POSITIVe NEWSLETTER

EUROPEAN COOPERATION IN THE FIELD OF SCIENTIFIC AND TECHNICAL RESEARCH

ISSUE VI, DECEMBER 2017

WELCOME

Dear partners, we are now approaching the end of 2017 and entering the last term of our COST Action POSITIVe. Once more, this December issue brings together summaries and snapshots of all the past year activities including meetings, workshops, training school, STSM, publications and various presentations as well as our regular expert opinion and collection of surveys from amid the POSITIVe participants.

Thus far, the FG has tried firmly to cover all the aspects dealt with during the past years and to reflect the efforts and the good work done by all the working groups. We have been very keen on including as many pictures as possible that clearly show all the many nice people from the different countries that have intervened in the different research tasks. The get-to-know-each-other section continues highlighting the story of POSITIVe partners so that we will end up the Action with as many friends and colleagues as possible. We honestly hope to continue fulfilling our dissemination job up until the very end of the Action by September 2018. We still have one more year to go and from the members of this FG we wish you all a wonderful and successful 2018.

Merry Christmas (the Focus Group)

IN THIS ISSUE:

NEWS FROM THE ACTION

6th COST Action POSITIVe Meeting, 2017
Organized by Dr. Kristos Kontogiorgis and Dr. Antonia Kaltsatou, Thessaloniki, GREECE

During September 19-23, 2017 Thessaloniki, Greece hosted major events crucial to a successful implementation of COST POSITIVe. The 6th Working Group and 4th Management Committee meetings allowed Action partners to network and share the results of activities performed so far as well as plan further tasks to progress towards implementation of POSITIVe final objectives. The WGs and MC meeting was accompanied with the 3rd Scientific Workshop attended by both renowned and promising young researchers who discussed their most recent findings on omics-based evidence of the health effects of plant food bioactives.

The events took place in a pleasant atmosphere built by a heartful hosting of our Greek partners with a sunny and warm weather in the background. Participants of the meetings had a chance to get advantage of very fruitful discussions and enjoy evening strolls around the city of Thessaloniki and the delicious Greek cuisine.

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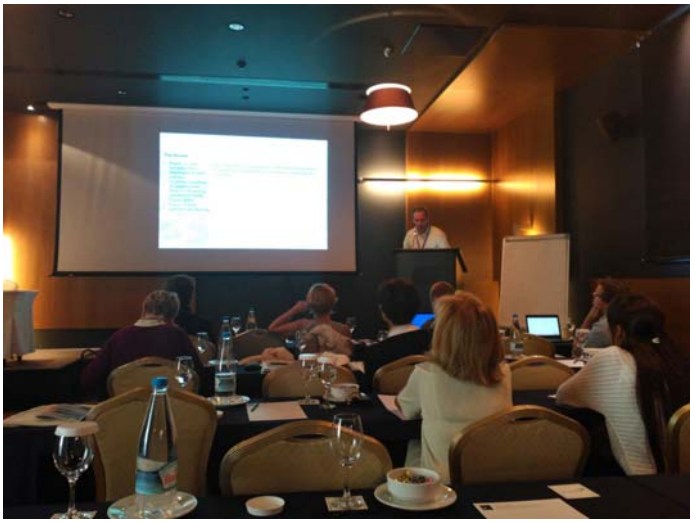
RESEARCH HIGHLIGHTS

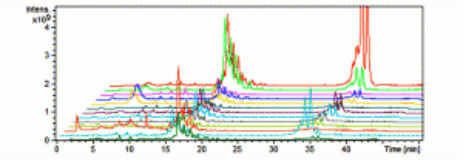
Work Group 1
Leader: Tom VAN DE WIELE
Co-leaders: Claudine MANACH & Rikard LANDBERG

The WG1 meeting was started off by Rikard Landberg who divided the initial session into one session dedicated to the Gene Variant group and the second one to the different subgroups looking at specific bioactive compounds. An important aspect to discuss was the current state of the work on the metabolic pathways for the various compounds investigated.

There were some presentations by Dr Torsten Bohn on the research about ADME pathways of carotenoids which is well advanced and almost ready for publication and also by Wiktor Jurkowski on the different web resources that can be used for modelling and visualization of metabolic pathways, where Pathwhiz and Minerva may be applicable for the objectives of the WG1.



The different subgroups need to complete and hand a template prepared for the purpose of getting the information needed for the drawing of the metabolic pathways of the different compounds.



The session about metabolomics and the compounds subgroups was led by Dr. Claudine Manach. Some tasks such as the compilation of key analytical issues needed for metabolomics analyses and identification of compounds and metabolites were reopened. Further work is guaranteed through web meetings and collaborative efforts. Presentation by Dr. Maria Bronze updated the progress of the multiplatform test analyses and the status of a new article due in December. Due to the various difficulties and problems in this area, further work is needed in order to reach consensus on how to perform wide coverage and accurate analyses and identification of metabolites. Issues such as the use of standards with different polarity, tools to predict retention times or stability of the mixed compounds were also discussed. More partners may join the platform and more web meetings and STSM will be organized to continue with this work.

On the second day of the WG1 meeting, the work focused on the status of the reviews about the different compounds subgroups: papers selection, data extraction and analysis, publications, etc. Changes and needs in the different subgroups were also discussed by different partners. An important number of papers have been published, submitted or will be completed in the next few months.

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Work Group 2
Leader: Ana RODRIGUEZ-MATEOS
Co-leaders: Eileen GIBNEY & Dragan MILENKOVIC

Meta-analysis subgroup

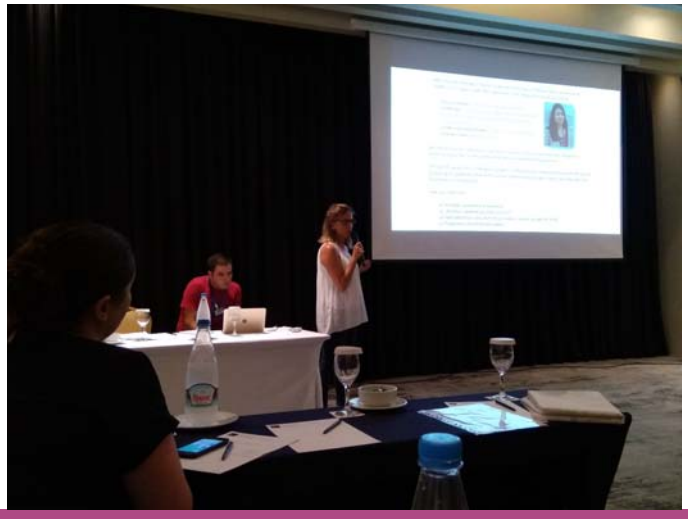
The WG2 meeting was led by Eileen Gibney who started the session by updating the current status of the meta-analyses published and in preparation. A general discussion followed about some critical issues on the results interpretation, especially in view of the data limitation and lack of significance of the subgroup analyses. Next, Paula Pinto presented all the work carried out on the flavanols meta-analysis looking at blood pressure (BP) and flow mediated dilation (FMD). Some of the problems found during this analysis were exposed so that future studies should include and consider important aspects such as better description of the methodology, clearer setup of the subgroups, and more research on the relationship dose-response. Her presentation was followed by others given by: Antonio González-Sarrías on the meta-analysis on ellagitannins and anthocyanins, Pedro Mena on hydroxycinnamic acids, Eileen Gibney (on behalf of Antonia Katsaltou and Christos Kontogiorgis) on the systematic review about the interaction between polyphenols and exercise and, Emilie Combet on the metanalysis of flavanols and glycemic function. Several important issues on these analyses were commented and the need of a summary of the key findings was proposed.

There was also a presentation by Eileen Gibney on the current status of dataset analyses and on the potential POSITIVe study. After examining the responses to the questionnaire previously sent around, it was found that problems such as funding, ethics, specific compound or product to investigate, and study design were of concern and that further discussion and consideration should be given to the planning of the study. Another key aspect was the importance of including the bioavailability as a factor affecting variability in the response. Overall, the idea needs to be further settled in order to prepare a feasible and valuable study.

Cell & Molecular Targets subgroup

The activities carried out in this subgroup were introduced by Laurent Monfoulet. During the meeting, Mayte García-Conesa also presented the work carried out by Biljana Pokimica during a STSM in Spain in her lab at CEBAS-CSIC (June 2017). A full and updated revision and selection of articles about gene expression effects of bioactive compounds in human clinical trials as well as data extraction has been completed and a draft article is being prepared. Further work on the results presentation and general discussion is on its way. The article may be published before the summer 2018.

Regarding other nutrigenomic studies in cell and animal models, although an important amount of work has been done, there is some concern about the completion of some of the tasks initially proposed and the collaboration of more people was requested. There was a general discussion as to how to tackle the work that still need to be done and more STSM were considered but not finalized.



