Lifestyle Genomics

Lifestyle Genomics 2018;11:169–193
DOI: 10.1159/000501177

Published online: July 8, 2019

Abstracts are available online only, free of charge,
at www.karger.com/doi/10.1159/000501177

13th Congress of the International Society of Nutrigenetics/Nutrigenomics (ISNN)

July 12-13, 2019, Cambridge, UK

Guest Editors
Martin Kohlmeier, Kannapolis, NC, USA
Adela Chirita, Timisoara, Romania
Emma Beckett, New Lambton Heights, NSW, Australia
Donato Angelino, Parma, Italy
Daniele Del Rio, Parma, Italy
Mihai Niculescu, Hillsborough, NC, USA

NNEdPro-ISNN Joint Nutrigenomics Education Session
Oral Presentation
ISNN Nutrigenetics Guidelines Working Groups
Poster Abstracts

KARGER

Basel · Freiburg · Paris · London · New York · Chennai · New Delhi · Bangkok · Beijing · Shanghai · Tokyo · Kuala Lumpur · Singapore · Sydney

Lifestyle Genomics®

NNEdPro-ISNN Joint Nutrigenomics Education Session

1

NGx case studies as teachable moments in health professionals' education

Martin Kohlmeier[1]

[1]UNC Nutrition Research Institute, University of North Carolina at Chapel Hill, Kannapolis, NC, USA

Healthcare providers commonly find it difficult to provide effective nutrition advice for preventing or treating disease, improving physical performance, or improving mood and cognition difficult. Lack of comprehensive training is a major reason. When the complexities of individual differences and the practical use of genetic and other omics information are added, many well-intentioned students and health professionals become discouraged. These double difficulties can be turned into a strength by explaining interesting examples, building use cases by integrating basic science concepts, detailed explanations of metabolic mechanisms, and established dietetic approaches. An illustrative example may consider the notably different vitamin B12 (B12) status of people with the common *FUT2* rs601338 allele G and of those without it (Kohlmeier, 2013). The secretors, who have one or two rs601338 G alleles, tend to have less B12 in blood. A next step could be to recognize that most people around the world do not have an rs601338 G allele, but many of them have functionally equivalent and similarly common null variants at nearby positions. The *FUT2* teaching moment can touch on the roles of intrinsic factor, haptocorrins, glycosylation, enterohepatic circulation, as well as blood group antigens, forensic significance of blood group secretors, or also the role of cell surface glycoproteins during infection with *H.pylori*. A practically relevant question may be about B12 depletion and metabolic changes in young teenagers starting a vegan lifestyle and what the presumed comparative consequences are in secretors versus non-secretors. There are numerous equally interesting examples that can help learners to link important molecular concepts to important differences in individual responses to nutrition exposures. Practical use cases are more likely to stimulate the interest of undergraduate as well as postgraduate learners in key nutritional and genetic concepts. It is much easier to take issues seriously when we find that they impact real people, including ourselves.

References

1. Kohlmeier M. Nutrigenetics. Applying the science of personal nutrition. Academic Press, San Diego, 2012, pp 185-6. ISBN 9-7801-2385-9-006
2. Velkova A, Diaz JEL, Pangilinan F, et al. The FUT2 secretor variant p.Trp154Ter influences serum vitamin B12 concentration via holo-haptocorrin, but not holo-transcobalamin, and is associated with haptocorrin glycosylation. Hum Mol Genet 2017; 26(24):4975-4988

2

IUNS and ISNN efforts for better Nutrient x Gene interactions education and practice

J Alfredo Martinez[1]

[1]Precision Nutrition and Cardiometabolic Health Program. IMDEA-Food Institute CEI UAM-CSIC, Madrid, and Centre for Nutrition Research, University of Navarra, Pamplona. CIBEROBN, Madrid, Spain. IdisNA Institute for Health Research, Pamplona, Spain.

