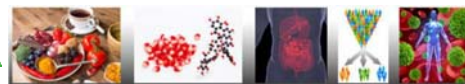




# POSITIVE NEWSLETTER



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH



ISSUE VII, JUNE 2018

## WELCOME

Dear All,

Even though the fourth year of our COST Action POSITIVE is getting to an end and the final meeting is just around the corner, we are neither thinking about the finish line nor slowing down the pace. We celebrated a very successful 7th Working Group meeting the past March in Dubrovnik, and are now getting ready for the Final POSITIVE Conference in September in Lisbon. The Action is in a high gear, with the partners strongly engaged in networking, research dissemination activities and effective implementation of short-term scientific missions, either hosting early stage researchers in their labs or undertaking the training themselves. The word "final" will probably be tossed around the coming months, however we should keep in mind that it is not the end. It is, indeed, the commence of new collaborations and projects that will allow us to continue working together and getting to know each other.

This time, more than ever, we wish to thank all contributors who devoted their time and efforts to make this issue as well as all the previous newsletters happen.

Hope to meet you all in Lisbon for a final meeting (and party!)

THE FG

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## NEWS FROM THE ACTION

### 7<sup>th</sup> COST Action POSITIVE Meeting, 2018 6<sup>th</sup> – 7<sup>th</sup> March Dubrovnik, CROATIA

The POSITIVE partners continue working hard towards the achievement of their respective objectives and met once more in March 2018, this time, in the beautiful surroundings of the city of Dubrovnik (Croatia). The meeting was held at the Valamar Lacroma Dubrovnik Hotel and it was kindly organized by **Dr. Nada Knezevic**, Director of the Regulatory Affairs Department and by **Dr. Suzana Rimac Brncic** from the University of Zagreb.

We take this opportunity to **thank them for the organization** of the meeting and for the great time spent in Dubrovnik!



## RESEARCH HIGHLIGHTS

### Work Group 1

Leader: Tom VAN DE WIELE

Co-leaders: Claudine MANACH & Rikard LANDBERG

The members of the WG1 gathered in Dubrovnik to continue working and discussing about the different tasks they still need to complete. They first talked about the **Data-base** that is under construction and will collect as many **Plant Bioactive Metabolites** as possible reported in urine and plasma samples, together with their known health benefits and analytical needs.

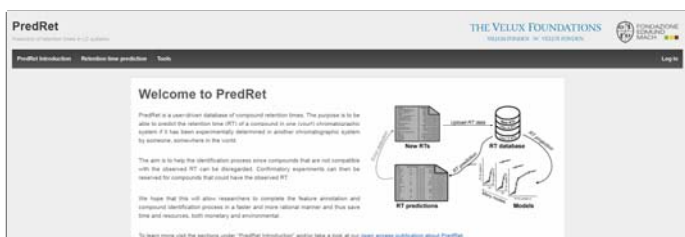
There were also further discussions in the area dedicated to **Metabolomics**. A few important issues still need to be done for the completion of the manuscript regarding the multiplatform coverage test such as the normalization of the retention times (RT) of the compounds analysed in the different platforms, and the preparation of some general guidelines for a reference method applied to untargeted analysis. A few journals are under consideration for this publication, after which, a few other activities will follow: validation of this method, preparation of combined spectra and comparison of sample preparation and extraction protocols provided by different partners.

Another interesting issue commented during the meeting was the utility of applying RT predictive tools such as the database **PredRet** (<http://predret.org/>) for the analysis of metabolites derived from plant food bioactive compounds. INRA will be testing this database with known compounds.



Progress on the work of the **Microbiome and Gene Variants** was also further discussed. Efforts are still directed towards the identification of key molecules (genes & proteins), both of human and microbial origin, and pathways involved in the metabolism and absorption of the plant bioactive compounds as well as for the related and relevance genomic information: polymorphisms, presence in different microbial groups, etc. Enhancing knowledge in this area remains essential for the understanding of the bioavailability of plant bioactive compounds and the variability in humans to metabolize and absorb these compounds. The need to reinforce the workflow in this area by improving means of sharing knowledge between subgroups was highlighted.

Last, but not least, a number of **Knowledge gaps and Research needs** for the specific types of plant bioactive compounds were revised and discussed. There are still many unclear aspects that need further and thorough investigation. Finding the key factors, i.e. most relevant microbial and human enzymatic activities, major metabolites derived from this activity, main transporters across the intestinal barrier, will allow for a better understanding of the interindividual variability in the bioavailability of the plant bioactive compounds and their link to variability in the cardiometabolic responses. A more integrated approach is needed bearing in mind the general idea that different compounds and metabolites from different diets may have the same benefits!





## RESEARCH HIGHLIGHTS

### Work Group 2

Leader: Ana RODRIGUEZ-MATEOS

Co-leaders: Eileen GIBNEY &  
Dragan MILENKOVIC

#### Meta-analysis subgroup

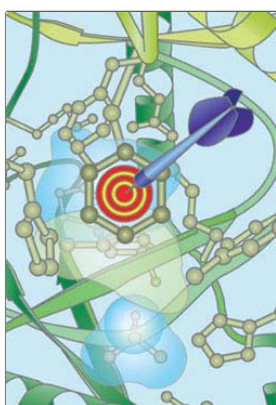
The activities programmed within this subgroup have progressed well and a number of meta-analyses have been now completed and published whereas a few others should be finished within this last period of the COST Action, covering like this the cardiometabolic effects of a variety of plant bioactive compounds and a thorough examination of the factors that may influence the responses and were identified and available in the published RCTs collected. In addition to a combined revision of all these publications to have a general overview of the current situation and the issues that still need to be further investigated, the collaboration with the WG1 to explore the feasibility of adding together bioavailability studies and cardiometabolic effects was considered and taken on board by some partners of both groups. Awareness of the importance of other key factors not yet incorporated into the analysis of the cardiometabolic effects such as microbiome and the host genetic variants were remarked. Potential reviews of publications related to these areas were proposed and will be discussed with the WG1 members.



In terms of future proposals, a working sub-group was organised with the aim of preparing some grant applications for future studies incorporating many of the recommendations and best practices that will emerge at the end of the Action from all the outcomes of the WG1 and WG2.



#### Cell & Molecular Targets subgroup



The meeting of the cell and molecular target subgroup was led by Dr. Tatjana Ruskovska who presented an overview of the progress done on the revision of pre-clinical evidences. The strategy employed was a combination of literature search, bioinformatics tools and docking studies to identify genes, transcription factors and pathways that may be implicated in the response to the bioactive compounds in relation with cardiometabolic endpoints.

The work done in animal models was well advanced for some groups of compounds (flavanols) with several genes and pathways identified. Further studies with those data were proposed such as finding out relevant information about those genes in humans and exploring the interindividual variability. After this study is completed, other bioactive compounds should follow. Regarding the revision of *in vitro* studies, the work on flavanols and phytosterols is still in progress, with data extraction completed and the bioinformatics analysis just started. The main aims are the same as in animal studies, i.e. finding key regulated genes and pathways in human cells exposed to these compounds.

Work on human clinical trials looking at gene expression regulation by plant bioactive compounds is now further reinforced with the organization of a new subgroup led by Dr. Vauzour. A considerable number of nutrigenomic studies using microarrays was collected and are ready for data extraction.