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RESEARCH HIGHLIGHTS

Work Group 3
Leader: Baujke DE ROOS
Co-leader: Marina HEINONEN

A WG3 plenary meeting gathered most of the Thessaloniki meeting attendants. During this session, the WG3 leader Baukje de Roos presented the results of a questionnaire distributed to Portuguese consumers that evidenced a considerable interest and knowledge on plant bioactive compounds as well as the importance of improving the knowledge about their efficacy for preparing new products applicable to specific populations. Other tasks proposed within the group such as the development of movies and webinars were a bit delayed but a short video with Zohar Kerem about a successful collaboration between academia and industry was filmed during the meeting. Other videos are in preparation. The presentation at VitaFoods in Geneve was also commented, as well as the development of a decision-tree style on-line tool and a final roadmap. The roadmap is essential to summarize the work done as part of POSITIVe to evidence the complexity of the aspects involved in inter-individual variability in response to the bioactive compounds. It is also very important to establish the gaps in knowledge and the needs for future research in the area.

Focus Group
Leader: Mayte GARCÍA-CONESA
Co-leader: Iwona KIEDA

The plenary Focus Group meeting was opened by the FG leader Mayte Garcia-Conesa who presented the past and ongoing communication activities within the Action, and invited attendees to consider future application of a preliminary questionnaire on food & health introduced to consumers at local science events in Spain. Partners discussed the possibilities of producing an improved version of the questionnaire by investigating participants' knowledge about: metabolic diseases, the role of diet in health, the importance of understanding differences between individuals, as well as identifying challenges that may show up when we try to apply it to other groups across COST partners in Europe for a larger survey.

Furthermore, new means of disseminating POSITIVe impacts and achievements were considered. FG intends to work on a 'template document' that will collect the most relevant information obtained from the WGs activities and publications. This information will then be exploited to design a brochure with the most relevant messages to be conveyed to different target groups, i.e. science community, food industry and general public. In addition, several FG members agreed to continue working on short videos with interviews to academic and industrial partners of the Action to introduce successful collaborations between research and industry, further distributed on the POSITIVe web page and social media channels.

Finally, upcoming events for informal presentation of POSITIVe were highlighted (POSITIVE workshop for school children during the European Researchers' Night in Poland, see page 19 for a summary of the activity).

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3rd POSITIVe Workshop

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

The 3rd Scientific Workshop of the COST Action POSITIVe entitled "Omics breakthroughs in the health effects of plant food bioactives" was carried out in Thessaloniki (Greece) the 20th and 21st of September, 2017. The workshop was focused on how Omics-based disciplines (including Nutrigenetics, Nutri (Epi)genomics, Metabolomics and Microbiomics) contribute to provide new findings on the health effects of plant food bioactives. The scientific programme was elaborated by members of the Think-Tank Group, the group constituted by Early-Career Investigators of the Action.

The workshop was organized in four sessions: one session about Metabolomics, two sessions on Nutrigenetics, Nutrigenomics and Nutriepigenomics, and one session on Microbiomics. Both renowned and promising young researchers presented the highest quality and most interesting recent findings resulting from the use of these approaches.

Each session consisted of three presentations delivered by recognized scientists from inside and outside the COST Action. The metabolomics session was opened by **Dr. Albert Koulman (**Cambridge University, UK). He presented a lipidomics approach to study the lipid metabolism of infants, validating key features of the lipid profiles as nutritional biomarkers. **Dra. Mireia Urpi Sarda (**University of Barcelona, Spain) showed the application of metabolomics approaches to study biomarkers of Mediterranean diet adherence and polyphenol-rich food intake (Nutrimetabolomics). **Dra. Marynka Ulaszewska** (Fondazione Edmund Mach, Italy), focused on nutrikinetics studies where the aim was to identify the metabolic products of apple polyphenols using an untargeted metabolomics approach and to evaluate their relation to individual members of the gut microbiota.

In the first Nutrigenetics, Nutrigenomics and Nutriepigenomics session, **Dr. George Patrinos** (University of Patras, Greece) discussed the difficulties to integrate Nutrigenomics into the everyday lives of consumers. He presented a recent study of 38 genes included in commercially available nutrigenomics tests and commented on the need for ethical considerations when approaching nutrigenomics. **Geoffrey Istas** (King´s College London, UK) discussed the results of a study that investigated the impact of chronic blueberry consumption on both gene and miRNA expression in peripheral blood mononuclear cell (PBMC) using integrated nutrigenomic analysis.

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3rd POSITIVe Workshop (cont.)

During the second session of Nutrigenetics, Nutrigenomics and Nutriepigenomics, **Dr. Clarissa Gerhäuser** (German Cancer Research Center, Heidelberg, Germany) gave a presentation of the PATHWAY-27 project, whose objective is to understand the role and mechanism of action of bioactive-enriched foods on risk factors of the metabolic syndrome combining advanced omics techniques (transcriptomics, metabolomics, epigenomics and microbiomics). **Dr. Dylan Mackay** (University of Manitoba, Canada) discussed an association between the variability in the LDL cholesterol in response to plant sterol consumption and genetic variations. The final presentation in this session, given by **Dr. Ken Declerck** (University of Antwerp, Belgium), focused on the integration of transcriptomics, epigenomics and kinomics to characterize the immunomodulatory properties of an *Echinacea* extract in monocyte cells.

The last session of the workshop was focussed on Microbiomics. In this session, **Dr. Kieran Tuohy** (Fondazione Edmund Mach, Italy) discussed several methodological approaches to study how the diet:microbe interactions contribute to the functioning of the gastrointestinal tract and health promoting diets and foods. **Dr. Alan Walker** (University of Aberdeen, UK) presented a recent work identifying diet-responsive microbes as drivers of inter-individual variation in response to consumption of plant food bioactives. The aim is to consider the importance of microbiota composition/activities in personalized nutrition-based strategies. Finally, **Dr. David Berry** (University of Vienna, Austria) discussed how individual variation in the gut microbiota can impact the metabolism of polyphenols using the example of the microbial degradation of rutin.

To conclude the workshop, some of the organizers and participants in the workshop: **Dr. Pedro Mena, Dr. Noemí Tejera, Dr. Albert Koulamn, Dr. Dylan Mackay, and Dr. María Teresa García Conesa** gathered to debate about the current status of the omics disciplines as well as about some of the main features presented during the workshop. Overall, the omics technologies have provided new and interesting insights into the health effects of dietary compounds and nutrients and have opened new research areas that warrant further investigation with promising POSITIVe results. The omics are here to stay and future research should adapt to the complex designs needed to obtain the best results of these disciplines.

The workshop was finalised with the handing of an honorary prize to the best poster presentation by **Irena Krga** (University of Belgrade, Serbia) and to the best flash-poster presentation by **Dr. Wim Vanden Berghe** (University of Antwerp, Belgium). The Scientific Committee of the Workshop thanked the Organising Committee (**Dr. Christos Kontogiorgis, Dr. Antonia Kaltsatou, and Dr. Eirini Deligiannidou**) and the audience for their help and participation.

Overall, the workshop was great!.

Πειρατές Στη Θεσσαλονίκη

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RESEARCH HIGHLIGHTS

SOCIAL EVENTS

During the meeting in Thessaloniki it was the privilege of the organizing committee to indulge the participants of the "Omics breakthroughs in the health effects of plant food bioactive" conference as well as all the attending POSITIVe partners into a city tour on foot. We took off from the city's landmark, the White Tower, and reached the historic district of Ladadika, enjoying a brief presentation of the city's long history delivered by the local organisers - Dr. Christos Kontogiorgis, Dr. Antonia Kaltsatou and Eirini Deligiannidou.

Living up to our nation's reputation, all the attendants were invited to try on some of the delicious foods that Thessalonikki has to offer. Ant this was done in more than one occasion throughout the meeting! Towards the end of the second day, after an educating set of presentations and with lots of ideas in our brains, all parties had the opportunity to enjoy a nice relaxing dinner in the heart of the city followed by a nice evening stroll by the seaside.

A dinner gala was held in the eastern part of the city in a traditional tavern with a vast variety of sea food combined with Greek "ouzo" for the braver of us as well as dancing initiated by professional dancers of a local school, who volunteered for our entertainment. Laughter and joy under the sounds of "sirtaki" lead most of the attendants to dare a spin on the dance floor, proving the open and welcoming spirit of the Action in general.

That was a meeting to remember for sure!