Precision nutrition based on Nutrigenetics and Nutrigenomics is associated with the principle that food or nutrients utilization depends on the genetic background of the individual (Nutrigenetics) and on the capacity of nutritional factors to modulate gene expression (Nutrigenomics). Expected advances in both scientific branches should improve current interests and value for individualized health to achieve personal wellbeing demands. The increasing availability of omics technologies, the need for newer recognized biomarkers and the potential of featuring nutritional targets based on genome knowledge and bioinformatic progress are boosting genotype-based and transcriptomic applications for personalized nutrition. Thus, the applications for precision nutrition depends on the genetic make-up (genotype and epigenetic signatures) and on clinical/medical information (previous diseases, intolerances/ allergy manifestations, family constraints) or metabolism (physical activity and dietary intake) plus social variation (food likes/dislikes and convenience or religious aspects) influencing individual's nutrient utilization. The cost of genetic analyses, a protocoled personalized advice based on nutritionally associated omics, the regulations and clearer information about the benefits and limitations of using genetic tests are pending issues as well as harmonization of ethical issues. The promotion of scientific activities in Nutrigenetics and Nutrigenomics areas and the coordination of existing Societies concerning this field, such as the International Society for Nutrigenetics and Nutrigenomics (ISNN) also must be prompted to interact with IUNS. Indeed, the development of nutritional teaching and skills learning based on online tools are declared endeavors of the IUNS Capacity Building Committee in order to implement and promote global IUNS missions, including Nutrigenetic/Nutrigenomic interactions. An expected outcome from these activities is to provide e-learning modules devised for the professional development of young Nutritionists members of IUNS Adhering bodies, preferentially in Africa, Latin-America

KARGER

E-Mail karger@karger.com
www.karger.com/lfg

and Asia Regions. The possibilities are varied through MOOCs, ONLINE Courses, Modules or Webinars within already existing Programs and a Textbook in collaboration with ISNN. Interestingly, the former "Nutrient- gene interactions: Knowledge to action" Task Force has evolved to "Precision Nutrition", which is benefiting from Nutrigenetics and Nutrigenomics progresses to provide an efficient individualized nutrition for a healthy life, where about 15000 citations appeared in PUBMED since 2001.

References

1. Ramos-Lopez O, et al. Guide for Current Nutrigenetic, Nutrigenomic, and Nutriepigenetic Approaches for Precision Nutrition Involving the Prevention and Management of Chronic Diseases Associated with Obesity. J Nutrigenet Nutrigenomics. 2017;10(1-2):43-62.
2. Kohlmeier M, et al. Guide and Position of the International Society of Nutrigenetics/Nutrigenomics on Personalized Nutrition: Part 2 Ethics, Challenges and Endeavors of Precision Nutrition. J Nutrigenet Nutrigenomics. 2016;9(1):28-46.
3. Ferguson LR, De Caterina R et al Guide and Position of the International Society of Nutrigenetics/Nutrigenomics on Personalised Nutrition: Part 1 - Fields of Precision Nutrition. J Nutrigenet Nutrigenomics. 2016;9(1):12-27.

3

The state of nutrigenomics education

Agata Chmurzynska[1]

[1]Institute of Human Nutrition and Hygiene, Poznań University of Life Sciences, Poland

Nutrigenomics examines the relationships between nutrients and the genome on the cellular, tissue, and whole-organism levels. Unraveling the genetic basis of inter-individual differences in dietary response, metabolism, and diet-related disease risk may eventually lead to genotype-based recommendations on nutrient intake and precise nutrition. Although health care professionals can benefit greatly from nutrigenomic education, nutrigenomic courses are not commonly included in undergraduate curricula. Moreover, the courses that do exist differ in duration and content. Some are offered during doctoral studies. There are also nutrigenomic education opportunities outside of higher education institutions, which include commercial online courses and traditional workshops. In addition, summer schools in nutrigenomics have been organized by the NuGO and the International Society of Nutrigenetics/Nutrigenomics (ISNN). There is also the European Summer School of Nutrigenomics in Camerino, Italy, as well as other national summer schools, such as in Poland and France. Students and health care practitioners usually do not perceive themselves to be well educated in nutrigenomics. Several recent studies have underscored the need to introduce nutrigenomic education into health profession curricula.

4

Nutrigenetics education in Eastern Europe: opportunities and challenges

Mihai Dinu Niculescu[1,2]

[1]Victor Babes University of Medicine and Pharmacy, Timisoara, Romania; [2]Advanced Nutrigenomics, Hillsborough, North Carolina, USA.