In the final gathering of WG2 a few other tasks were proposed such as the collaboration with the Gene Variant group to progress on the understanding of gene variants with an effect on cardiometabolic responses to plant bioactives. Other various discussion as to how to complete data analyses and presentation of the meta-analyses took also place during the meetings.

## RESEARCH HIGHLIGHTS

### Work Group 3

Leader: Baujke DE ROOS

Co-leader: Marina HEINONEN



The WG3 meeting was moderated in place by Professor Tomás Barberan and was focused mostly on the development of a **Roadmap** with all the Action outputs and specifically directed to stakeholders and Brussels. It was

proposed the preparation of several white papers that will include the main results of the work done in the Action and that will contribute to increase awareness of the complexity of the human interindividual variability in response to the intake of bioactive compounds. These articles will translate the main results of the Action into practical applications and what are the things that remain to be done in future research plans with a focus on 1) stakeholders, 2) policymakers and 3) scientist working in the field. Regarding the scientific community, the work will be published in the form of reviews in a relevant journal.



During the Working Group meetings in Dubrovnik the upcoming activities of the Focus Group have been revised. It was decided that members of the FG will be actively involved in the elaboration of the POSITIVE Research Roadmap and will contribute to the production of the dissemination material dedicated to stakeholders. In addition to the regular actions connected with reporting on ongoing progress of the Action, research papers published and scientific missions completed, the Focus Group will commit to further dissemination of POSITIVE outputs during events dedicated to general public and industrial stakeholders. Additionally, potential ways of leveraging the ECI-oriented networking base developed by the Think Thank group (Getting to know initiative) were discussed.

### Focus Group

Leader: Mayte GARCÍA-CONESA

Co-leader: Iwona KIEDA





## RESEARCH HIGHLIGHTS

## Think Thank Group

Leaders: Rocío GARCÍA-VILLALBA &amp; Pedro MENA



The 5<sup>th</sup> Think Tank Group (TTG) meeting in Dubrovnik was scheduled as an ordinary meeting of the Early Career Investigators (ECIs). The meeting was open to the whole ECI community since online participation was available. This helped to increase the numbers of attendees, being a good way to continue building the network of young scientist in plant bioactives and inter-individual variability. The meeting gathered 11 participants: Rocío García Villalba, Geoffrey Istas, Banu Bayram, Viktorija Maksimova, Eirini Deligiannidou, Paul Young Tie Yang, Dorrain Low, Mar García-Aloy, Teresa Serra, Maria Rosa Tumulo, and Pedro Mena. Three of them were introduced as new members, which showed the interest of the ECIs to be involved in the Action activities, even if it is finishing. The meeting started with a short introduction to the new ECI members about the goals reached in the last three years and the progresses that some ECI members have achieved in: 1) the TTG project 'How to report interindividual

variability in scientific publications', and 2) writing a perspective article as a result of the Workshop in Thessaloniki (September 2017). Three important issues were discussed throughout the meeting:

**New steps for a perspective paper related to the 3rd Sci. WS.** This project had been somehow inactive during the last 5 months. The strategy to finish the paper was discussed and now there is a final manuscript ready to be reviewed by all the authors and sent to the POSITIVE leaders for comments and approval.

**New steps within the 'How to Report Interindividual Variability in Publications' project.** This project needs to be finished quite soon since it could be part of a Special Issue with the main conclusions of the Action. Moreover, the project will be presented by Dr. Aleksandra Konic-Ristic at the last Sci. Workshop (to be held in Lisbon, September 25-26, 2018). In order to finish this project, a Short Term Short Mission will be carried out by Marina Nikolić, from the Center of Research Excellence in Nutrition and Metabolism, Institute for Medical Research, University of Belgrade (Serbia), in the research group of Dr. Pedro Mena and Prof. Daniele Del Rio at the University of Parma (Italy) during June 2018. Dr. Konic-Ristic will also take active part in this collaboration.

**Ideas for the coming online meetings and the "Get to Know" sessions.** All the attendees agreed on the need for new activities favouring the participation of all the ECIs in the monthly online meetings. After discussion, it was decided that the new ECIs will introduce themselves and that a new, quick round of presentations will be carried out. The new round will be focused on presenting the current situation of each ECI and the possibilities to collaborate in the future. Following these ideas, a successful meeting was carried out in April. Up to 12 ECIs attended the online conference. We had 3 very nice presentations and subsequent discussions with Margherita Dall'Asta, Viktorija Maksimova, and Paul Young. A new meeting has been scheduled for June.



## RESEARCH HIGHLIGHTS

### SOCIAL EVENTS

Thanks to the great hospitality of the local organizers, POSITIVE partners were offered the opportunity to experience the wonderful culture, heritage and cuisine of Dubrovnik. During a guided tour we had a chance to trace the mighty city walls, explore the shooting scenes from Game of Thrones, and admire incredible sea views. After a day-long discussions the partners were also invited to a **traditional Croatian dinner**, where they could taste local specialties and carry on networking in a pleasant and relaxing atmosphere.



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## SAVE THE DATES

### Lisbon welcomes you to the ...

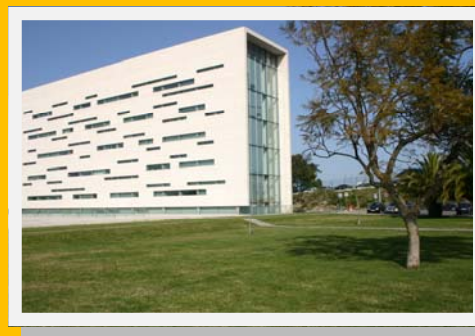
**COST Action POSITIVE  
JOINT WG & MC Meetings**



**VENUE:**

Vip Executive Art's Hotel  
Avenida D. Joao II, n°47  
1998-028 Lisboa

**Final POSITIVE Conference  
25-26<sup>th</sup> September 2018**



**VENUE:**

NOVA University rectory building  
Campus de Campolide, Lisboa

### LOCAL ORGANIZERS:

Dr. Claudia Nunes-dos Santos ([csantos@ibet.pt](mailto:csantos@ibet.pt)) (iBET, Oeiras, Portugal)  
Dr. Maria Bronze (FFU Lisboa, Portugal)  
Dr. Paula Pinto (IPS-ESA, Santarem, Portugal)

## JOIN US ON TWITTER



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**@Cost\_POSITIVE**

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

## SAVE THE DATES

And Lisbon also welcomes you to the...

2<sup>ND</sup> CONFERENCE ON

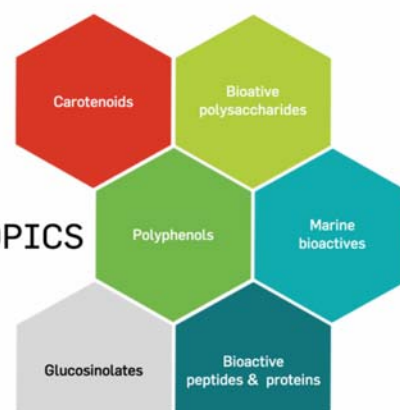
# FOOD BIOACTIVES & HEALTH



26-28 SEPTEMBER 2018 LISBON PT



### MAIN TOPICS



**T**he conference will gather experts on different types of food bioactive compounds and will cover a wide range of aspects of the research in this area: metabolism, effects & mechanisms, functionalisation, characterisation, bio-transformation, interactions, novel compounds.