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TRAINING SCHOOL

Attending the training school on "Use of Nutrigenetics & Nutri (epi)genomics in nutrition" has been an outstanding experience. It was my first time attending a Training School of this kind and I had great expectations of the results. All the topics covered in the course were stimulating and all the teachers were very knowledgeable of their subject, and explained step by step everything they presented. They also encouraged us to maintain an open dialog rather than just giving their presentations without interacting.

Use of Nutrigenetics & Nutri(epi)genomics in nutrition

Regarding the subjects imparted, that about Clinical trials in Nutrigenetics presented by Dylan S. MacKay, PhD of the University of Manitoba, offered me a much clear understanding of the requirements to properly perform a clinical trial on Nutrigenetics. This helped me get started on designing my own proposal. There was a general talk considering all the steps required for such a project, from picking the genetic variant(s) to designing the trial and taking under consideration the aspects that might affect it in terms of reliability. What was even more helpful was the tasks we had to do in groups in which we had to draft and present our own design to the class and discuss its feasibility as well as its strengths and limitations.

There were three main outcomes for which I consider that attending this training school was very beneficial for my research and future work. First, I had the chance to work in groups with the other participants and this forced me to explore my own knowledge and capabilities as well as to learn from all the colleagues attending the school. Second, I was introduced to interesting yet occasionally complex subjects such as: i) bioinformatic analyses, presented by Ken Declerck of the Department of Biomedical Sciences – University Antwer and, ii) DNA sequencing, presented by Sarah Bastkowski of the Earlham Institute, in a very amenable way. Last, but not least, I got to keep in touch with both the teachers and the other attendants for future collaborations. Overall, it has been an amazing event that both met my needs and exceeded my expectations.

By Eirini Deligiannidou

The training also included some webinars that can be seen at:
https://www6.inra.fr/cost-positive/Trainings-Webinars

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SAVE THE DATES

COST Action POSITIVe
7th WG Meeting, 6th and 7th March 2018

VENUE: VALAMAR LACROMA DUBROVNIK HOTEL

ORGANIZERS: Dr. Nada Knezevic, Director of Regulatory Affairs Department & Dr. Suzana Rimac Brncic, University of Zagreb

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Final COST Action POSITIVe
WG Meeting and Final Conference,
24th - 27th September 2018

VENUE: OEIRAS (PORTUGAL)

ORGANIZERS: Dr. Claudia Do Santos

iBET - Instituto de Biologia Experimental e Tecnológica

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SHORT TERM SCIENTIFIC MISSIONS

BILJANA POKIMICA from Serbia went to CEBAS-CSIC, Murcia, SPAIN

Thanks to the COST Action POSITIVe and to Dr Mayte Garcia Conesa, I spent the most useful and pleasant time during the past month of June 2017, being a STSM intern at the CEBAS-CSIC in Murcia (SPAIN). There, I learnt how to prepare and write a Review Article on 'Human gene expression regulated by plant bioactives'.

I had to read and revise a total of 63 articles all looking at the influence of the supplementation with a range of bioactive compounds and products (foods, extracts, mixtures) from diverse plant origin on the expression of a number of genes in different human tissues. All the articles were based on RT-PCR analysis. Once I read the articles, my main assignment was to carefully extract detailed information about different sections of the research (study design, quality of the gene expression studies, results, etc) into template Excel and Word tables. Dr Mayte García-Conesa helped me through the whole procedure, double-checked the work I had done, and explained to me what was the best way to do it and what was the most important details that we neede to obtain for the purpose of the Review. Thanks to her I have learnt a lot regarding quality of studies and articles, gene expression regulation and review preparation. Therefore, the knowledge I have attained during this STSM is very useful for my PhD thesis, that I am currently writting, as well as for my future work in general.

Murcia is a faboulous University town where I met a lot of nice students from different countries, and I made lifetime friendship with two students from Turkey and Russia. I enjoyed being in Murcia also because of its wonderful landscapes. I walked near beautiful trees, cactuses, flowers and lemon trees every day on my way from University dorms to CEBAS-CSIC, both located at the University Espinardo Campus.

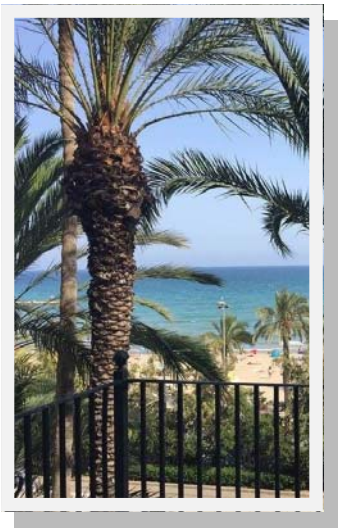
STSM Topic: Gene expression regulation in human trials following intervention with bioactive compounds: a literature survey

Dr Mayte García-Conesa was both my supervisor and a sincere friend. Every working day we had lunch and coffee together, she showed me around the city and introduced me to her friends and colleagues, who were all very nice to me.

During the weekends, I visited amazing sandy beaches near Murcia, located in Cabo de Palos, Torrevieja, Alicante and La Manga, where I enjoyed swimming.

Also, I had a great time sightseeing Cartagena from the boat.

This STSM made me richer in both scientific knowledge and friendships, and enabled me to spend one month in the beautiful country of Spain.



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SHORT TERM SCIENTIFIC MISSIONS

DITTA KOLIMÁR from Hungary went to the university of Vienna (AUSTRIA)

STSM Topic: Studying the relationship between microbiome genetic variation and polyphenol metabolic conversions

Gut microbiota plays a key role in the metabolism of many plant bioactives, such as certain polyphenols. Gut microbiome is not uniform among individuals, which suggests that different individuals or groups of individuals might respond differently to the intake of plant polyphenols. An STSM was initiated in December 2016 by COST POSITIVe to address this question. In the framework of the STSM entitled studying the relationship between microbiome genetic variation and polyphenol metabolic conversions, Ditta Kolimár a postgraduate researcher of the Szent István University, Faculty of Food Science (Budapest, Hungary) spent three months at the group of Dr David Berry, at the University of Vienna, Division of Microbial Ecology between Jan-March 2017. The actual goal of this research was to increase the level of understanding of the effect of interindividual variation of human gut microbiome on the metabolism of rutin (quercetin-3-O-rutinoside), one of the most abundant flavonol conjugates present in widely consumed plant foods. *In vitro* modelling of gut microbial fermentation of rutin was carried out utilising the microbial consortium of human faecal samples of 10 healthy volunteers. The microbial response to acute rutin treatment was followed with a specific fluorescent staining technique called BONCAT, which enables the selective detection and quantification of metabolically active members of the highly complex microbial community at the single-cell level. After completing some basic training and gaining hands-on experience in the experimental work, Ditta carried out the planned incubations and fluorescent imaging under the supervision of Dr Alessandra Riva, a post-doc of the Vienna group. Due to the focussed work plan, this short-term stay provided valuable experimental results and the hypothesised inter-individual variability in microbial activity could be experimentally confirmed.

In addition to the gained actual scientific output, this STSM moved one step further. It has contributed to the fundamental aim of the COST action, namely to initiate or foster further collaborations between COST members. In particular, after closing the STSM stay, results from the STSM were completed with metabolomic profiling at the host institute of the applicant in Budapest under the supervision of Dr László Abrankó. Combined results of this collaborative research were recently presented as an oral talk at the XIX EurFoodChem conference, held between the 4 and 6 of October (2017) in Budapest.

This is still not the end of this successful story. Results of the STSM were used as a proof of concept in a proposal to the call of a bilateral Austrian-Hungarian science foundation. The idea got granted and, at present, this collaborative research on interindividual variability of gut microbial polyphenol metabolism keeps going on between Dr Abrankó and Dr Berry. Finally, it should be proudly noted that this successful collaboration was initiated by an STSM grant of COST POSITIVe. And no doubt, the initial momentum gained during the STSM was absolutely essential for this evolution process, and enabled to go beyond the original scope.

SZENT ISTVÁN UNIVERSITY
FACULTY OF FOOD SCIENCE, BUDAPEST

DOME
Division of Microbial Ecology

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SHORT TERM SCIENTIFIC MISSIONS

Kateřina Valentová from CZECH REPUBLIC went to ITQB-UNL/IBET, Oeiras, PORTUGAL

The past July 2017, I had the opportunity to spend one week at the Disease & Stress Biology Laboratory, ITQB-UNL/IBET in Oeiras, which is located in the Lisbon Metropolitan Area, Portugal. My visit was one of the STSM funded by the COST Action POSITIVe and gave me the opportunity of working with Dr. Cláudia Nunes dos Santos. The aim of this STMS was to finalize our review on the Inter-individual variability of quercetin ADME in humans. We had been working on the review together with other POSITIVe WG1 members: A. Filipa Almeida, Grethe Iren Borge, Marius Piskula, Adriana Tudose, Liliana Tudoreanu, and Gary Williamson. This work commenced during the first POSITIVe meeting in Belgrade in March 2015. By the time we had the meeting in Olsztyn (February 2017), all the relevant data had been extracted and a number of tables grouping the results were prepared. We had also written by then, the Introduction and Experimental section of the manuscript. We realized that the working hours during the WG meetings were not sufficient and that between meetings, people were busy attending other pieces of work. It was decided that in order to finalize the manuscript as soon as possible, we needed to focus on it and work in close collaboration between, at least, the main authors.