As nutrigenetics is transitioning from the status of an emerging science to one of a fully-fledged scientific field, the aspect of education in nutrigenetics received less attention. However, teaching nutrigenetics to either graduate or post-graduate students remains a challenging endeavor, stemming from multiple causes. This presentation discusses the challenges encountered, and the opportunities discovered when teaching nutrigenetics to a post-graduate, Eastern European audience. While not completely homogenous, the cultural settings in Eastern Europe are remarkably different from those in Western Europe and USA. In addition, and in part due to different priorities in medical and nutritional education, as well as due to differences in the functioning of the health care systems, students' expectations are different. These contribute to a different set of premises, from which students may derive a different set of motivational vectors that powers their interest for studying nutrigenetics. However, opportunities are also discussed, arising from the same causal pool from which challenges emerge.

As a consequence, building a curriculum in nutrigenetics, structuring a course, and adding the motivational framework to the teaching effort, are elements that have to be particularized to these audiences, sometimes in contrast to the usual techniques previously used in USA and Western Europe.

Acknowledgements: This work was partially funded by the POC Project NutriGen, SMIS 104852.

Oral Presentation

5

Weaving together omics and food intake patterns

Martin Kohlmeier[1]

[1]UNC Nutrition Research Institute, University of North Carolina at Chapel Hill, Kannapolis, NC, USA

Responses to nutrition exposures can vary greatly between individuals. This creates challenges for regulators who define adequate intake levels, to nutrition educators who want to teach what works and what does not, and to practitioners who want to guide their patients and clients towards effective nutrition solutions. Genetic information (genomics) is becoming increasingly useful to predict whether individuals are likely to respond to a particular intervention in a certain way (responders) or not (non-responders). At the same time, the investigation of intestinal microbes (microbiomics) helps us to understand how these organisms modify human nutrition exposure by metabolizing unabsorbed food residue and by generating useful nutrients for the host. Detailed analysis of the metabolites and other small molecules (metabolomics) in blood, urine and other accessible fluids can help us to

understand how all these moving parts work together to cause observable effects and outcomes. The goal of integrating information from these different domains is to guide us towards better nutrition solutions for specific individuals with their particular health challenges. We want to find effective nutrition patterns that transcend one-size-fits-all advice. We want to be able to tell individual patients and clients how they can shed excess body fat most effectively by adjusting their nutritional environment to be more conducive to achieving this goal. We want tools that can guide individuals toward food patterns that align better with their genetic framework and the behavior of their microbial companions. We want nutrition that works. The participants of the 13th Congress of the International Society of Nutrigenetics/Nutrigenomics are adding yet more tools for effective Precision Nutrition practices that can improve well-being, performance, health and longevity for all of us.

6

Exercise intensity-dependent regulation of FTO mRNA expression is associated with glucose accumulation in skeletal muscle of homozygous FTO rs9939609 A-allele genotypes

Jessica Danaher[1], *Alba Moreno-Asso*[2,3], *Robin A. Wilson*[2,3], *R. Mark Wellard*[4], *Christos G. Stathis*[2], *Matthew B. Cooke*[5]

[1]School of Science, College of Science, Engineering and Health, Royal Melbourne Institute of Technology (RMIT) University, Melbourne, Australia; [2]Institute for Health and Sport, Victoria University, Melbourne, Australia; [3]Australian Institute for Musculoskeletal Science (AIMSS), Department of Medicine-Western Health, Melbourne Medical School, The University of Melbourne, Melbourne, Australia; [4]Science and Engineering Faculty, Queensland University of Technology, Brisbane, Australia; [5]Department of Health and Medical Sciences, Faculty of Health, Arts and Design, Swinburne University of Technology, Melbourne, Australia
Email: jessica.danaher@rmit.edu.au

The association between the Fat Mass and Obesity-Associated (*FTO*) gene and the odds of obesity can be attenuated by approximately a third in physically active adults, suggesting a possible relationship between exercise and FTO protein function. To date, no studies have determined whether FTO is modifiable by exercise and whether changes in FTO function play any peripheral role in mediating skeletal muscle metabolism. Twenty-eight healthy males and females were genotyped for the *FTO* rs9939609 (T>A) polymorphism, prior to performing continuous isocaloric (400 kcal) cycle ergometer exercise on two separate occasions at 80% (HI) and 40% (LO) VO2peak. Skeletal muscle biopsies were sampled from the vastus lateralis pre-exercise, and at 10 and 90 minutes post-exercise. No significant interaction was detected for either exercise or genotype on FTO protein expression ($p > 0.05$). A main effect for time was observed for *FTO* mRNA expression following HI intensity exercise ($p = 0.002$), and for m6A methylation levels on RNA following both exercise protocols (HI, $p = 0.032$; LO, $p = 0.032$). GC-MS analysis detected greater skeletal muscle glucose accumulation at 10 minutes following HI ($p = 0.021$) and LO ($p = 0.033$) intensity exercise in AA genotypes compared to TT genotypes. A negative correlation was observed between skeletal muscle *FTO* mRNA expression and muscle glucose accumulation in AA genotypes ($p = 0.033$) during the HI intensity exercise trial. This is the first study to show an acute exercise intensity-dependent regulation of skeletal muscle *FTO* gene expression. The association between muscle glucose and *FTO* mRNA levels suggests an impact of *FTO* on carbohydrate metabolism.