If you need further information please contact:

**FBHC 2018 Organizing Committee**  
**2<sup>nd</sup> International Conference on Food Bioactives and Health 2018**

E-mai: [fbhc2018@itqb.unl.pt](mailto:fbhc2018@itqb.unl.pt) or visit the website at: <http://www.itqb.unl.pt/fbhc2018>



## SHORT TERM SCIENTIFIC MISSIONS

### EIRINI Deligiannidou from Greece went to the UEA, Norwich, UK

Winter in the UK can be rather bad, however, in this Action we share the belief that there is enough sun for everyone, so I packed a bit of the Greek sunshine and started my journey to the beautiful city of Norwich. From January the 8<sup>th</sup> till March the 15<sup>th</sup> I was privileged to work in two well respected institutions: The Norwich Medical School of the University of East Anglia and The Earlham Institute in Norwich, UK, under the joined supervising of Prof. Anne Marie Minihane (MED) and Dr. Wiktor Jurkowski (EI) on the subject of "Data integration to study flavonoid metabolism".



Madrid to Mumbai.

Both my supervisors have been with me every step of this mission, providing guidance and support and encouraging me to do more and aim higher, which I find priceless. Never have I missed a smile from them, which made Norwich feel like home even more and professional business aside, we had great fun!



On a non-scientific point of view, I have experienced living abroad which was life changing, visited the beautiful Leeds Castle in Canterbury and also picked up the habit of drinking my tea with milk! Regarding the city, long walks, is something

## STSM Topic: Data integration to study flavonoid metabolism



During this mission I was located at The Bob Champion Research and Education Building, working closely with both my supervisors on finding the best possible way to put the knowledge of published papers on flavonoid

metabolism, into an illustration that would be publicly available to the research community to further investigate, amend and improve. My task was to extract information from older and new literature, regarding the metabolic fate of flavan-3-ols and use illustrating tools such as PathWhiz and PathVisio to visualize the pathway. Using existing knowledge from the POSITIVE members as well as databases such as PhytoHub and PubChem, I have gathered information on the metabolites involved in this pathway which led to its illustration via PathVisio and publication on WikiPathways.

Through this mission I have gained knowledge on the use of metabolic pathway illustrating tools, the importance of keeping track of your work via (sometimes endless) spreadsheets and also created a picture that was actually a thousand words (or rather reactions!). Furthermore, I have learned how an open office works, participated in the monthly meetings of the department of Medicine learning even more about ongoing research projects and have met amazing people from

to do in Norwich, which is a lovely small city with warm people to make up for the cold weather and also England's first UNESCO City of Literature!

The University of East Anglia is a huge institute with a beautiful campus that I can only describe as a "condensed version of the world". Surely this mission had widened my horizons personally and professionally and for this I am thankful to this Action and especially to the STSM coordinator Dr. Aleksandra Konic Ristic, who helped to every step of my application and to my mentor Dr. Christos Kontogiorgis who introduced me to POSITIVE.

Lesson learned: **"Amazing things happen, if you just stay POSITIVE!"**



## SHORT TERM SCIENTIFIC MISSIONS

Our STSM took place at King's College of London under the supervision of Dr. Ana Rodríguez Mateos. Casually, our STSM coincided at the same time of the year and we were able to work together enriching more the STSM experience. Our mission was focused in the analysis of phenolic compounds in plasma and urine of high cardiovascular risk patients after beer and non-alcoholic beer ingestion (Víctor's job) and measurement of anthocyanin-derived metabolites after consumption of capsules enriched with anthocyanins (Michele's task). For these purposes we used a solid phase extraction (SPE) protocol and the samples were analysed using an Orbitrap mass spectrometer. These new approaches are needed to enhance the knowledge of how the ingestion of food with high amount of polyphenols could affect and modulate health.

## Víctor Micó Moreno & Michele Tassotti visited King's College London, UK



### STSM Topics:

**Michele Tassotti: Measurement of anthocyanin-derived metabolites in plasma using LC-MS.**

**Víctor Micó Moreno: Measurement of beer's polyphenol levels in urine of an interventional study with beer in high cardiovascular risk patients.**

For us, the realization of this STSM was a great opportunity to know other laboratories and other ways of working different from our respective laboratories.

We would like to thank Dr. Ana Rodríguez Mateos' group the great welcome to both of us and all the help and support provided to carry out the STSM. In addition to this, the possibility to know other researchers will have a great impact in our career and it could open future opportunities and collaborations among our groups.

But, The STSM means more things. It was a great personal experience. To us, this STSM was also the chance to meet with the lab group after work, visit beautiful places in London, take a lovely lunch by the Thames riverside enjoying the sun (yes! Sun exists in London!) and meet new people. To conclude, we want to thank the POSITIVE COST Action the opportunity given to us by these STSM and we would like to highly recommend them to other researchers due to the **great experience both professionally and personally.**



**Michele Tassotti**

**Víctor Micó Moreno**



## SHORT TERM SCIENTIFIC MISSIONS

### Ralph Rühl from Hungary visited University of Vigo, Spain

As the plan was to stay for two months, I had the fantastic idea to drive my car across the whole of Europe. Well, it's just 3200 km and 31 h of driving without a break. Sounds easy, so let's go ! Vamos a la playa ! Car was checked and all packed. A short stop at my family's in Germany and the Atlantic coast in France went all smoothly, till we drove passed the sign '50 km to Vigo' at the highway. At this exact point my car



started making very strange noises. Lucky enough Vigo was reached and we got to our apartment by the harbor. Just when the car made extremely loud not-normal noises. It's better not to mention which car brand.

The next day we initiated intercultural relationships with some local car-repair guys, Diego and Carmen, manager and sister, respectively. And quickly we learned that there are small differences between the German way of organization and the Spanish one. Especially measures of time were handled slightly in a different way. Diego and Carmen tried to teach us Spanish, starting with the most famous Spanish word 'mañana'. Diego and Carmen learned also, like all young Spanish people, the language of their autonomous region at school. In this case the 'autonomous region of Galicia', so, Galego. We even learned this language: "mañá". English, German, French or Hungarian were not so well distributed in Galicia as I experienced, but thank God at the University we could communicate well. After 2-weeks, the car was finally repaired, immediately

Research went very well and all in time, till we had a gigantic wood fire coming from Portugal and entering Vigo. The whole University surrounding was under fire and the University closed down for a couple of days. The apartment in the top floors of the building was filled completely with black smoke. This night was spent at the harbor, near the water, while the air was like cigar smoke till the next morning.



With a small delay, our project was finalized like planned. We found for our novel identified lipid hormone, new unique nutritional precursors present in food as well as in the human organism. Usually nutritional precursors of hormones were named Vitamins and **together with our Vigo cooperators, we patented and will publish ours and named it: Vitamin A5.**

**PATENTED**

### STSM Topic: Identification of the new lipid hormone 9-cis-13,14-dihydro-retinoic acid (9CDHRA) after supplementation of nutritional

broken again at the same place and so on. Thank God, we had a guy named "Jesus" as our colleague in our labs and he thought us devotion and patience.