Indeed, during the STSM, I worked very hard together with Claudia and A. Filipa Almeida and had regular consultations with Dr Gary Williamson by Skype. The concentrated effort on the manuscript allowed us to finalize all the sections of the manuscript: tables and results, discussion, conclusion and the full list of references. The complete draft was then circulated among the remaining authors for final remarks and the paper was submitted to the *Comprehensive Reviews in Food Science and Food Safety* in September 2017.

Overall, my stay was a really nice experience, the host team was great and I am especially grateful to Cláudia for the wonderful welcome dinner in family on the amazing Carcavelos beach, located at a walking distance from my hotel. I´m looking forward to visiting the place again during the last POSITIVe meeting September 2018!

STSM Topic: Inter-individual variability of quercetin ADME in humans

UNIVERSIDADE NOVA DE LISBOA

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EUROPEAN COOPERATION IN THE FIELD OF SCIENTIFIC AND TECHNICAL RESEARCH

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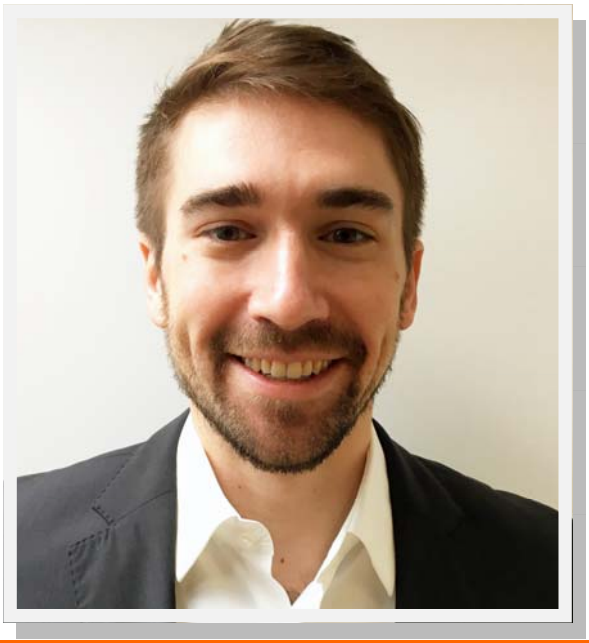
SCIENTIFIC EXPERT'S OPINION



Dr. David BERRY
Associate Professor,
University of Vienna, AUSTRIA

Individuality in the gut microbiota: State of Knowledge and Future Directions

Each of us is home to a diverse and complex community of microorganisms – including *Bacteria*, *Archaea*, and *Fungi* – collectively termed the human microbiome. The intestinal tract is an especially rich microbial environment, with hundreds of species totaling an estimated 10^{14} cells that together form a highly dense and diverse ecosystem. The intestinal microbiome has drawn widespread attention as it has become clear that it plays important roles in human health, affecting nutrition, immunity, metabolism, and susceptibility to enteropathogenic infection (Subramanian *et al.*, 2015). Technological progress in the field of next-generation sequencing technology has advanced our understanding of both the genetic diversity of the microbiome as well as the physiological and pathological processes that are influenced by the commensal microbiota. A clearer picture is now emerging of the composition of the human microbiota in healthy individuals and the diverse factors affecting its variability (Yatsunenko *et al.*, 2012).

The gut is initially colonized at birth - though there are reports that even the fetus is not sterile - by taxa such as *Bifidobacterium*, *Lactobacillus*, *Staphylococcus*, and *Enterobacteriaceae*, and pioneer colonizers are derived in part from the mother's vaginal microbiota, skin and fecal microbiota of parents and siblings, breast milk, and other infants. In the first three years of life, the gut microbiota develops into a "mature microbiota" with increased species richness, predominance of the bacterial phyla *Bacteroidetes* and *Firmicutes* (with lesser phyla including *Actinobacteria*, *Verrucomicrobia*, and *Proteobacteria*), capacity of the microbiota to degrade and transform dietary compounds, increased abundance of vitamin biosynthesis pathways, and higher numbers of butyrate-producing bacteria (Yatsunenko *et al.*, 2012). Generally, the composition of the gut microbiota is known to be shaped by diet, health state, host genetics, and environmental/lifestyle factors (Clemente *et al.*, 2012). From studies of the gut microbiota in healthy individuals it has become clear that adults have a relatively stable microbiota, the composition of which is person-specific, which raises the question: what are the implications of the inter-individual variation in gut microbiota?

A well-studied example for inter-individual variability in plant bioactives is the polyphenol equol, which is an agonist of the estrogen receptor β and exerts manifold effects, including anti-inflammatory and anti-cancer activities (Duda-Chodak *et al.*, 2015). Equol is formed in the intestine by the bacterially-mediated transformation of the soy isoflavone daidzein. Only a small number of bacteria have been identified to be able to form equol from daidzein, such as *Eggerthella* spp., *Slackia* spp. and *Adlercreutzia equolifaciens*. The variability in abundances in equol-producing bacteria is thought to be an important factor explaining that the prevalence of equol producers is approximately 30–50% of the population. While equol has been the subject of much study, little is known about the metabolism of many other plant bioactives and interactions between plant bioactives and the gut microbiota. One of the aims of the COST Action POSITIVe is to identify for which plant bioactives the microbiome is an underlying factor of variability for ADME processes. In order to gain deeper insights into the molecular mechanisms of this variability, it is essential to move forward and identify critical metabolic steps and microbial enzymes for the transport and metabolism of these compounds. With this information in hand, it will be possible to screen large metagenomic datasets generated by major microbiome sequencing projects such as the Human Microbiome Project and the MetaHIT project to evaluate the variability in the abundances of these key genes across the human population.

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SCIENTIFIC EXPERT'S OPINION

How can we use microbiome information to inform therapeutic practice or dietary recommendations? There are interesting examples from nutrition research suggesting that microbiome composition can be a useful diagnostic marker. Cotillard et al. (2013) conducted diet-induced weight-loss and weight-stabilization interventions in obese and overweight individuals. They found that individuals with reduced microbial gene richness had increased metabolic dysfunction and low-grade inflammation. Interestingly, though the dietary intervention was able to improve low gene richness and clinical phenotypes, it was less efficient for inflammation parameters in individuals with lower gene richness. Therefore, low gene richness may be a useful diagnostic parameter to stratify individuals and predict the efficacy of an intervention. Another recent example was a crossover trial of the effect of industrial white or artisanal sourdough bread consumption on glycemic response based on an oral glucose tolerance test (Korem *et al.*, 2017). They found that there was high inter-individual variability in the cohort and that neither bread type elicited a better glycemic response. However, looking into the microbiome of the participants, they were able to predict whether an individual would have a better glycemic response to industrial white bread or artisanal sourdough bread based on distinctive signatures in the microbiome. As the glycemic response to bread type was person-specific and microbiome-associated, this study suggests that it may be possible to use microbiome information for personalized nutrition.

The other possibility in the future is to "improve" microbiomes by adding bacteria that perform desired metabolisms, which have been termed functional probiotics (Bolca *et al.*, 2013). Probiotics have had a variable track record, in some cases producing positive short-term clinical responses, yet rarely leading to the stable establishment of a beneficial bacterium in the intestinal ecosystem (Walker & Lawley, 2013). However, by using gut-derived probiotic bacterium and screening of microbiomes to identify missing microbial components, it was possible to engraft an exogenous *Bifidobacterium* species in the human gut (Maldonado-Gómez *et al.*, 2016). The time may be coming when microbiome monitoring and modification is a routine part of personalized nutrition and medicine. While it will likely be a long road before this is standard practice, identifying the microbial factors driving inter-individual variation in plant bioactives ADME processes is an important challenge that we must address in order to be able to consider diagnostic and therapeutic applications.

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Dr. David Berry, member of POSITIVe Working Group 1 received
CITY OF VIENNA PROMOTION AWARD!

The City of Vienna Awards are awarded anually to individuals who have made major achievements in areas ranging from architecture, literature and art to humanities and natural sciences. David Berry received the City of Vienna Promotion Award 2017 (Förderungspreis der Stadt Wien) in the category Natural Sciences.

