic Biomarkers: A Meta-Analysis of Randomized Controlled Human Trials to Explore the Role of Inter-Individual Variability

Regina Menezes <sup>1</sup>, Ana Rodríguez-Mateos <sup>2</sup>, Antonia Kaltsatou <sup>3</sup>, Antonio González-Sarriás <sup>4</sup>, Arno Greyling <sup>5</sup>, Christoforos Giannaki <sup>6</sup>, Cristina Andres-Lacueva <sup>7</sup>, Dragan Milenkovic <sup>8</sup>, Eileen R. Gibney <sup>9</sup>, Julie Dumont <sup>10</sup>, Manuel Schär <sup>11</sup>, Mar Garcia-Aloy <sup>7</sup>, Susana Alejandra Palma-Duran <sup>12</sup>, Tatjana Ruskovska <sup>13</sup>, Viktorija Maksimova <sup>13</sup>, Emilie Combet <sup>12</sup> and Paula Pinto <sup>1,14,\*</sup>



Paula Pinto

nutrients MDPI

Review

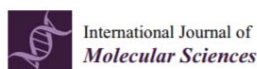
## A Systematic Review and Meta-Analysis of the Effects of Flavanol-Containing Tea, Cocoa and Apple Products on Body Composition and Blood Lipids: Exploring the Factors Responsible for Variability in Their Efficacy

Antonio González-Sarriás <sup>1,\*</sup>, Emilie Combet <sup>2</sup>, Paula Pinto <sup>3</sup>, Pedro Mena <sup>4</sup>, Margherita Dall'Asta <sup>4</sup>, Mar Garcia-Aloy <sup>5,6</sup>, Ana Rodríguez-Mateos <sup>7</sup>, Eileen R. Gibney <sup>8</sup>, Julie Dumont <sup>9</sup>, Marika Massaro <sup>10</sup>, Julio Sánchez-Meca <sup>11</sup>, Christine Morand <sup>12</sup> and María-Teresa García-Conesa <sup>1,\*</sup>

María-Teresa  
García-Conesa

## RESEARCH DISSEMINATION

## OUR MAIN POSITIVE COLLABORATIVE PUBLICATIONS



Review

## Meta-Analysis of the Effects of Foods and Derived Products Containing Ellagitannins and Anthocyanins on Cardiometabolic Biomarkers: Analysis of Factors Influencing Variability of the Individual Responses

María-Teresa García-Conesa <sup>1,\*</sup>, Karen Chambers <sup>2</sup>, Emilie Combet <sup>3</sup>, Paula Pinto <sup>4,5</sup>, Mar Garcia-Aloy <sup>6,7</sup>, Cristina Andrés-Lacueva <sup>6,7</sup>, Sonia de Pascual-Teresa <sup>8</sup>, Pedro Mena <sup>9</sup>, Aleksandra Konic Ristic <sup>10,11</sup>, Wendy J. Hollands <sup>2</sup>, Paul A. Kroon <sup>2</sup>, Ana Rodríguez-Mateos <sup>12</sup>, Geoffrey Istaş <sup>12</sup>, Christos A. Kontogiorgis <sup>13</sup>, Dilip K. Rai <sup>14</sup>, Eileen R. Gibney <sup>15</sup>, Christine Morand <sup>16</sup>, Juan Carlos Espín <sup>1</sup> and Antonio González-Sarrías <sup>1,\*</sup>



Antonio González Sarrías

TTG

JOURNAL OF  
AGRICULTURAL AND  
FOOD CHEMISTRY

Perspective

Cite This: *J. Agric. Food Chem.* XXXX, XXX, XXX–XXX

pubs.acs.org/JAFC

## Breakthroughs in the Health Effects of Plant Food Bioactives: A Perspective on Microbiomics, Nutri(epi)genomics, and Metabolomics

Banu Bayram,<sup>†</sup> Antonio González-Sarrías,<sup>‡</sup> Geoffrey Istaş,<sup>§</sup> Mar Garcia-Aloy,<sup>||,○</sup> Christine Morand,<sup>⊥</sup> Kieran Tuohv,<sup>#</sup> Rocío García-Villalba,<sup>\*,&‡</sup> and Pedro Mena<sup>\*,∇,○</sup>



Pedro Mena

## VISIT US ON FACEBOOK



<https://www.facebook.com/costpositive/>

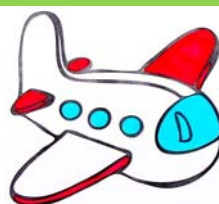
## RESEARCH DISSEMINATION

## POSITIVE SPREADING ALL OVER THE WORLD

## 19<sup>th</sup> World Congress of Food Science & Technology (IUFOST),

October 23-27, 2018, Mumbai, India

Once more and, before the end of our COST Action, POSITIVE has spread the main messages and lessons learnt about Interindividual Variability & Food Bioactives and Health to the scientific community. The job was in the hands and voice of our Chair, Dr. Christine Morand, who travelled all the way to Mombay to present POSITIVE at one of the largest Food Science & Technology Conferences, IUFOST-2018. The meeting also counted with the presence and active participation of Prof. Mariusz Piskula, General Director of the Institute of Animal Reproduction and Food Research, Polish Academy of Sciences, Olsztyn (Poland) and a partner of POSITIVE.