In the lab, we started quickly our projects and all went like expected, more complicated and slowly like planned. But, nevertheless, the nice food in Galicia (and in general in Spain), and especially some of the Spanish wines (Rioja) diluted all troubles quickly. As Vigo is the second biggest fishery harbor in the world, after Tokio, all what the sea contained was eaten, like crabs and 'calamares' and mostly the local specialty 'percebes'. They look like aliens, but it is an animal which is attached to the ground and filters plankton out of the sea water. The only thing which we didn't eat, were our new friends in the bay: the five dolphin families.



The way back from lovely Vigo by car went very well and the 45 bottle of excellent Spanish/Portuguese wine arrived also in well shape back to Hungary. Thanks to the COST "POSITIVE" and to Vigo and all it's people, except two. Hasta la vista, hasta luego, Vigo, I'll be back ! **Ralph Rühl**

## SHORT TERM SCIENTIFIC MISSIONS

My STSM took place between the 5<sup>th</sup> of December 2017 and the 15<sup>th</sup> of December 2017. I was hosted by Dr. Cláudia Santos at the Molecular Nutrition and Health research from ITQB, Universidade Nova de Lisboa, Portugal. The aim of my mission, as part of the WG2, was to update an ongoing meta-analysis exploring inter-individual variability after consumption of flavanols from cocoa, apple and tea on the cardiovascular system. During this short stay, under the supervision of Dr. Paula Pinto, I learned how to perform a meta-analysis using the Comprehensive Meta-Analysis software to assess the overall effect of flavanol consumption. In addition, I familiarized with subgroup analyses by studying how flavanol consumption is affected by individual variables such BMI or gender. With Paula's great help, I managed to extract and patch the required papers in an intensive short period of time.

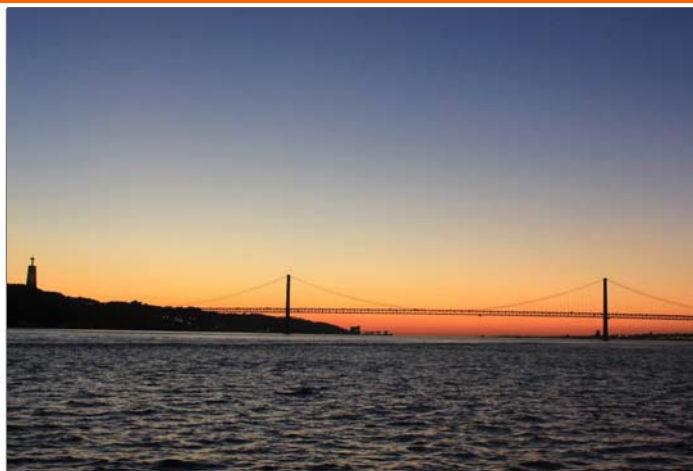
## Paul Young Tie Yang from UK visited ITQB Nova, Portugal



## STSM Topic: Inter-individual variability on the effects flavanols on the cardiovascular system: systematic review and meta-analysis

Aside of learning about meta-analysis, this STSM has been an opportunity for me to meet young researchers, attend a PhD Viva and meet other members of the COST action. From the touristic point of view, Lisboa has a lot to offer, wonderful historic places, sunny terraces, great food and a very positive atmosphere. All this contributed to make my STSM a great experience.

Once again, I would like to thank everyone from Cláudia's lab for such a great and warm welcome from the very first day and I am definitely looking forward to meet the group again for the final COST POSITIVE meeting in Lisboa.



Paul Young





## SCIENTIFIC EXPERT'S OPINION

**Dr. ANNE-MARIE MINIHAHE**  
 Nutrition and Preventive Medicine,  
 Norwich Medical School, UEA, Norwich, UK



**T**he health benefits of plants foods and plant bioactives are widely recognised, which is the basis for typical recommendations to consume at least two servings of fruits and three servings of vegetables per day. Low intake of fruit and vegetables is among the top 10 risk factors for mortality worldwide. In the global *PURE* cohort, up to a 40% reduction in the risk of chronic diseases was evident in high versus low consumers of fruit, vegetables and legumes [1]. Although popula-

tion effects-sizes have been widely reported, our understanding of how an individual will respond to increased intakes is

[NCT01922869?term=COB&cntry=GB&rank=1](https://doi.org/10.1093/ajcn/88.5.1171) ).

Prospective cohort and genome wide analysis studies, where power allows, should investigate response to treatment in population subgroups (e.g. males vs. females, old vs. young). A greater use of individual participant data meta-analyses will allow data from smaller investigations to contribute collectively to a more comprehensive understanding. Models may be built from the acquired knowledge, which will be improved as new data and knowledge are generated.

Given the large effect of plant bioactives on health, and the fact that <25% of global populations meet current recommendations, **the identification of key determinants of metabolism and bio-efficacy is a worthy journey**. Such knowledge will inform refinement of current dietary guidelines (dose and plant foods), and the targeting of products and recommendations towards consumers who are likely to be most responsive and gain most health benefits. Developments in pharmacogenetics, and increasingly bespoke approaches to prescribing, should provide us with encouragement.

1. Miller, V, et al., *Lancet*, 2017. 390:2037-2049;
2. Cassidy, A and Minihane, AM. *Am J Clin Nutr*, 2017, 105:10-22.
3. Manach, C, et al., *Mol Nutr Food Res*, 2017, 61:1600557-1600573.



## UNRAVELLING THE SOURCES OF INTER-INDIVIDUAL VARIABILITY IN RESPONSE TO PLANT BIOACTIVES: A long way to go, but worth the 'journey'

almost entirely lacking.

The aetiology of the large heterogeneity in response is likely to be an inter-play between (epi) genetic profile, physiological status (e.g. sex, microbiome speciation and metabolism, and menopausal status) and behavioural attributes (e.g. prescribed medications, and habitual diet) [2, 3]. Such variables affect bioactive bioavailability, metabolism and bio-efficacy. Many argue that gaining an understanding of determinants of response is a mammoth task, with the picture likely to be too complex, and the impact of individual variables too small to allow a meaningful predictive framework to be derived. This is a pessimistic view. *'Rome was not built in a day'*. We need to be patient. Although a comprehensive understanding is lacking, and research is somewhat fragmented, investigating the impact of one factor at a time, a growing number of studies are beginning to describe potential sources of variability. Unravelling factor\*plant bioactive effects on health is best approached using prospective recruitment methodologies on the basis of the variable(s) of interest in adequately powered studies, such as the approach taken in the ongoing COB trial (<https://clinicaltrials.gov/ct2/show/>



**RESEARCH DISSEMINATION**
**PUBLICATIONS- WG1**

The research on a natural colorants is an important part of current science regarding food technology and nutrition. In this context, betalains - water-soluble natural pigments - are an interesting and important group of phytochemicals which chemical structure is based on the skeleton of betalamic acid linked with a cyclo-3,4-dihydroxyphenylalanine residue in case of betacyanins or with different amino acid in case of betaxanthins. Betalains are pigments responsible for **red-purple (betacyanins)** and yellow-orange color (betaxanthins) present only in plants belonging to Caryophyllales and in some species of higher fungi.



