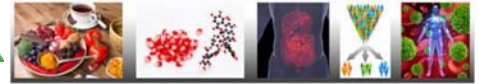


# POSITIVE NEWSLETTER



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.



© paco portillo

\* 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

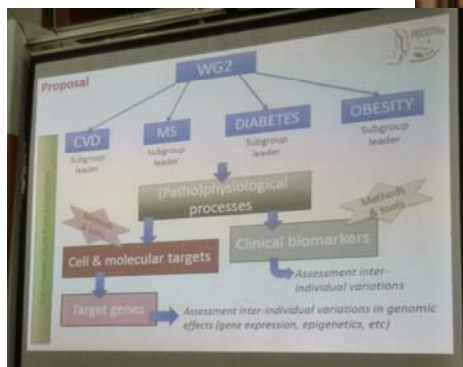
WG2 Leader

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*

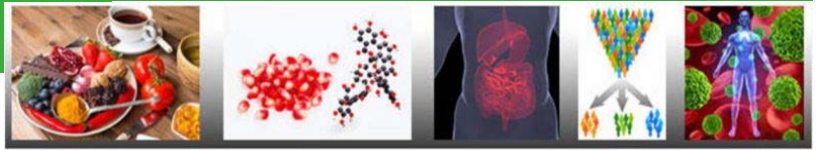


specially benefited by this dietary pattern in terms of stroke protection<sup>6</sup>. However, most of the studies have focused on macronutrients (i.e., dietary fat), leaving a huge gap of knowledge regarding other micronutrients and non-nutrients components of our food. This is especially true for 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  
© The Authors 2015

**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,

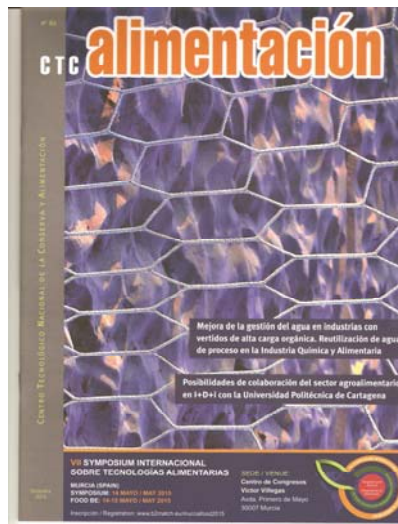
ii) encourage citizens' participation stressing the relevance and impact of the European institutions in everyday life.

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)