## PARTNERS' VIEWS & OPINIONS

### POSITIVE EXPERIENCE

We asked all the POSITIVE partners about their views and opinions regarding their experience during the course of the four-years Action. These were some of our questions and some of their responses ...

#### Main lessons from POSITIVE

What are the new issues you acquired during the Action which you have incorporated/will incorporate into your future research?

Individual variation is one of the key issues which need to be tackled one way or another. The division between responders and non-responders and studies related to factors causing the response or its absence seems to me a reasonable way to continue. Easy, it is not, but feasible and reasonable....!

Some of the topics I didn't know so much before joining the COST POSITIVE: knowledge about other bioactives such as carotenoids; how to conduct meta-analysis of cardiometabolic effects; EU or other initiatives on bioactives that some colleagues are working on; status of research regarding inter-individual variability (...) upon bioactives consumption.

For a successful scientific work, an interdisciplinary and regular exchange between specialists is indispensable. Digitalisation is more and more important to deal with the vast quantity of data !!!

(...) applying bioinformatic tools to identify genes, transcription factors and pathways targeted by plant food bioactives in relation with cardiometabolic disorders, have significantly enhanced my skills (...) a better understand of anthocyanin bioavailability, which gave me new insight in interindividual responses of plant food bioactives on human health.

I think the omics approach of some of the groups and the training schools and webinar have been really useful for us, giving us direct access to real data and examples that are already being used in our lab. Also, the participation in the meta-analysis work has been very productive, not only for the publications, but also for the acquisition of new knowledge in the methodology used.

Improved networking, additional publications, further knowledge on metabolism of bioactive' phytochemicals.



## PARTNERS' VIEWS &amp; OPINIONS

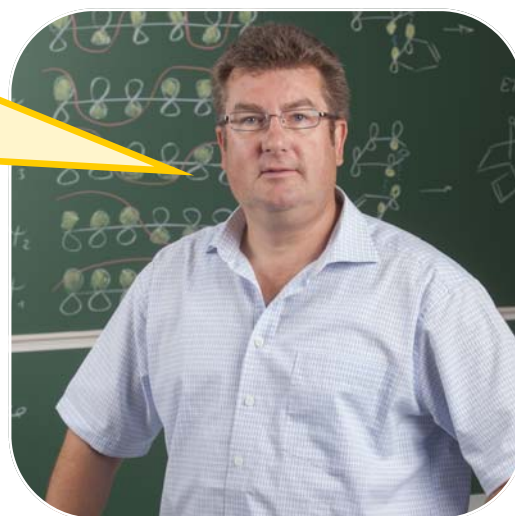
## Networking at POSITIVE

How did you find the opportunity to interact and work with new colleagues from other countries and research institutions?



I only knew some of the colleagues before, some I knew from publications, but the majority I didn't know. So, the COST was a good opportunity to get to know them. With some people I am sure I will continue to have contact with. It would be great to continue the action, although I am not sure how that will be possible from a practical perspective. Maybe to associate the POSITIVE network meetings after or before relevant scientific meetings, so that people can meet more easily and avoid additional travelling costs...

It was inspiring to meet old friends and new researchers and to exchange results and opinions. There are always possibilities to launch new projects, especially between peripheral European countries and Switzerland. The contacts made during the action will intensify these collaborations. Networking will continue through the participation at international meetings....!!!



Very good exchange within WG, perhaps across WG more interaction time could have been allowed for, and, perhaps, further time for poster presentations. Overall however great possibility to broaden network....!!!



## PARTNERS' VIEWS & OPINIONS

Have you developed any fruitful collaboration that you will continue in the near future?

I have developed fruitful collaboration with prof. Ruskovska, my supervisor and mentor who has also become my sincere friend and taught me during STSM and give me much clear understanding of the requirements to perform a extraction of nutrigenomics data from the literature for further bioinformatics analysis. This was beneficial for my research and future work and this collaboration will be continue in the near future.



Would you like to maintain your involvement in the POSITIVE network after the end of the Action?

I would greatly appreciate efforts of particular participants who will have initiative to continue our work after the end of Action. Also, I express my willingness to be involved in the POSITIVE network in the near future.

If activities are continued, I would be very interested to stay involved, perhaps, at a somewhat lower frequency of meetings (1/year?).

Yes, of course!!





## PARTNERS' VIEWS & OPINIONS

### Social life at POSITIVE

Did you enjoy the meetings and associated social events?

The social events are as important as the scientific meetings. I was very pleased about the side activities during the COST



Yes quite a lot! Great organization in all the meetings I attended.

Very nice meetings, though perhaps time for social interaction could be enhanced (i.e. more time set aside) to allow for further networking !!!



## PARTNERS' VIEWS & OPINIONS



Meetings were well-organized and entertaining at best. I specially wish to thank the partners who amply used their time and effort to guide or organize the guided tours to show us around the historic sites of the meeting venue cities.