Food Research International 108 (2018) 530–538


 Contents lists available at [ScienceDirect](https://www.sciencedirect.com)
**Food Research International**

 journal homepage: [www.elsevier.com/locate/foodres](http://www.elsevier.com/locate/foodres)


## The impact of the matrix of red beet products and interindividual variability on betacyanins bioavailability in humans

 Wieslaw Wiczowski<sup>a,\*</sup>, Ewa Romaszko<sup>b</sup>, Dorota Szawara-Nowak<sup>a</sup>, Mariusz K. Piskula<sup>a</sup>
<sup>a</sup> Institute of Animal Reproduction and Food Research, Polish Academy of Sciences in Olsztyn, Tuwima 10 Str., 10-748 Olsztyn, Poland

<sup>b</sup> NZOZ Atarax, 1 Maja 3 Str., 10-117 Olsztyn, Poland


Due to their relative stability and their very interesting color, betalains are widely used in the food industry for the coloring of a wide range of food products. The human body is very often exposed to these natural compounds. In addition, there are evidences that betalains display strong biological activities. In spite of the above facts, the fate of betalains in the human organism has not been well recognized yet. To exhibit positive effects of betalains in the human organism, these compounds have to first enter the human systemic circulation. Since consumption of food rich in these pigments does not have to imply at the same time its good bioavailability, adequate estimation of betalains bioavailability from different foods is a prerequisite for further consideration of their involvement in the physiological processes. In addition, in the course of bioavailability studies, apart from the analysis of which compounds were absorbed and metabolized, it is also necessary to track the impact of the food matrix on bioavailability as well as the effect of interindividual variability. With regards to the food matrix influence, the bioavailability of phytochemicals from liquid matrix will be different from that from the solid matrix. Equally, it will be different from a raw matrix than from the macerated/softened matrix.

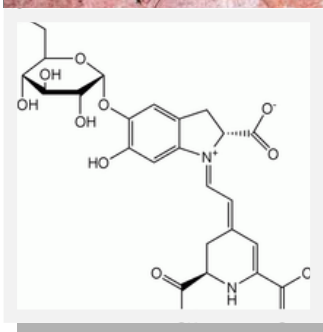
In relation with the interindividual variability influence, bioactive compounds considered bioavailable for one individual may not behave in the same way for another. A significant role in these processes may be imputed to factors addressed as genetics, sex, age and disease states. Genetic variation of enzymes involved in the absorption and metabolism of phytochemicals may result in a complete absence or enhanced expression of a functional enzyme. Up- and down-regulation of gene expression in response to an altered cellular environment may achieve the same range of metabolic function, but often in a less reliable, predictable and time-dependent manner. Hence, these important issues are under consideration of the POSITIVE Action.

Overall, there was no data on the differences in betalains bioavailability for various food matrices and comprehensive studies in relation to interindividual differences as far as the absorption and biotransformation of betalains. In Poland, and also in Europe and worldwide, betalains are known mainly as the pigments of a red beetroot - a vegetable which is very often eaten in a cooked form as a salad, fresh juice, soup or as a fermented product.



## RESEARCH DISSEMINATION

## PUBLICATIONS– WG1



Red beetroot is a very rich source of betalains, and because betalains are potent antioxidants resulting from the structure of their molecules, therefore, among other, red

beet is placed among the ten vegetables characterized by the strongest antioxidant properties.

The analysis of the red beet products matrix and interindividual variability impact on **betacyanins bioavailability** in humans presented in the recent article of Wiczkowski et al. (Food Research International, 2018, 108, 530-538) showed that betacyanins bioavailability from juice and crunchy slices is similar, with the matrix of products consumed having an impact on betacyanins excretion profile, and the phenotype of volunteers affecting betacyanins excretion rate. Briefly characterizing this work, it should be pointed out that except for the difference in the matrix, red beet products, namely juice and crunchy slices, used in that study contained betanin and isobetanin but in different ratio of these pigments, i.e. 9 : 1 and 6 : 4, respectively. Further, urine samples examined by HPLC-DAD-MS method after the consumption of both products contained not only native betacyanins but also their aglycones. In the case of juice, the highest betacyanins urine excretion rate was observed within the first 2 hours, while in case of crunchy slices within the period of 2-4 h. As the Authors suggested, this phenomenon may result from a more easier absorption of betacyanins from juice than from the matrix of crunchy slices which had to undergo softening under the influence of the digestive process to allow the release of betacyanins from this matrix.

Further, among volunteers, a high interindividual variability in the average total betacyanins excretion rate and in the fraction of betacyanins dose eliminated in urine was found. However, it should be emphasised that the same volunteers were characterized with the highest and the lowest value of these parameters. The Authors indicate that two

reasons for the variability observed may occur, namely the activity of intestinal bacteria, and the genetic variation which may influence the degree of absorption, metabolism, and excretion of betacyanins.

Taking into account the aims of POSITIVE, further studies are now needed to discover the gut metabolism of red beet betacyanins as well as how the paths of absorption and metabolism of betacyanins in regard to this process are exactly shaped.

**Genetic variation of enzymes involved in the absorption and metabolism of phytochemicals may result in the complete absence or enhanced expression of a functional enzyme. Up- and down-regulation of gene expression in response to an altered cellular environment may achieve the same range of metabolic function, but often in a less reliable, predictable and time-dependent manner.**

This article is available at.

<https://reader.elsevier.com/reader/sd/90504A54036B5A147BCBD04A3D82508E1E09AA200E6EB5CCAC0785FD6871BAF47E8FC100EC7D4F883BB7E22CF22C77BE>



## RESEARCH DISSEMINATION

## PUBLICATIONS– WG2



In the Protein chemistry, Proteome analysis and Epigenetic signaling (PPES) lab, PhD candidate Ken Declerck's and Prof. Wim Vanden Berghe's research is focusing on identifying molecular inflammaging mechanisms that drive epigenetic clock progression.

Full article available at: <https://www.sciencedirect.com/science/article/pii/S0047637417302476>

Videocast of interest: <https://videocast.nih.gov/summary.asp?Live=19257&bhcp=1>

Mechanisms of Ageing and Development xxx (xxxx) xxx–xxx



Contents lists available at ScienceDirect

## Mechanisms of Ageing and Development

journal homepage: [www.elsevier.com/locate/mechagedev](http://www.elsevier.com/locate/mechagedev)



### Back to the future: Epigenetic clock plasticity towards healthy aging

Ken Declerck, Wim Vanden Berghe\*

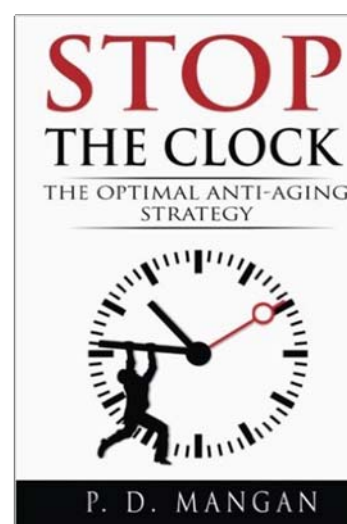
*Laboratory of Protein Chemistry, Proteomics and Epigenetic Signaling (PPES), Department of Biomedical Sciences, University of Antwerp (UA), Belgium*

A deeper understanding of the epigenetic mechanisms that might be implicated in aging can be applied in therapeutic nutritional or pharmaceutical rejuvenating interventions to promote healthy aging, or to prevent inflammatory-related disorders such as cancer, cardio-metabolic and neurodegenerative aging diseases.