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RESEARCH DISSEMINATION

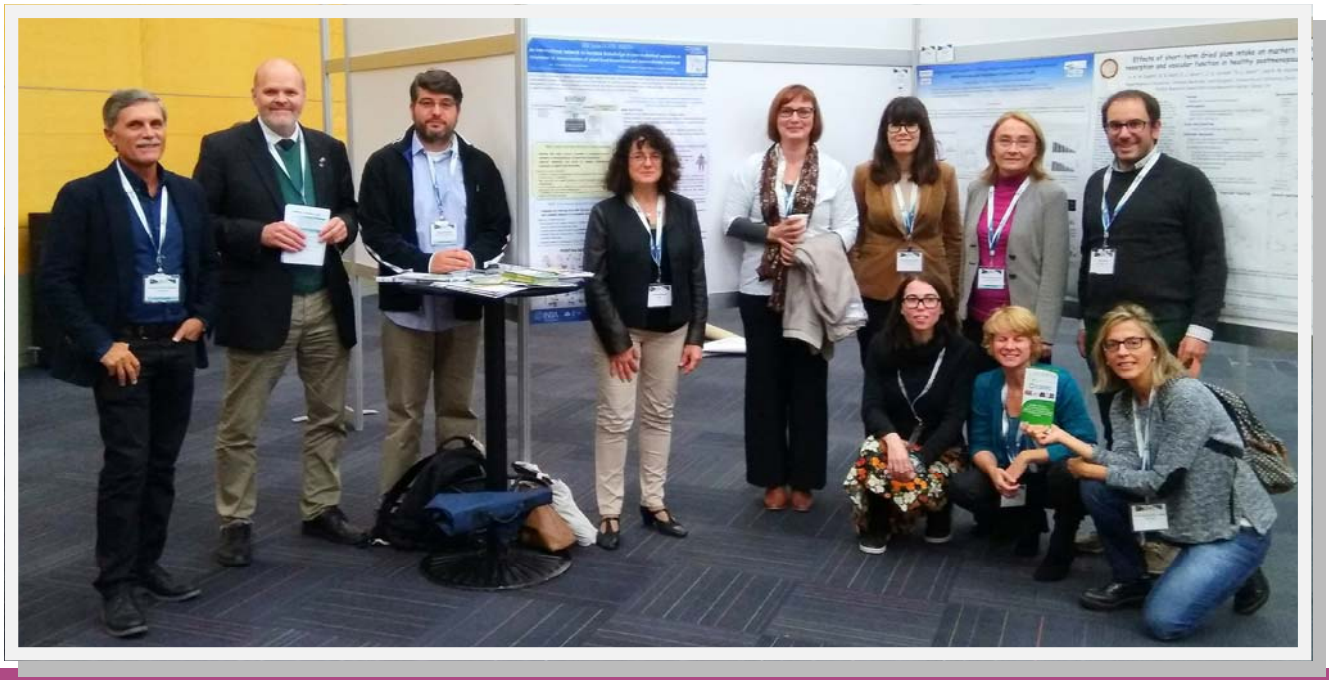
Significant and extensive participation of the members of the COST Action POSITIVe at the 8th edition of the 'International Conference of Polyphenols and Health' in Quebec (Canada)

The 8th edition of the 'International Conference of Polyphenols and Health' was successfully held at Quebec (Canada) the past 3rd to 6th of October, 2017. With the participation of more than 500 researchers from all over the world, the conference gathered a number of oral presentations given by members of the COST Action POSITIVe (FA1403) covering several research areas of polyphenols and health i.e., bioavailability and metabolism, role of bacteria, health effects of polyphenols (cardiovascular effects, aging, epigenetic and nutrigenomic effects), new databases available, and all of these under the common frame of the 'Inter-individual variability in response to the consumption of these bioactive compounds'.

Some of the keynotes and plenary lectures introduced by POSITIVe members were: 'Epigenetic control of cardiovascular health by polyphenols' by Dr. W. van der Berghe; 'Microbial metabolism of polyphenols, inter-individual response' by Dr. F. Tomás-Barberán; 'Polyphenols on modulation of gut microbiota in vitro' by Dr. T. van de Wiele; 'The frailty phenotype and polyphenol exposure towards healthy aging' by Dr. C. Andrés La Cueva; 'Polyphenols modulation of miRNA' by Dr. D. Milenkovic. In addition, several other oral shorter presentations by POSITIVe members were included in the different sections of the conference such as: 'Gut metabolism of quinic acid' by Dr. S. Mocco; 'Bioavailability of cranberry polyphenols' by Dr. A. Rodríguez-Mateos; 'Bacterial enzymes as a tool to prepare polyphenol metabolites' by Dr. K. Valentová; 'Phyothub online platform' by Dr. C. Manach; 'Interindividual variability in the nutrigenomic response to curcumin' by Dr.C. Morand or 'Contrasting in vitro vs. in vivo molecular effects of the ellagitannins metabolites urolithins' by Dr. M.T. García-Conesa. All these talks covered the main objectives and research carried out within the WG1 and WG2 of the Action.

To strengthen the presence of POSITIVe in the conference, a poster with the main objectives and tasks developed by the Action was put up, and the tryptic and newsletters about POSITIVe were distributed during the poster sessions.

The principal objective and message of POSITIVe has been definitively widely spread to the scientific community in the field during the conference.



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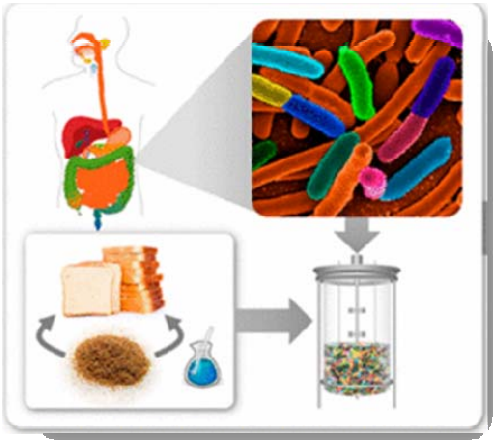
RESEARCH DISSEMINATION

PUBLICATIONS– WG1



Elucidating the colonic microbial metabolism of phenolic acids: an essential step towards the understanding of interindividual variability in the response to dietary polyphenols

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Article

pubs.acs.org/JAFC

Effect of Bioprocessing on the *In Vitro* Colonic Microbial Metabolism of Phenolic Acids from Rye Bran Fortified Breads

Ville M. Koistinen,[†] Emilia Nordlund,[‡] Kati Katina,[‡,§] Ismo Mattila,[‡,∥] Kaisa Poutanen,[‡] Kati Hanhineva,[†] and Anna-Marja Aura*[,‡]

COST-Positive partners from UEF and VTT Ltd (Finland) have published this collaborative article combining techniques of cereal bioprocessing, an *in vitro* colon model and state-of-the-art metabolite analyses using targeted and non-targeted mass spectrometry.

The current article compared phenolic acid metabolism of native and bioprocessed rye bran fortified wheat breads and elucidated the microbial metabolic route of ferulic acid from food matrix. The breads were first subjected to a simulated upper intestinal *in vitro* digestion and the digested samples were inoculated with faecal microbiota in an *in vitro* colon model. In this study, the faecal inoculum was pooled from several donors to eliminate the possible variability, as we focused on the metabolic routes themselves.

The time course of the metabolite formation was followed using mass spectrometry (GCxGC-TOFMS and UPLC-QTOF). While original cereal phenolic acids were released more extensively from the bioprocessed bran bread and ferulic acid had consistently higher concentrations in the bread type during fermentation, there were only minor differences in the appearance of microbial metabolites. The only difference was that the resilient native rye bran bread showed better the intermediary metabolites of ferulic acid, other hydroxycinnamic acids among them. Therefore, the authors conclude that the microbial metabolites formed by the faecal microbiota are common for all hydroxycinnamic acids, namely hydroxylated phenylpropionic acids, phenylacetic acids and benzoic acids, which can be connected to many flavonoids and polymeric flavanols. When metabolites are scattered to different small phenolic and organic acids, their detection may be challenging. Moreover, when the source is a complex dietary fibre matrix, such as whole grain cereals, the release and conversion is slow and may not be distinguished from other sources.

The best sample for human intervention for detection of microbial metabolites is 24-hour urine, which gives a history of metabolites circulating in the body during the past 24 hours. The metabolites have a long residence time in the body fluids, and they are gradually excreted to urine. Therefore, the health benefits of microbial metabolites may come *via* synergistic effects from several sources and the correct approach would be a comparison of whole diets instead of individual foods. It is not well known how interindividual differences in the ecology of colonic microbes or metabolite-related genes affect the metabolism of phenolic acids and more research is thus warranted on the metabolizing capabilities of individual microbial strains or individual communities.