... I will keep you all in my heart !

I enjoyed attending the meetings in Belgrade and Olsztyn very much. For me it was opportunity to meet colleagues of POSITIVE for the first time, to enjoy the city's sightseeing and local food at national restaurants which had been organized by the local POSITIVE partners as a very good hosts.



The social events were always quite nice given the great efforts of the local organisers (although I not always stayed to attend them due to travelling schedules)...



# POSITIVE NEWSLETTER

ISSUE VIII, DECEMBER 2018

## POSITIVE New Generation !!!!

Our POSITIVE Action has certainly proven to be very productive not only from a scientific point of view but also providing a handful of beautiful babies and ...

...Who knows??? This may be the next generation of POSITIVE scientists ...

What is evident (or not???) is the **high inter-individual variability** among all of them !!!! Here is a good sample.

**Congrats to all !!!!**



ALEXIA-CHRISTINA KALTSATOU,  
BORN JANUARY 28, 2017  
DAUGHTER OF ANTONIA KALTSATOU



LUCIA RODRIGUEZ HEISS,  
BORN OCTOBER 1, 2014  
DAUGHTER OF ANA & CHRISTIAN

# POSITIVE NEWSLETTER

ISSUE VIII, DECEMBER 2018

## POSITIVE New Generation !!!!



**DEFNE BESTEPE, BORN MAY 23, 2017  
DAUGHTER OF SENEM KAMILOGLU**



**MADALENA BRONZE, BORN JULY 8, 2017  
GRANDDAUGHTER OF MARIA ROSÁRIO BRONZE**



# POSITIVE NEWSLETTER

ISSUE VIII, DECEMBER 2018

## POSITIVE New Generation !!!!



LUCAS GONZÁLEZ, BORN APRIL 4, 2017  
SON OF ANTONIO GONZÁLEZ SARRÍAS



My mum is a scientist



MARTÍN PÉREZ, BORN AUGUST 11, 2016  
SON OF ROCÍO GARCÍA VILLALBA



## POSITIVE Network - Achievements

- **8 WG meetings** (Belgrade / Murcia / Norwich / Bucarest /  
/ Olsztyn / Thessalonique / Dubrovnik / Lisbon)
- **4 Scientific Workshops and Conference** (Tours /  
Norwich / Thessaloniki / Lisbon)
- **2 Training Schools** (Barcelona / Thessaloniki)



## POSITIVE Network - Achievements

➤ **35 Short-Term Scientific Missions**

➤ **6 ITC Conference grants**

➤ **10 collaborative reviews published**    
15 additionnal in preparation

➤ **8 Newsletters**

➤ **Website** <http://www6.inra.fr/cost-positive>



COST is supported by the  
EU Framework Programme  
Horizon 2020.

Organisation

Working Groups

Events



## CONTACT US



EUROPEAN COOPERATION IN THE FIELD OF  
SCIENTIFIC AND TECHNICAL RESEARCH

### Contact us:

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: christne.morand@clermont.inra.fr

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: fatomas@cebas.csic.es

## CHAIR'S CORNER

Dear POSITIVE partners,  
Dear Friends,

This time it's the end, the Action has officially ended on December 9<sup>th</sup>. We hope you have enjoyed being involved as much as we did! In any case, from our side, it was a great pleasure to coordinate the COST POSITIVE network during the last four years. All together we have performed a great job and put forward at the international level the scientific importance and the impact of increasing our understanding of why some individuals respond to plant food bioactives consumption, while others do not. We must recognize that despite the huge and constant dedication of the POSITIVE partners, we have not yet provided a clear response. Indeed, this topic is a difficult concept, probably much more than we initially thought, that cannot be fully addressed based only on a systematic analysis of existing published studies, which were never designed to respond to this question.



However, the extensive networking activities within POSITIVE have provided some key insights and identified the gaps in knowledge and the needs for future research. And now, with the help of the Steering Committee, we will do our best to promote the POSITIVE findings towards policy makers and funding bodies, to help in getting research calls/funding to carry out concrete research on this relevant and exciting topic. Some papers are still under finalization, and we expect their publication in 2019, thanks to the maintenance of the collaborative dynamics within the POSITIVE sub-groups! Of course, The POSITIVE website will continue to be fed with the new outcomes as well as with any information of relevance for the POSITIVE community.

**So we keep in touch !!!**

**With our best wishes for Christmas and New Year !!!**

**THANK YOU ALL &  
HAPPY 2019**







EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH

**Chair:** Dr. Christine MORAND, INRA - France,  
e-mail: [christne.morand@clermont.inra.fr](mailto:christne.morand@clermont.inra.fr)

**Co-Chair:** Prof. Francisco TOMAS-BARBERAN, CEBAS-CSIC, Spain,  
e-mail: [fatomas@cebas.csic.es](mailto:fatomas@cebas.csic.es)

**Webpage:**

[www6.inra.fr/cost-positive](http://www6.inra.fr/cost-positive)