Approximately 100 years ago, Albert Einstein proposed that time is a relative concept. Einstein's theory of relativity states that time and space are not as constant as everyday life would suggest. He suggested that the only true constant, the speed of light, meant that time can run faster or slower depending on gravity in space, and how fast you are travelling. Today, we face another paradigm of nonlinear dynamic time scale in biological aging. In contrast to your chronological aging since birth, biological aging is more variable and flexible in response to the environment.

Variable speed of biological aging can be determined by measuring DNA methylation intensities of your epigenetic clock. Remarkably, different lifestyle factors (smoking, stress, high caloric food, pollution) can speed up biological aging relative to your chronological age, whereas other factors (healthy diet, exercise) make you younger. For example, healthy centenarians with a Mediterranean diet may have a biological age of 80, but a chronological age of 100. Reciprocally, heavy smokers may have a biological age of 100, but a

chronological age of 80, with advanced disease/mortality risk. As such, **the epigenetic clock signature could be used as a lifestyle management tool to monitor healthy aging, to evaluate preventive interventions against chronic aging disorders and to extend healthy lifespan.** In addition, the epigenetic DNA methylation clock signature is increasingly used as a biomarker to estimate aging-related disease susceptibility and mortality risk.





## RESEARCH DISSEMINATION

## PUBLICATIONS– WG2










Overall analyses corroborate the benefits of Anthocyanins and Ellagitannins but factors influencing these effects remain poorly understood: Further research in the area is needed.



International Journal of  
Molecular Sciences

Review

## Meta-Analysis of the Effects of Foods and Derived Products Containing Ellagitannins and Anthocyanins on Cardiometabolic Biomarkers: Analysis of Factors Influencing Variability of the Individual Responses

María-Teresa García-Conesa <sup>1,\*</sup> , Karen Chambers <sup>2</sup>, Emilie Combet <sup>3</sup> , Paula Pinto <sup>4,5</sup> ,  
 Mar Garcia-Aloy <sup>6,7</sup> , Cristina Andrés-Lacueva <sup>6,7</sup>, Sonia de Pascual-Teresa <sup>8</sup> , Pedro Mena <sup>9</sup> ,  
 Aleksandra Konic Ristic <sup>10,11</sup>, Wendy J. Hollands <sup>2</sup>, Paul A. Kroon <sup>2</sup>, Ana Rodríguez-Mateos <sup>12</sup>,  
 Geoffrey Istaş <sup>12</sup>, Christos A. Kontogiorgis <sup>13</sup>, Dilip K. Rai <sup>14</sup> , Eileen R. Gibney <sup>15</sup> ,  
 Christine Morand <sup>16</sup>, Juan Carlos Espín <sup>1</sup> and Antonio González-Sarrías <sup>1,\*</sup> 

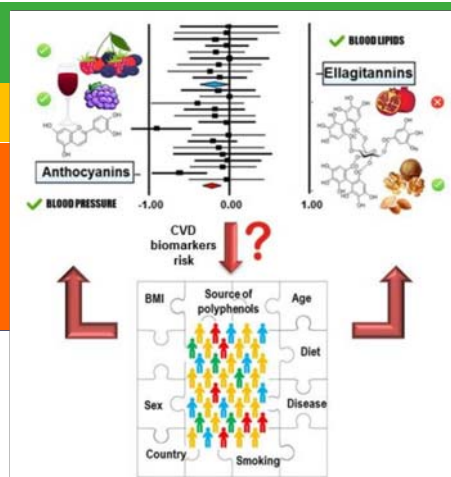
Following the main aims of POSITIVE, and, in particular, the objectives of the WG2, i.e. understanding the interindividual variation in the responsiveness to plant bioactive compounds regarding cardiometabolic endpoints, we have now completed and published a 3<sup>rd</sup> meta-analysis in which we have compiled the effects of berries, grapes, nuts and pomegranate containing as the major bioactives, ellagitannins and (or) anthocyanins, on a number of cardiometabolic markers. The results corroborated that, globally, these products have a benefit on some lipid markers (waist circumference, WC, total-cholesterol, HDL-cholesterol), blood pressure or flow mediated dilation (FMD). The size of these effects is small to moderate but continued intake of these products may contribute to reduce or maintain lower levels of these biomarkers. We detected some differences between products with: i) berries and grapes being more effective at reducing blood pressure, ii) nuts and pomegranate resulted better regulators of LDL-cholesterol, triglycerides (TAGs) or glucose. But these differences cannot be yet solely attributed to differences in ellagitannins or anthocyanins composition.

Nevertheless, and as already stated in our previous meta-analyses, the analysis of the influence of various factors (baseline BMI, sex, age, health status, smoking, country where the study was carried out) on the effects of these foods and

food products is limited and inconclusive mostly due to the small number of studies carried out with specific subpopulations e.g., only women or men, or people with normal BMI (<25 Kg/m<sup>2</sup>), or patients with a specific condition, etc. Also, and, very importantly, the studies carried out so far did not describe thoroughly some of these characteristics in the investigated subpopulation and have missed out other important ones such as the ethnic group, dietary habits, lifestyle, etc... It is thus not yet possible to come up with any conclusion as to any particular condition or subpopulation that could benefit from the intake of these products better than others. More and better studies are surely needed in this direction.

Equally important is to understand whether the benefits of the intake of bioactive compounds are specific of each type of product and compound or whether we are looking at some common benefits of a wide range of these dietary bioactive compounds, perhaps acting through common mechanisms *via* the intestine? Doses and duration of the interventions still remain poorly understood and should also be further investigated.

Although we are still a long way to reaching specific recommendations of these products/compounds for specific groups of consumers, **the way forward is now more clearly set up: Research in the area should continue to decipher inter-individual variability in response to all bioactive compounds.**



## RESEARCH DISSEMINATION

**PUBLICATIONS– FG:**  
The views of the consumers



**Research Open**

Nutrition Research and Food Science Journal

Volume 1 Issue 1

Research Article

## Spanish Consumers' General Understanding of Metabolic Diseases and how they may be Influenced by Diet and Novel Foods: a Preliminary Survey

Laura Laguna<sup>1</sup>, Begoña Bartolomé<sup>1</sup>, Victoria Moreno-Arribas<sup>1</sup>, María-Teresa García-Conesa<sup>2\*</sup>

<sup>1</sup>Institute of Food Science Research (CIAL), CSIC-UAM, C/Nicolás Cabrera 9, 28049 Madrid, Spain

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**SCIENTISTS IN DIRECT CONTACT WITH COSUMERS: The need to improve the communication and translation of our understanding of the binomial 'HEALTH-DIET' to the general public**

**T**his article collects the results of a simple preliminary survey distributed to a Spanish random population sample constituted by casual visitors to a general public Science event. Researchers from the Spanish Research Institution CSIC (CIAL & CEBAS) were interested in finding out how much the general public was aware of their metabolic health status and how much they knew about some very basic concepts related with metabolic disorders such as hypercholesterolemia or diabetes and about the influence of diet and lifestyle on their health. The survey also included some very simple questions about novel healthy products such as 'Functional Foods' and 'Nutraceuticals' and one final question regarding the understanding of the consumers about the potential differences of the effects of diet in different people.

The analyses of the results showed that despite a general concern about maintaining a good health status and some notions about the importance of eating well and keeping good life habits, the participants had a very limited knowledge of chronic disorders and manifested little familiarity and understanding of novel foods or nutraceuticals. The concept of inter-individual variability in response to diet was poorly understood by most participants.