7

Greek adolescents with higher BMI are more likely to adhere to a diet regimen. Synergistic effect of common genetic variants

Katerina Meimari[1,4], *Maria Kafyra*[1,4], *Ioanna Ntalla*[2,3], *Konstantinos Apostolou-Karampelis*[1], *Georgios Dedoussis*[1]

[1]Department of Nutrition and Dietetics, Harokopio University of Athens, Athens, Greece; [2]Clinical Pharmacology William Harvey Research Institute, Barts and the London Medical School, Queen Mary University of London, London, UK; [3]Centre for Genomic Health, Queen Mary University of London, London, UK [4]These authors contributed equally to this work.
Email: dedousi@hua.gr

Genetic predisposition is a major contributing factor to the development of obesity. Diet also plays an important role in obesity development, by increasing the risk for elevated adiposity. The present project investigates the impact of dietary patterns of Greek adolescents and established common genetic variants on BMI. Dietary patterns deriving from Principal Component Analysis (PCA) on the food frequency questionnaires of the TEENAGE Study (n = 857) were examined for their effect size on log(BMI). We assessed the combined effect size of these patterns with 34 established childhood obesity variants via multivariate linear regression, adjusting for age and gender. A forward stepwise variable selection was subsequently conducted to provide the optimal regression model, based on Akaike information criterion (AIC). PCA provided 5 dietary patterns explaining 45.5% of the adolescents' dietary choices. Only the "Healthy Diet" Pattern, including low fat dairy and unprocessed cereal, was significantly related with log(BMI) ($p < 0.001$). This indicates that adolescents with higher BMI are mostly the ones who follow a diet. Of the 34 variants examined, 5 SNPs were associated with log(BMI) ($p < 0.05$) (rs13107325{C} *SLC39A8*, 0.034±0.015; rs987237{A} *TFAP-2BI*, 0.025±0.012; rs7138803{G} *FAIM2*, 0.019±0.009; rs2287019{C} *QPCTL*, -0.026±0.012, and rs1558902{T} *FTO*, 0.021±0.009). The variable selection showed that the synergistic effect of the rs13107325 polymorphism and the adherence to the "Healthy Diet" pattern (0.037±0.015; $p = 0.013$) was associated with higher log(BMI) (AIC = -574.1). Adolescents with higher BMI are more likely to follow a diet. The synergistic effect displays great interest and may influence dietary choice via its effect on gut permeability and gut microbiota composition.

8

Biological basis of human variability: genetic influences on weight loss

John C Mathers[1]

[1]Human Nutrition Research Centre, Newcastle University, UK

There is considerable inter-individual variation in human phenotype due to inter-individual differences in genotype. In addition, phenotype varies between individuals, and within any individual over time, because of interactions between genotype and multiple environmental exposures including nutrition. Weight gain, and the risk of becoming obese, are influenced by genetic make-up. In the general population, >100 genetic variants are associated with measures of adiposity and, on average, variants in the *FTO* gene have the biggest individual effect. This raises the question "*If the risk variant in FTO helps to make people fatter, does it also make it more difficult to lose weight?*". Using data from 8 large weight loss studies involving about 9,500 participants, we found that carriage of the risk allele for *FTO* had no effect of weight loss (Livingstone *et al.* 2016). This lack of effect was evident for both genders, at younger and older ages and regardless of the type of intervention (diet, physical activity or drugs). Similarly, in a recent intervention study in the USA, there was no effect of variants in 3 other genes on weight loss (Gardner *et al.* 2018). This is good news for those wishing to lose weight since it shows that one's genes are not always one's destiny and that weight loss can be just as successful in those who carry risk alleles for increased adiposity.