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RESEARCH DISSEMINATION

PUBLICATIONS– WG2

Access to all dissemination products:
https://www6.inra.fr/cost-positive/Dissemination

Nutrients **2017**, *9*(7), 746; doi:10.3390/nu9070746

Open Access Review

A Systematic Review and Meta-Analysis of the Effects of Flavanol-Containing Tea, Cocoa and Apple Products on Body Composition and Blood Lipids: Exploring the Factors Responsible for Variability in Their Efficacy

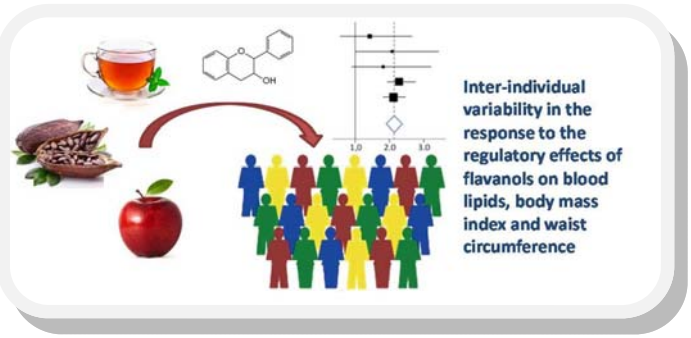
Antonio González-Sarrías [1,*], Emilie Combet [2], Paula Pinto [3], Pedro Mena [4], Margherita Dall'Asta [4], Mar Garcia-Aloy [5,6], Ana Rodríguez-Mateos [7], Eileen R. Gibney [8], Julie Dumont [9], Marika Massaro [10], Julio Sánchez-Meca [11], Christine Morand [12] and María-Teresa García-Conesa [1,*]

Flavanols against cardiometabolic risk factors: accumulated evidence of their efficacy supports their beneficial effects and the relevance of population estratification

This is the second published article of a series of metanalyses that the members of POSITIVe are conducting as part of the activities planned within the WG2 of the Action. With the collaboration of partners from different research institutions from Spain, UK, Portugal, Italy, & France, we have collected and critically revised a total of 120 randomized controlled clinical trials (RCTs) in the search for the current evidence of the efficacy of flavanol-containing tea, cocoa and apples, on body mass index (BMI), waist circumference (WC) and blood levels of cholesterol and triglycerides (TAGs). In addition, various factors considered to have an influence on the response to the consumption of these type of compounds have been explored.

A number of important issues have come out of this analysis. First of all, the heterogeneity of the trials is very high and thus, a considerable number of the studies need to be pooled in order to achieve significant results. Indeed, when all the studies were pooled together the overall evidence of the reduction of BMI, WC, total and LDL-cholesterol, and TAGs and of the increase in HDL-cholesterol was very significant. These effects were quantitatively comparable to those produced by some drugs, life-style changes or other natural products.

On the other hand, grouping the studies taking into account factors such as the baseline-BMI, sex, or health status of the participants, or the source and form of administration of the compounds, or the country were the study was conducted gave us some preliminary indication of the potential influence of these factors on some of the outcomes. The results suggested that the flavanols may be more effective in specific subpopulations such as in overweight/obese people or when administered as part of tea drinks or tea extracts. Nevertheless and given the still high heterogeneity of the studies and the reduced number of them per subgroup the significance of these results is very limited.



It is important to remark that, so far, the description of the participants in the different human studies has not always been very thorough and thus, important features such as the ethnicity, sex, age, menopausal stage, smoking or disease condition have not been properly described. Often, the intervention has been conducted in mixed populations making difficult the extraction of data useful for the study of the factors affecting interindividual variability in the response to these compounds. Further, other important factors such as life-style habits (sport practising, alcohol intake, etc) have not been usually considered.

In the future, these and other critical factors such as intestinal microbiota composition or genetic make-up will have to be incorporated into the human intervention studies. Also, full characterization of the products used in the intervention is required so that proper doses and metabolism of the flavanols (or other bioactive compounds) can be estimated. Improved design of future studies taking into account all these will definitively enhance our understanding of interindividual variability in response to bioactive compounds and of their efficacy against cardiovascular and metabolic diseases.

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RESEARCH DISSEMINATION

PUBLICATIONS– WG3

The NATCONSERV Project: persuading the food industry to use berry extracts as a natural source of bioactive antioxidants for the meat industry: A successful story of the POSITIVe Romanian partners in collaboration with the Romanian Food Industry stakeholders.

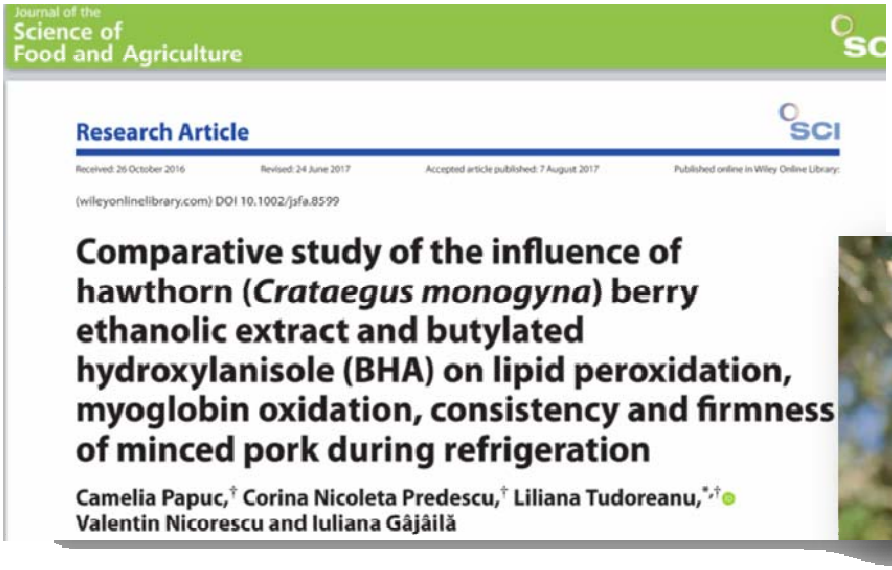
Following public concern about the use of synthetic food antioxidants, there is an increasing demand for the application of mixed or purified natural alternatives to maintain the quality of meat and meat products during storage. Moreover the texture, flavour and mouthfeel arising from the intake of foods are critical to consumer choice and acceptability.

The rules to design food structure for existing meat products have been well established although not necessarily completely and scientifically described and understood. Currently, there is a strong drive to produce healthy consumer acceptable meat products, pushing products into a formulation space whereby some of the well-known rules no longer apply. On the other hand, the costs of developing formulation production replacing the so called traditional additives are of concern to many producers.

Members of the POSITIVe's Romanian group (Prof. Camellia Papuc and Prof. Liliana Tudoreanu) in collaboration with other colleagues from the Faculty of Veterinary Medicine of Bucharest (Dr. Corina Nicoleta Predescu, Dr.Valentin Nicorescu and Dr. Iuliana Gâjaila) conducted a research project to find the most suitable natural bioactives as antioxidants in the formulation of several minced meat products. The project NATCONSERV- Natural food preservatives for functional safe and healthy foods ended in August of 2017. The Romanian food company involved was Group ANGST Romania (www.angst.ro) which is a Romanian-Swiss company specialized in meat products. The project was funded by the Executive Agency for Higher Education, Research, Development and Innovation Funding (https://www.uefiscdi.ro/) and by the Group ANGST (Romania).

The main objective of the project was to develop new meat products reducing the use of synthetic food antioxidants and applying instead, natural bioactive compounds from hawthorn berries and fermented juices. The results so far have been excellent and the natural extracts rich in bioactive compounds tested were more effective antioxidants than the synthetic counterpart butylated hydroxylanisole (BHA) in minced meat products (see article below).

As a result of this project, two patents have been submitted to the Romanian office for patents OSIM (http://www.osim.ro/) for natural antioxidants to be used by the meat industry and two new products developed (frankfurters). One of the main outcomes is that the good quality of the products obtained with the natural antioxidants persuaded Group Angst Romania to start designing a new formulation of products based on natural antioxidants.