Despite the limitations of this preliminary study, the results support the importance and need to continue providing more and updated information to the general population about metabolic diseases and how to prevent them. **New products, such as foods or tablets enriched in beneficial constituents and, new concepts, such as the relevance of the interindividual variability in response to diet and personalized nutrition should be clearly translated and explained to the consumers.**



## GET TO KNOW YOUR POSITIVE

### SENIOR RESEARCHERS

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

I am a pediatric gastroenterologist. I joined the School of Nutritional Sciences at the Hebrew university with the vision of carrying out research that would serve as a bridge between clinical and basic sciences regarding issues relevant to malnutrition. Specifically, I have devoted the majority of my career to investigating vitamin A and vitamin A deficiency. My research work on vitamin A encompasses three spheres: *nutrition, inflammation and growth*, and their inter-relationships. Because my academic training began in the area of Paediatric Gastroenterology, the impetus for my first research projects was based on clinical observations; from there my focus moved to identifying animal and in-vitro models that characterized specific phenomena of interest and then my work expanded to intensive investigation dedicated to unravelling underlying mechanisms of action. Recently I founded a start-up where we have an IP protected technology to produce high quality isolate of chickpea protein which is as an excellent source of plant protein, non-allergenic with negligible amounts of phytoestrogens, non-GMO and of course lactose and gluten free. This is a result of longstanding research on enhancement of the nutritional qualities and more than 15 years of work in the developing world to alleviate malnutrition.

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

I went to medical school and did my pediatrics training in Hadassah Medical School at the Hebrew University of Jerusalem. My training in gastroenterology and later nutrition were at the Hospital for sick children in Toronto Canada. I also did a master program in Nutritional biochemistry at the University of Toronto. I spent a year with Prof Crawford in London on omega 3 fatty acids research. Lately I did a master in business administration in Israel as well.

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

I think that we may have contributed to a better understanding of the function of vitamin A especially deficiency of vitamin A and to link it to many phenomena other than vision. We were among the first that used microarray in nutritional research and pointed out that vitamin A deficiency is associated with inflammation and iron deficiency and most of all our humble contribution to find ways to supplement vitamin A in various areas in the developing world.

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

We were among the first to link nutritional work to in collaboration with colleagues in Wageningen. We were able to show the expression of relevant genes in the presence and absence of vitamin A but our recent reviews on both vitamin A deficiency and chickpea summarizes our work over the last 20 years. As a head of nutrition in our university I also had a chance to influence the curriculum of under and graduate students and possibly to improve their education.



**PROFESSOR RAM REIFEN**  
HEBREW UNIVERSITY OF JERUSALEM

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

Dr Hagit Hurvitz - an outstanding paediatrician who had an open mind and a unique ability to see beyond symptoms, and many years later Prof Crawford who had a wide angle and a global view on things without neglecting detailed and thorough research. My parents were my role models for life beyond science and medicine. I often ask myself what would my father do or how would my mother react in a certain situation that I am facing.

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

To prepare themselves for a long journey with ups and downs. To use passion in their work. To be attentive to the environment and to keep an open mind, also, to collaborate with people who do different things than they do.

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

By far Jerusalem, our cultural and historical centre which has got beyond history magic and beauty and a unique atmosphere. The second favourite place is Florence full of culture and beauty.

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

I am a musician at heart and for a short time I debated whether I should pursue a career as a musician.. I love the seventh symphony of Beethoven and violin concerto of Mendelson. I love listening to Adele and Amy Winehouse and I read almost all the new books by Israeli writers. My favorite one is David Grossman.

**What is your favorite sport(s)?** Swimming and jogging. We have a short winter in Israel and therefore it is easy to do both almost all year round.

## GET TO KNOW YOUR POSITIVE PARTNER

### SENIOR RESEARCHERS



**KIERAN TUOHY**  
**FONDAZIONE EDMUND MACH**

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

The focus of my research is diet: microbe interactions in the gut and how they can influence host health and disease risk. To study these interactions we use both *in vitro* models (gut models and cell lines) and small dietary interventions in people. We collaborate with others for mechanistic studies in laboratory animals. From a technological view point, we use a mix of metagenomics and metabolomics, as it is becoming apparent that it is not sufficient to know your microbiome by name, you must understand how they contribute to the human system at a molecular level through both metabolic and immune interactions.

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

I received my degree (Industrial Microbiology), a long time ago now, from University College Dublin in Ireland, a Masters degree (Environmental Microbiology) from the University of Aberdeen, Scotland, and my PhD, entitled, "Measurement of DNA transfer in the gut using *in vitro* and *in vivo* models", from the University of Surrey in England in 2000. Since then I worked for about 10 years at the University of Reading before moving to Italy in 2010 and joining Fondazione Edmund Mach (FEM). I am now Head of the Department of Food Quality and Nutrition at FEM.

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

This is a difficult question, since most scientific research careers in my experience are built using small, steady but consistent steps over many years. However, if pushed, I'd pick one from the beginning of my career – publishing my first research paper (and realising that the most important thing is to get the papers out and not to procrastinate too long worrying about how they will be received), and one recent highlight, leading my first European project, CABALA\_diet&health (<http://cabalaproject.eu/>).

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

It is probably a review article from a few years ago entitled, "The way to a man's heart is through his gut microbiota" – dietary pro- and prebiotics for the management of cardiovascular risk." Although getting a bit old now, at the time it did serve to concentrate my thinking about how diet as a whole, rather than individual ingredients, can impact on microbiota composition and metabolic output, and consequently influence chronic disease risk. In fact, I would advise young researchers to write review articles on their chosen topics. Regularly. It really does help to advance your thinking, improve your writing skills and give you the confidence to challenge existing dogma. Just reading is not enough, you need to write to really think about of topic, focus your ideas and get your research directions clear in your head.

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

I was exceptionally lucky in my career to have some fantastic role models, Professors Ian Rowland, Glenn Gibson, Christine Williams and most recently Fulvio Mattivi. All very different characters, all with very different approaches to their science and life as a researcher, but also all fantastic teachers and scientists, always leading from the front, and brave!

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

See above about reviews and writing, and also to help as many people as you can on the way up – makes life a lot easier when your older and pass over the hill!

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

I usually have a favourite place wherever I live – at the moment it's a small outcrop of rock jutting into a local cool mountain stream. Sometimes I fantasise about jumping in – Irish man in hot country syndrome ;)

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

The Police, Paul Simon, Beethoven and Placebo, depending on mood, and book, still "In the Name of the Rose".

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

Rugby and Gaelic Football – Up Mayo!



## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHERS

**What is the focus of your research?** My main research interests are orientated to the medicinal plants closely related to the antioxidative activity due to different phytochemical compounds. Acting as antioxidants, these molecules are capable to neutralize or scavenge the free radicals, which are responsible for many degenerative processes (cardiovascular diseases, aging), as well as progression of cancer. Therefore, I assume that antioxidative potential of many plant metabolites are in high demand at the current phytotherapy, as well as in nutrition. In this aim, we are using an electrochemical voltammetric method, which has many advantages versus the previous in vitro antioxidants assays. This electrochemical method could be effectively used in revealing the mechanism of oxidation/reduction of plant metabolites, or predicting their interaction with other plant constituents as well as conventional medicines or heavy metals.