References

1. Gardner CD *et al.* (2018) *JAMA*. 319(7):667-679.
2. Livingstone KM *et al.* (2016) *BMJ*. 354:i4707.

9

Genetics of obesity and eating behaviors

Louis Pérusse[1]

[1]Department of Kinesiology and Institute of Nutrition and Functional Foods, Laval University, Quebec, Canada

Although the dramatic increase in the prevalence of obesity observed worldwide could largely be explained by changes in our lifestyle (unhealthy eating habits, reduced physical activity level) and our environment (food supply, social and physical environments), not everyone is becoming obese despite being exposed to the same "obesogenic" environment, which suggests that genetic factors play an important role in explaining this differential susceptibility to obesity. The objective of this presentation is to provide a brief overview of the evidence for a role of genetic factors in obesity and eating behavior traits. Results from twin and family studies have clearly established that obesity is influenced by genetic factors. Heritability estimates are higher when derived from twin (50%-80%) compared to family (25-50%) studies and tend to be higher for phenotypes indexing fat distribution and abdominal fat than for those indexing total body fatness. The evidence showing that eating habits and eating behaviors are themselves influenced by genetic factors will be reviewed. Results from large-scale genome-wide association studies (GWAS) have identified > 800 genetic variants showing robust associations with various obesity phenotypes. Many of the genes associated with these variants are expressed in regions of the brain involved not only in the regulation of appetite (hypothalamus and pituitary gland), but also in learning, cognition, emotion and memory (hippocampus and limbic system), suggesting that traits related to eating behaviors might represent key mediators of the genetic susceptibility to obesity. Recent data from the Quebec Family Study suggesting that eating-behavior traits partly mediate genetic susceptibility to obesity will be reviewed.

10

Novel genotype-driven weight loss strategies

Lu Qi[1]

[1]HCA Regents Distinguished Chair and Professor, Director, Tulane University Obesity Research Center, Department of Epidemiology, Tulane University, School of Public Health and Tropical Medicine, New Orleans, LA, USA

Genetic research in the past decade has led to identification of numerous variations in human genome associated with obesity. These findings have been applied to detect gene-diet interactions on obesity and weight changes in population based studies and clinical trials. In large cohort studies such as the Nurses' Health Study and Health Professionals' Follow-up Study, we have analyzed the interactions between the genetic variations and various dietary factors such as sugar sweetened beverage, fried foods, fruits and vegetable, as well as dietary patterns in relation to obesity and weight gain. In long-term diet intervention trials such as the POUNDS LOST trial, we also investigated the roles of genetic variations in modulation of weight loss in response to diet interventions. Data from our studies indicate that this new research area holds great promise to improve genotype-driven weight loss strategies.

11

Pharmaconutrigenetics of antipsychotic-induced weight gain

Olivia Dong[1]

[1]Center for Applied Genomics and Precision Medicine, Department of Medicine, Duke University School of Medicine, Durham, NC, USA

Antipsychotic medications treat a variety of psychiatric disorders, including schizophrenia and bipolar disorder. Antipsychotic medications are routinely used off-label for aggression, autism spectrum disorders, dementia, obsessive-compulsive disorder, pervasive developmental disorder, sleep disorders, and treatment-resistant depression (1,2). First generation (typical) antipsychotics are associated with extrapyramidal side effects (i.e. Parkinsonism, tardive dyskinesia), which are minimized with second generation (atypical) antipsychotics although there is a greater risk of weight gain, impaired glucose tolerance, and lipid abnormalities (2–4). Antipsychotic-induced weight gain increases the risk for diabetes, metabolic syndrome, cardiovascular disease, and a 20% reduction in lifespan (4). Weight gain risk can vary by the specific antipsychotic agent (4).

Given the negative health consequences of antipsychotic-induced weight gain, it is critical to optimize selection of antipsychotics that maximizes drug efficacy and minimizes the risk of weight gain. From a pharmacogenetic standpoint, there are 10 antipsychotics that have pharmacogenetic guidance from FDA or have high evidence level (A or B) from the Clinical Pharmacogenetics Implementation Consortium (CPIC). These pharmacogenetic guidances are associated with *CYP2D6* genotypes and can help clinicians optimize therapeutic agent selection or dose selection of these antipsychotics. From a nutrigenetic standpoint, genetic markers in several genes (i.e. *ADRA2A, 5-HTR2C, DRD2, MC4R*) can help explain, and to some extent predict individual variation observed in antipsychotic-induced weight gain (3,4). Taken together, genetic information can be used to help select the optimal antipsychotic therapy that maximizes drug efficacy while minimizing adverse side effects.