Journal of the Science of Food and Agriculture

Research Article

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(wileyonlinelibrary.com) DOI 10.1002/jsfa.8599

Comparative study of the influence of hawthorn (*Crataegus monogyna*) berry ethanolic extract and butylated hydroxylanisole (BHA) on lipid peroxidation, myoglobin oxidation, consistency and firmness of minced pork during refrigeration

Camelia Papuc,† Corina Nicoleta Predescu,† Liliana Tudoreanu,*† Valentin Nicorescu and Iuliana Gâjâilă

POSITIVe NEWSLETTER
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RESEARCH DISSEMINATION

INTRODUCING POSITIVe TO THE GENERAL AUDIENCE

On September 29, 2017, POSITIVe Partner, Institute of Animal Reproduction and Food Research PAS organized in Olsztyn (Poland) one of the largest science celebration events in Europe – Researchers' Night. Through a vast array of experiments, science shows and workshops researchers advocated a crucial role of science in our everyday life, dispelling negative stereotypes around research work, and building mutual trust with the society at large. Everyone could find first-hand answers to the questions concerning health, nutrition, technology or engineering. Institute invited Night's guests to visit usually inaccessible laboratories offering experiments with antioxidants, workshops on microbiology and methods of assessing the prohealth value of everyday food products.

Institute's researchers prepared a presentation introducing school children, their teachers and parents to the mission of COST POSITIVe, pro-health values of plant food bioactives and the phenomenon of inter-individual variability. During workshops "Build your health", young students learnt what is the new food pyramid, how it is built, what are the factors affecting its composition (age, sex, lifestyle), and how did it change over the last decades. Kids and youngsters built a proper, up-to-date pyramid using magnets representing different food products, paying a special attention to those containing plant-based bioactive compounds. Then, participants were challenged to differentiate products as to their beneficial and potentially harmful effects on a human body. Here they were familiarized with the aspects of interindividual variability and other determinants affecting the response of our organism to biologically active compounds. During the entire event, children acquired a new knowledge concerning informed nutritional choices and importance of physical activity.

EUROPEAN RESEARCHER´S NIGHT IN POLAND

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GET TO KNOW YOUR POSITIVe PARTNER

EARLY STAGE RESEARCHERS

JAROSLAV HAVLIK

Czech University of Life Sciences, Czech Republic

What is the focus of your research?
My research is focused on the bioactivity of natural products. It is quite broad, driven by the interest to get an insight into the related areas. In my early career I investigated the antimicrobial activities of essential oils chemistry and their effect on food pathogens. Later, I focused on phenolics and other classes of natural compounds, studying their inhibitory properties against enzymes, as well as the cytotoxic and antimicrobial activity they exhibit. In the meantime, together with my research group, we have discovered honey bees as an interesting model to study antimicrobial interactions between food and natural product supplements and microbiota. Invertebrates as a model can overcome many obstacles associated with ethics and health safety measures. To better understand our model, we had to get a better understanding of the insect-associated microorganisms. Two years ago I joined the team of Christine Edwards and Emilie Combet at the University of Glasgow as a postdoc working on a BBSRC project. We studied the mutual interactions of human microbiota, food-derived polyphenols and dietary fibres. After finishing my postdoc, I returned to the Czech Republic and now continue studying human catabolism of polyphenols, especially stilbenoids, and some aspects of foodomics.

In what countries/organisations have your studied or worked in?
After obtaining my degree in life sciences at the Czech University of Life Sciences, I started working at the same university as a postdoc, than as a lecturer, and finally as a senior lecturer in agricultural chemistry and nutrition. Having returned from Scotland, I now work as a researcher and senior lecturer in a metabolomics facility at the Czech University of Life Sciences.

What has been the greatest achievement in your career?
Fundamental research does not always lead to something that can be practically useful. However, when it happens, you feel great satisfaction. We are now trying to commercialise the plant-based antimicrobial substituents for honey bees and some other things, running a spin-off company. It is very different from the lab work we have been used to.

Which is your favourite paper you have written/co-authored and why?
With Christine Edwards, Emilie Combet and other scientists from Glasgow University, we are now finishing a manuscript on the influence of dietary fibre on the large intestinal catabolism of polyphenols, also focusing on the interindividual differences. Different kinds of dietary fibre are certainly interacting with bacterial groups, facilitating their growth and changing their metabolic activities. The profile, latency and quantities of metabolites change in the presence of certain fermentable fibres. Usually, polyphenol metabolism is studied apart from the food matrix, therefore our novel approach will provide very interesting data to be available in the paper that will be published early next year.

Who is/was your most influential mentor/colleague and why?
In my early career, it was my PhD. supervisor, Prof. Ladislav Kokoska. He has a wonderful ability to motivate his students to not give up hope, especially when our first experimental do not confirm the hypothesis. In my recent career it was Prof. Christine Edwards, who I value for her leadership skills.

Where is your favourite place in the world and why?
Somewhere in the South-East Asia. I have travelled to Indonesia, Thailand, Cambodia, Malaysia, but spent the longest time in central Vietnam with the Czech Aid project, and later shortly at the Food Technology Department in Saigon. Only in Vietnam you can sit at the table, eat a snake and discuss whether a dog tastes better than a cat. Despite cultural differences many people have a western-like way of thinking. In Indonesia, Java, Bali and Lombok, the hospitality of local people is like nowhere else in the world. As a student-backpacker, I was invited to the families to stay overnight, and these were very memorable moments of my journey.

What is your favourite music/book
I enjoy Electronic rock, Teddybears, Chemical Brothers, Pendulum, electroswing or experimental music like Einsturzende Neubauten. My favourite writer is Haruki Murakami. His *Hard-Boiled Wonderland and the End of the World* or *Kafka on the Shore* magic realism novels really captivate imagination.

What is your favourite sport(s)?
I enjoy running marathons. In Istanbul, when thousands of runners run over the Bosporus Bridge connecting Asia and Europe, you can feel the bridge shaking. In Vienna or Prague, it is really touching when you hear waltz or The Moldau melodies when crossing the finishing line. Besides, I enjoy swimming, cycling and hiking. Scotland was a perfect place for this.

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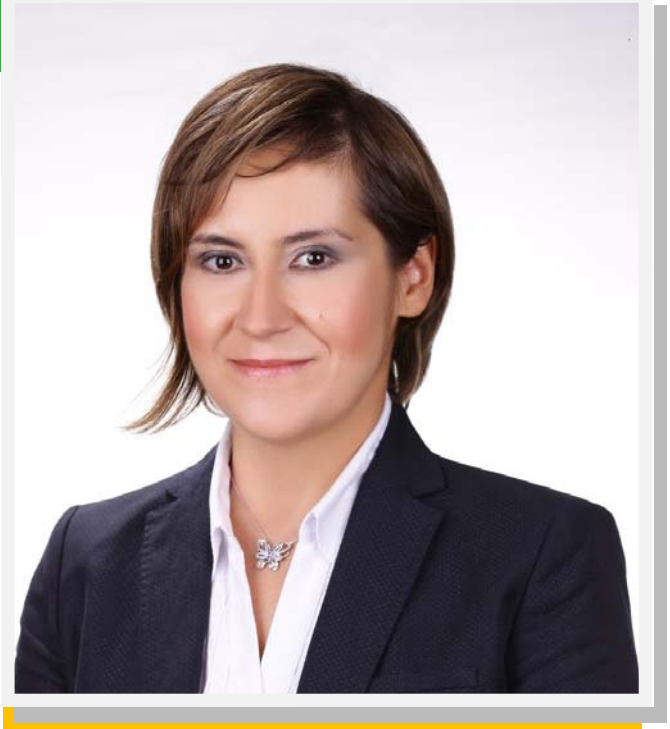
GET TO KNOW YOUR POSITIVe

EARLY STAGE RESEARCHERS



BANU BAYRAM

University of Health Sciences, Turkey

What is the focus of your research?
The focus of my research is development, validation and application of analytical methods for the quantification of food bioactive compounds. Besides, we investigate the bioavailability, biological activity and metabolism of phytochemicals by means of cellular models, animal and human studies for the prevention and treatment of diseases.

In what countries/organisations have your studied or worked in?
I graduated from Istanbul University Department of Biology. Then I got my MSc and PhD degrees at the Istanbul Technical University, Department of Food Engineering. During my PhD I got a scholarship from the government and joined the research group of Prof. Gerald Rimbach at the Christian Albrechts University (Kiel, Germany), Institute of Human Nutrition and Food Science, to perform the practical part of my thesis, and stayed there for 3.5 years. During my PhD I had chance to work at the University of Hohenheim (Stuttgart, Germany), Department of Biofunctionality and Safety of Food, for 2 months. After I completed my PhD thesis, I started to work again with Prof. Rimbach as a postdoc for 14 months. When I came back to Turkey, I got a position at the TUBITAK Food Institute. As a senior researcher, under an EU Project, I visited the Institute of Food Research (Norwich, UK) for 6 months.

What has been the greatest achievement in your career?
The greatest achievement in my career is to get the scholarship from the government and go to Germany for the PhD studies. This was a great experience for me and it allowed me to improve myself personally and scientifically.