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

I have studied pharmacy at the Faculty of pharmacy at Cyril and Methodius University in Skopje, the capital of Republic of Macedonia. On this integrated 5-year study program, I have acquired the degree of master of pharmacy. Then, in 2011, I have continued on the doctoral studies and defended my PhD thesis in 2016 in Stip, at Goce Delcev University, where I have the permanent teaching position (assistant professor), now. During my PhD studies, I have had a few study stays in Leipzig, Germany where I had a chance to work on a cytotoxicity assays and cell cultures and these results were incorporated in my doctoral thesis. During this stay, I have also had a short practical experience in Ca-fluorescence imaging methods, PCR and electrophoresis.

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

As an early career investigator, the publication of the results of my PhD study in a high quality scientific papers, has been the greatest achievement. I am also very proud that as a member of WG2 in our COST Action, I have been included in the meta analyses related to the interindividual variations in the effects of flavonols on cardiovascular risk factors which have been published in a prestige journal.

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

Both original scientific papers: Maksimova, Viktorija and Mirceski, Valentin and Gulaboski, Rubin and Koleva Gudeva, Liljana and Arsova-Sarafinovska, Zorica (2016) [Electrochemical Evaluation of the Synergistic Effect of the Antioxidant Activity of Capsaicin and Other Bioactive Compounds in Capsicum sp. Extracts](#). International Journal of Electrochemical Science, 11. pp. 6673-6687. & Maksimova, Viktorija and Koleva Gudeva, Liljana and Gulaboski, Rubin and Nieber, Karen (2016) [Co-extracted bioactive compounds in Capsicum fruit extracts prevents the cytotoxic effects of capsaicin on B104](#)



**VIKTORIJA MAKSIMOVA**  
Univerzitet Goce Delcev, Macedonia

[neuroblastoma cells](#). Revista Brasileira de Farmacognosia. pp. 1-7. published on the results of my doctoral thesis makes me really happy because they are integrating my research interests in a whole picture about a plant fruit (hot pepper) that is very often used in nutrition in my country, as well as world wide. Because of the possible health effects of Capsicum I consider that they are both very important in my career.

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

There are many people whose contributions have been very important to my research and to me. Among others, as the most inspiring I will have to emphasize a few of them. Prof. Karen Nieber, prof. Valentin Mirceski and prof. Rubin Gulaboski have influenced a lot in my research and professional upgrade. Their implication on my practical working skills as well as scientific expression style are enormous and I am very grateful to their unselfish advises and suggestions.

**Where is your favorite place in the world and why?** The tallest sand dune in Europe, The Dune of Pilat, located in the Arcachon Bay area, in Bordeaux, France is the most impressive place that I have visited. I had a chance to visit it through one of my short study stays in France and I was impressed by the view of the Atlantic Ocean on one side and an enormous pine forest on the other side of the Arcachon Bay, a sandbank and a peninsula!

**What is your favorite music/book?** As a romantic type, I love to hear the popular rock ballads as well as pop hits. The books of life philosophy and criminal book novels are also interesting to me.

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

I am not really a sport style girl, but I love to watch figure skating.

## GET TO KNOW YOUR POSITIVE PARTNER

### EARLY STAGE RESEARCHERS

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

I am a PhD student investigating the effects of berry (poly) phenols on cardiovascular health, their bioavailability and potential mechanisms of action in the vascular system. Over the past three years, I have conducted several randomized controlled trials assessing the effects of different berries on vascular function in humans, and also looking at plasma and urinary polyphenol metabolites using liquid chromatography-mass spectrometry. I have used murine models and in vitro approaches to provide mechanistic insights and complement the findings from human trials, together with nutrigenomic analysis to understand the biological pathways affected by (poly)phenol intake in the context of cardiovascular diseases.

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

I studied a Master degree in Biochemistry and Biotechnology at the University of Antwerp (Belgium). As part of an Erasmus program I performed a 6-month research internship in Epigenetics at the Chemoprevention Department in the German Cancer Research Center (Heidelberg, Germany). Under supervision of Dr. Ana Rodriguez-Mateos, I started my PhD at Dusseldorf University (Germany) in 2014. In 2016, our group moved to King's College London, where I am now currently in my last year of PhD.

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

Over the course of my PhD, I developed a network of connections with scientists all over the world, mainly thanks to the COST-POSITIVE action. The relationships I have made are not only helping me throughout my PhD, but will most certainly prove valuable in future endeavors.

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

*Istas et al. Identification of differentially methylated BRCA1 and CRISP2 DNA regions as blood surrogate markers for cardiovascular disease. Scientific Reports. 2017.* Is the paper based on the research I performed during my Master project and it is my first "first author" paper. The aim was to compare the epigenome of healthy individuals and atherosclerotic patients and to identify potential biomarkers of cardiovascular disease. Our analysis shows that *BRCA1* and *CRISP2* promoter methylation status in blood leukocytes might predict development of atherosclerosis.

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

Ana Rodriguez-Mateos is my most influential mentor. She has been very supportive, patient and inspiring over the course of my PhD. Most of my knowledge and skills are thanks to her.



**GEOFFREY ISTAS**  
 King's College London, UK

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

Italy. In my opinion Italy as a holiday destination has everything you need: delicious food, quality wine, good weather, amazing landscapes (beaches, mountains and fields) and nice people!

#### What is your favourite music/book

I am currently reading the "century trilogy" by Ken Follet. It feeds my passion for history and also presents basic knowledge about politics and social structures in an accessible and interesting manner. I love all kinds of music genres including jazz, indie pop, reggae, house and relaxing music.

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

I am a big fan of Capoeira, a Brazilian martial art that also incorporates dance. As a fervent practitioner for the past 15 years, Capoeira has kept me fit, has provided me with a social network in every country I moved to and embeds me with a warm Latin culture/vibe. I am a strong believer of the quote "a healthy mind in a healthy body" and Capoeira can give me just that!



## Chair's Corner

Dear POSITIVE partners,

The time goes definitely very fast since the Action is entering its fourth and last year! The quality of the collaborative works performed by the WGs since the beginning has already led to the publications of seven open access reviews in good scientific journals, and also several other manuscripts that are either under peer review or being completed. Each of these papers contributes to increasing the state of the art and the knowledge on the interindividual variation in response to plant food bioactives consumption and will provide a cornerstone for elaborating a new and concrete research programme on that topic. The POSITIVE Action has also fostered scientific exchanges within the network, by offering possibilities to more than thirty scientists to perform short-term scientific missions in partner labs.

The next and last major event organized by the Action will be its **Final Scientific Conference** that will be held in **Lisbon (25-26<sup>th</sup> September 2018)**, as a satellite activity of the 2<sup>nd</sup> Food Bioactives & Health Conference. During this two-day POSITIVE Conference (<https://www6.inra.fr/cost-positive/Home/News/Final-Conference>), the main findings of the Action will be presented, and the future of research and concrete applications related to individual response to dietary interventions will be exposed and discussed through the view of international experts and stakeholders. We hope that this event will largely attract scientists from and outside the POSITIVE community and, in any case, the Action will work in that direction by maximizing its efforts to refund the widest possible number of partners for attendance.

**Looking forward to seeing you at the Final Conference of POSITIVE!**

**Christine & Paco**



## CONTACT US



EUROPEAN COOPERATION IN THE FIELD  
OF SCIENTIFIC AND TECHNICAL RESEARCH

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