References

1. Correll CU, Lencz T, Malhotra AK. Antipsychotic drugs and obesity. Trends Mol Med. 2011 Feb;17(2):97–107.
2. Meltzer HY. Update on typical and atypical antipsychotic drugs. Annu Rev Med. 2013;64:393–406.
3. Dayabandara M, Hanwella R, Ratnatunga S, Seneviratne S, Suraweera C, de Silva VA. Antipsychotic-associated weight gain: management strategies and impact on treatment adherence. Neuropsychiatr Dis Treat. 2017;13:2231–41.
4. Lett TA, Wallace TJM, Chowdhury NI, Tiwari AK, Kennedy JL, Müller DJ. Pharmacogenetics of antipsychotic-induced weight gain: review and clinical implications. Mol Psychiatry. 2012 Mar;17(3):242–66.

12

Inaugural presentation of the new ISNN textbook: *Principles of Nutrigenetics and Nutrigenomics - Fundamentals for Individualized Nutrition*

Raffaele De Caterina[1]

[1]Università degli Studi di Pisa, Pisa, Italy

Principles of Nutrigenetics and Nutrigenomics: Fundamentals for Individualized Nutrition is the most comprehensive foundational text on the complex topics of nutrigenetics and nutrigenomics. Edited by Raffaele De Caterina, Alfredo Martinez and Martin Kohlmeier, three scientists deeply involved in the field and in the International Society of Nutrigenetics/Nutrigenomics (ISNN) as Past- or current Presidents, with contributions from the most well-cited researchers conducting groundbreaking research in the field, this book addresses how the genetic makeup influences the response to foods and nutrients as well as how nutrients affect gene expression. *Principles of Nutrigenetics and Nutrigenomics: Fundamentals for Individualized Nutrition* is broken into four parts, providing a valuable overview of genetics, nutrigenetics, and nutrigenomics, as well as a conclusion translates research into practice.

With an overview of the background, evidence, challenges, and opportunities in the field, readers will come away with a strong understanding of how this new science is the frontier of medical nutrition. *Principles of Nutrigenetics and Nutrigenomics: Fundamentals for Individualized Nutrition* is a valuable reference for students and researchers studying nutrition, genetics, medicine, and related fields.

Key Features

- Offers a uniquely foundational, comprehensive, and systematic approach with full evidence-based coverage of established and emerging topics in nutrigenetics and nutrigenomics
- Includes a valuable guide to ethics for genetic testing for nutritional advice
- Contains definitions, methods, summaries, figures, and tables to help students and researchers grasp key concepts

The Textbook will be eventually accompanied by a Companion Website, with PowerPoint presentations of several chapters, with audio recordings by the authors, as a source of presentation material for teaching purposes.

13

The nutrigenomics education session at the NNEdPro Summit

Sumantra Ray[1,2,3]

[1]University of Cambridge, UK; [2]NNEdPro Global Centre for Nutrition and Health, Cambridge, UK; [3]Ulster University, NI, UK

The NNEdPro Global Centre for Nutrition and Health is a not-for-profit social enterprise, headquartered at St John's Innovation Centre Cambridge and operating internationally via a network of partner organisations including the British Dietetic Association, University of Cambridge, Ulster University, Imperial College London and University of Parma. The NNEdPro Global Centre brings together complementary domains of knowledge across Human Nutrition, spanning molecules to mankind. One key strategy of this consortium is to leverage the nutrition education and training of health professionals, including medical doctors and other regulated health practitioners, to translate good quality nutrition evidence into practice. Nutrition education and training needs to be sensitive to both the changing tide of breaking evidence as it is published and to this effect the NNEdPro Global Centre has recently co-established the peer reviewed journal, BMJ Nutrition, Prevention and Health, in conjunction with the British Medical Journal Group. In addition to this, education and training in nutrition must also take account of inter-individual variation in the response to nutritional exposures, not least owing to genetic diversity. The ability to apply an evidence-informed approach to nutritional practices in real time along with the skills to discriminate between individuals with varying nutritional requirements or responses, are paramount to building a robust future workforce in nutrition and health. Hence the juxtaposition as well as crossover between the 2019 NNEdPro Summit on Medical/Healthcare Nutrition Education and Research and the 13th Congress of the International Society for Nutrigenomics/Nutrigenetics (ISNN) in the academic location of Cambridge. The ISNN session during the NNEdPro Summit directly preceding the ISNN Congress showcases several practical examples of inserting nutrigenomics content and teaching approaches into general nutrition education. In fact, highlighting genetic diversity in nutrition responses can strengthen nutrition education by delineating the affected pathways and explaining opportunities for adapting dietary patterns to specifically identified individual needs. Joining forces will enable synergies between these two important knowledge networks, with future convergence within learned societies such as the International Union of Nutrition Sciences (IUNS).