Which is your favourite paper you have written/co-authored and why?
My paper demonstrating the results of my *in vivo* study entitled "A diet rich in olive oil phenolics reduces oxidative stress in the heart of SAMP8 mice by induction of Nrf2-dependent gene expression" (*Rejuvenation Research, 2012, 15: 71-81*) is my favourite. It was the first paper to use my scientific skills in and it has the highest citation number among all my papers. Besides, the paper entitled "A validated method for the determination of selected phenolics in olive oil using high-performance liquid chromatography with coulometric electrochemical detection and a fused-core column" (*Food Chemistry, 2014, 138: 1663-1669*) is also important to me, because I published it after I faced many technical problems.

Who is/was your most influential mentor/colleague and why?
The most influential mentors in my life are Prof. Gerald Rimbach and Prof. Jan Frank. Prof. Rimbach, who was the supervisor of my thesis and I worked in his lab for 4.5 years. He is a very experienced scientist with a profound knowledge. He always encouraged me and taught many scientific skills that I needed to progress in my research career such as accurate scientific writing. Prof. Frank was a post-doc in Kiel while I was doing my PhD, now he is a professor at the University of Hohenheim. He is a very good friend of mine, a great personality and a very successful excellent scientist. I learned all about analytical techniques from him. Both mentors strongly supported me during my PhD and I learned almost everything what I know in the scientific world from them.

Where is your favourite place in the world and why?
The magnificent city of Istanbul is my favourite place in the world. It is an exciting, living city where I was born and still live in. Istanbul is one of the most important historical and cultural centres in the world and I am in love with the view of Bosphorus.

What is your favourite music/ book
I like listening to R&B, Latin and Greek music. Ricky Martin, Shakira, Rihanna, Pitbull, Enrique Iglesias, and Keti Garbi are my favourite singers. I like reading books of Carlos Ruiz Zafon, and Dan Brown.

What is your favourite sport(s)?
Unfortunately, I am not actively involved in any sport, but I go to matches of basketball, volleyball, football and tennis very often. Besides, I go to the gym a few times in a week.

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GET TO KNOW YOUR POSITIVe PARTNER

SENIOR RESEARCHERS

ELENA KISTANOVA

Bulgarian Academy of Sciences, Bulgaria

What is the focus of your research?

I have been working in the field of biology and biotechnology of animal reproduction for about 20 years**.** Since 2006 EU and many other countries banned antibiotics as feed additives and synthetic hormones as growth promotors in animal husbandry, based on their negative consequences for animal health and food safety. These restrictions accelerated the process of searching possible substitutes. Herbs and herbal extracts, by-products of fruits and vegetables processing proved as a valuable alternative, being useful as growth promoters and therapeutic agents. We started to analyse the effect of new phytogenic feed additives on the reproductive system of animals (plant exctract from *Tribulus terrestris*, micro algae *Spirulina platensis*). Ovulation rate and oocyte quality are important determinants of reproductive efficiency in females. The processes of follicular growth are closely regulated by endocrine and paracrine factors, including the gonadotrophins, metabolic factors and several local growth factors. Nutritional manipulations, especially supplementation of plant bioactive substances, can affect fertility. **Focus of my research is on understanding how they do that or how they can regulate the follicular growth leading to ovulation**. There are many questions to be clarified, e.g. whether bioactives (and which ones) can affect hormonal level or local growth factors (GDF9, BMP15), or whether they can affect the epigenetic reprogramming of developing oocytes? Inter-individual variation in response to bioactives from the reproductive system is also a very interesting topic, and we have started to pay more attention to this fact in our research.

In what countries/organisations have you studied or worked?

I finished my PhD at the Research Institute of Children and Adolescence Physiology in Moscow, Russia. Although my main scientific work is related to the area of reproduction, my PhD thesis was related to the cardiovascular system. I investigated the micro vascularization of rat's mesentery during the sexual maturation period. Having taken part in COST Action MITOFOOD, I was able to participate in the STSMs programme and perform research activities in the Institute of Physiology of the Czech Academy of Science in Prague. Under the leadership of Prof. Josef Houstek, we analysed the activity of mitochondrial enzymes in the ovaries of mouse treated with *Spirulina platesis* and organic selenium-selenopyran. My another valuable scientific visit took place in China, in the State Key Laboratory of Reproductive Biology, Chinese Academy of Science, headed by professor Qing-Yuan Sun, where I investigated mitochondria in oocytes with the methods of confocal microscopy. In Italy, Milano, in the lab of professor F.Gandolfi, I had the opportunity to perform studies related to the *in vitro* fertilisation. All in all, these scientific missions allowed me to get familiarized with different cultures, various approaches to research work, and to be part of a useful transfer of knowledge.

What has been the greatest achievement in your career?

There are many achievements in my career I consider important. They are all related to different parts of my work. I was the scientific expert in a significant FP7 – ReProForce project (http://reproforce.ibir.bas.bg/en), worked as a deputy director of our Institute (till 2014), and initiated a broad international collaboration while working in the COST Actions, bi- and multilateral projects.

However, my most important achievement is the education of future generations of scientists– the people, who I have transferred my knowledge and passion for science to. I am proud that my daughter caught "the bug for science" (she is a PhD student now) and that my two my PhD students (Desislava Abadjieva and Vanya Mladenova- members of POSITIVe) are now holding research positions in our Institute. I believe that they will continue our investigations and keep developing their scientific careers. They give me a hope that my scientific legacy will be continued.

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

It is Abadjieva D., Kistanova E. (2016) *Tribulus terrestris Alters the Expression of Growth Differentiation Factor 9 and Bone Morphogenetic Protein 15 in Rabbit Ovaries of Mothers and F1 Female Offspring. PLoS ONE 11(2): e0150400. doi:10.1371/journal.pone.0150400.* There are two reasons for choosing this paper as my favourite: a) we published interesting results proving the transgenerational effect of the aphrodisiac plant on the reproductive performance; b) the article was accepted and published in a recognized peer-review journal. It is no secret how difficult it is to publish articles from eastern European countries in peer-review journals with the IF. That is why we consider having our article published a great success.

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

It was my PhD mentor Prof. V.I Kozlov, DSc. Now he is the head of the Anatomy Department at the Medical Faculty of Peoples' Friendship University of Russia. He was a pioneer in the area of investigating blood microcirculation by bio(vital) microcopy. Our group included 6 PhD students who investigated the micro vascularization in different organs. He taught us to be creative, to work together, and to be ready to help each other. The basic knowledge and skills obtained during my PhD studies have helped me throughout my whole scientific life and allowed me to adapt to different scientific environments The friendship between all of us is maintained until now.

What is your advice for young scientists?

Maybe these are more than enough, but I believe everyone can choose the right ones for themselves:

- Respect ethical code in career development and remember that you are a human first.
- Do not put success in a competition or in a career above friendship.
- Be creative and dispel stereotypes.
- Don't use the already known pathways – try to find your own.
- Don't feel discouraged if something goes wrong - you are young and have the time to keep trying.
- Be open to mobility;
- Respect your colleagues and get inspired by their experience.

Only through working together and having a common contribution to science challenges we can achieve significant results and discoveries.

Where is your favorite place in the world and why?

I've travelled a lot, but not everywhere. It may be I' ve not reached this place yet. However, my heart belongs to two magnificent places: the white birch grove of Russia and the mountains of Bulgaria.

What is your favorite music/book?

It may sound old fashioned but I prefer classical music. Its harmony is the best relaxing tool in our competitive life. Also classical and modern ballet has not stopped to amaze me all my life. I am happy that I had the occasion to see the best performances in the most famous theatres – as in Bolshoi in Moscow, in Covent Garden in London, in Albert Hall in London, in Mariinsky in Saint-Petersburg. Among chansons, my favourite song is "Dance me to the end of love" of a Canadian singer-songwriter Leonard Cohen. I was pretty surprised to find out that I share the same favourite book with the colleague from Serbia – "The Alchemist" of P.Coelho. Sofia theatre "199" produced an amazing performance based on this novel. It is unbelievable how Coelho described in a few simple words the depth of feelings, people's relationships, and the necessity to follow a Personal Legend (something like our purpose in life). I read all of his subsequent books, but none of them moved me so deep like "The Alchemist."

What is your favorite sport(s)?

I'm not really a sport kind of a person. I am convinced that the physical and motor activity should serve to strengthen health and not be subject to competition. For me, walking in the forest and mountains is the best way to stay fit. I grew up on the plain. When I moved to Bulgaria and saw the mountains, I fell in love with them. They have this magic that attracts you more and more, they change during the day, during the seasons, however, always remain beautiful and share their positive energy!

OF INTEREST TO POSITIVE COMMUNITY

BIOAVAILABILITY 2018

"Understanding the bioavailability of micronutrients and bioactive compounds for improved public health"

DATE: 12-13 September, 2018

PLACE: John Innes Conference Centre, Norwich, UK

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