



POSITIVE NEWSLETTER

cost
EUROPEAN COOPERATION IN SCIENCE
AND TECHNOLOGY



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WELCOME



To introduce this 2nd 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 2nd 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

2nd COST Action POSITIVE Meeting 22nd-23rd September 2015, Murcia, Spain

The second WG1, WG2 and FG meeting of the COST Action POSITIVE FA1403 took place during the 22nd and 23rd 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.



2nd 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

15th - 17th 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 2nd 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 1st 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 phytosterols.

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 1st 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 1st online meeting took place on the 10th 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 2nd online meeting was organized the 18th 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 3rd online meeting was held the past 2nd 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 15-17th, 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,

Laurent-Emmanuel Monfoulet,
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,
Univariada de Barcelona
SPAIN



Laurent-Emmanuel
Monfoulet, INRA,
FRANCE



Antonio González-Sarrias
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

1st POSITIVE Scientific Workshop 26-27 October 2015, Tours, France



The 1st Scientific Workshop of the Cost Action FA1403 POSITIVE was held on the 26th and 27th of October 2015 in Tours, France, as a satellite symposium of the 7th International Conference on Polyphenols and Health, 2015 (ICPH: 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)¹.



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.

1st 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.

¹You 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

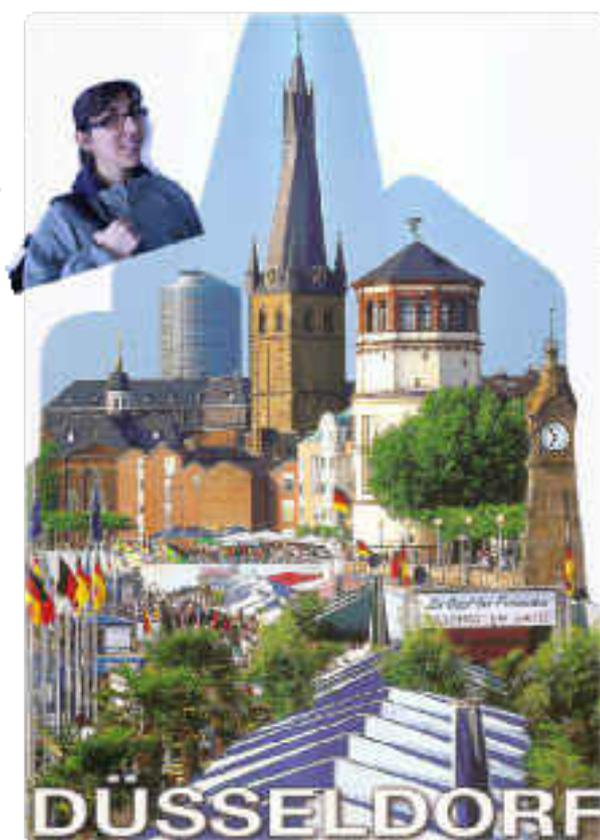
Myström. My research objective is to develop highly accurate detection methods for phytosteryl conjugates in natural sources as well as to study their bioactive properties and intestinal absorption. Phytosteryl conjugates have a high potential to reduce cholesterol levels. However, the exact mechanism 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 1st 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



*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.

***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-

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.



RESEARCH DISSEMINATION

Volunteers need to be stratified for citrus flavanone absorption in clinical

AGRICULTURAL AND FOOD CHEMISTRY

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

Marta Tomás-Navarro¹
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José L. Navarro³
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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 7th 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 1st 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

AGRICULTURAL AND FOOD CHEMISTRY

Encapsulation and Micronization Effectively Improve Orange Beverage Flavanone Bioavailability in Humans

Marta Tomás-Navarro,¹ Fernando Vallejo,² Francisco Borrego,³ and Francisco A. Tomás-Barberán^{1,4*}

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 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 Sausone¹, Ana Rodriguez-Mateos¹, Jan Heusel¹, David Falk¹, Dominik Schuler¹, Ruben Wagnhoff², Gunter G. C. Kuhnle³, Jeremy P. E. Spencer³, Hagen Schroeter³, Marc W. Merz⁴, Malte Kelm^{1,4} and Christian Heiss^{1*} for the FLAVIOLA Consortium, European Union 7th Framework Program

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

Christian Heiss • Roberto Sausone • 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. Merz • Malte Kelm • for the FLAVIOLA Consortium, European Union 7th Framework Program

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

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 ± 1 y) and older (60 ± 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

COST BRANDING REQUIREMENTS

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

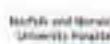
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14th -16th September

4th POSITIVE COST MEETING
and 2nd 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 2nd WG meeting gathering 57 participants. During this 1st 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 2nd 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



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