14

The interaction of dietary polyphenols with the human gut microbiota: inter-individual variability and effects on human health

Daniele Del Rio[1]

[1]School of Advanced Studies on Food and Nutrition, University of Parma, Parma, Italy

A growing amount of research has provided evidence for protective effects of various (poly)phenol-rich foods against chronic disease, including cardiovascular disease, neurodegeneration, and cancer. Bioactivity investigations using cell lines have made an extensive use of both (poly)phenolic aglycones and sugar conjugates, these being the typical forms that exist in planta, at micromolar or even millimolar concentrations. However, after ingestion, dietary (poly)phenolics appear in the circulatory system not as the parent compounds, but as phase II-generated metabolites, and their presence in plasma after dietary intake rarely exceeds nano-molar concentrations. Substantial quantities of both the parent compounds and their metabolites pass then to the colon where they are degraded by the action of the local microbiota, giving rise principally to small phenolic acid and aromatic catabolites that are absorbed into the circulatory system. These catabolic steps introduce a clear variability factor into the picture of polyphenol health effects, namely the existence of different genotypes in the human and, mostly, microbial capacity to transform phenolic compounds. This lecture will provide the basic knowledge on polyphenol metabolism and absorption, an update on the reports identifying "metabotypes", and a first account of the different effects these different metabotypes might have in experimental models of various diseases, including models where gene expression was tested.

15

The postprandial metabolome: a source of biomarkers to differentiate the nutritional properties of foods as well as the genotypic and phenotypic status of humans

Guy Vergères[1]

[1]Agroscope, Schwarzenburgstrasse 161, 3003 Bern, Switzerland
Email: guy.vergeres@agroscope.admin.ch

The glycemic response of humans to the ingestion of foods is a key parameter in food and medical sciences as it provides information on both the quality of the ingested foods and the health status of patients. On the other hand, hundreds of metabolites in blood react to food intake. Thus, in addition to glucose, the postprandial metabolome must contain specific, yet undiscovered, markers of food intake as well as markers of the genotypic and phenotypic status of humans. This paper explores these questions by analyzing the postprandial metabolomes derived from three human intervention studies. The first study investigates how the postprandial serum metabolome responds to increasing caloric doses of a high-fat meal. This analysis highlights saturation at

Lifestyle Genomics 2018;11:169–193
DOI: 10.1159/000501177

higher caloric doses as well as global differences in the response of normal weight and obese subjects. The second and third study compare the postprandial serum and urine metabolome of healthy subjects having ingested milk, yoghurt, cheese, and a soy drink. The results highlight the ability of metabolomics to differentiate foods based on the postprandial response of specific metabolites as well as on metabolite signatures. Interestingly, a dichotomic response to milk ingestion is observed in blood and urine for galactonate and galactitol, two metabolites derived from lactose. These metabolites associate with the lactase-persistence genotype of the subjects. A dichotomic response is also observed in serum for the Lewis a antigen suggesting that genetic polymorphisms related to the metabolism of oligosaccharides interact with the intestinal microbiome to modulate the production of this trisaccharide. The metabolome of biosamples from human nutritional trials is a source of markers, which will eventually foster personalized nutrition by complementing genetic data with phenotypic data.

16

Exploring responder status of the gut microbiome for calcium absorption during adolescent growth

Corrie M. Whisner[1], *Owen Ma*[2], *Arindam Dutta*[2], *Daniel W. Bliss*[2]

[1]College of Health Solutions, Arizona State University, Phoenix, AZ; [2]BLISS Lab, Arizona State University, School of Electrical, Computer and Energy Engineering, Tempe, AZ

During the adolescent growth spurt, many teens do not meet dietary recommendations for calcium (Ca) and vitamin D, nutrients critical for reaching one's genetic potential for peak bone mass. Previously, we demonstrated that prebiotics may provide an alternative or complementary means of increasing Ca absorption in adolescents. While Ca absorption positively correlated with specific microbes, not all children responded to prebiotic treatment suggesting that other factors may influence the interaction of gut microbiota and human cells to improve Ca metabolism. In this secondary analysis, we compared the difference in baseline dietary intake (24-h recalls) and microbiota proportions (at beginning of control period) between responders (≥ 3% increase in Ca absorption) and non-responders (< 3% increase in Ca absorption). Dual stable isotope methodologies were used to assess fractional Ca absorption. Sequencing of the 16S rRNA gene was used to taxonomically characterize the gut microbiome. Machine learning techniques were used to build a predictive equation for identifying responders. A total of 65.0% and 35.0% of participants classified as responders and non-responders, respectively. Habitual diets did not differ by group but non-responders consumed more fat than responders (83±28 g vs. 64±19 g; p = 0.063). Fractional Ca absorption was greater in non-responders compared to responders (0.69±0.15 vs. 0.55±0.12; p = 0.036) on the control diet without prebiotics. We identified 23 microbial features, including *Roseburia, Parabacteroides, Megasphaera, Mogibacterium, other Clostridales, Odoribacter, Fusobacterium, Dorea, Anaerofustis,* and *Paraprevotella,* that predicted responders with ~80% accuracy. These findings suggest that habitual diet and baseline microbial profiles may be predictive of prebiotic benefits.

17

Nutrigenetics of the intestinal microbiome; a cautionary tale

Hannelore Daniel[1]

[1]Technische Universitaet Muenchen, Fraunhofer Institute IVV, Freising, Germany

Given the fact that the genetic influence of the host on the intestinal microbiome is rather low, (estimated from population and twin studies to account for less than 10% of the overall composition) it is not surprising that only a very few individual gene variants of the host have so far been found that could affect microbiome composition and function. On the contrary, hundreds of environmental and intrinsic factors (age, disease states etc.) have been associated with microbiome diversity and changes. Yet, less than 25% of the variance in composition is currently explained by these determinants. The Bristol stool scale (colour and consistency of faeces) is the most influential variable for composition and associates with the classified enterotypes. However, the stool features are mainly the result of the handling of intestinal contents in the large intestine and the transit time. Any alteration in gastrointestinal transit time (with pharmacological treatments for example) has been shown to affect faecal composition (water content and microbial mass) and is thus a major driver of microbiome composition and functionality. I shall also address overall mass of the gut microbiome that becomes a particularly relevant feature when its metabolic capacity is predicted from sequence information. In addition, overall bacterial mass relative to host body mass may be a critical factor when translating findings in rodents to the human condition. Taken together, microbiome research is largely ignoring key features of gut physiology, is also not taking into account mass phenomena and builds/relies on relative composition data. This argues for more caution in making scientific claims.

18

Epidemiologic study of nutrigenetics and microbiome

Katie Meyer[1]

[1]UNC Nutrition Research Institute, University of North Carolina at Chapel Hill, Kannapolis, NC, USA

The field of nutrigenetics has focused on interactions between genetic variants and nutritional exposures, but there is growing interest in the possible relevance of the gut microbiome in nutrigenetic pathways. The role of the gut microbiota in mediating physiologic effects of dietary exposures has long been appreciated, and recent technological and analytic advances have accelerated our ability to study gut microbiota-related pathways and mechanisms, with the potential to advance discovery and delineate specific intervention targets related to diet/nutrition, gut microbiota, and metabolites. Integration of data on host genetics, gut microbial composition and function, and diet and nutrition in human population studies has revealed instances for which the intersection of nutrigenetics and the gut microbiome may refine

our understanding of individual variability in biologic response to dietary/nutritional exposures (e.g., associations between lactase gene (*LCT*) and *Bifidobacterium*). However, there remain several critical challenges to inferential interpretation of data from epidemiologic studies. We will describe major limitations in the field and propose future directions that may contribute to enhancing the rigor of research in this area.

19

Genotype-microbiome interactions in lactose intolerance

Victor Schmidt[1], *Liam Fitzstevens*[1], *Thirumalaisamy Velavan*[2,3], *Le Huu Song*[3], *Akim Adegnika*[2,5], *Meral Esen*[2], *Peter Kremsner*[2], *Ruth Ley*[1]

[1]Max Planck Institute for Developmental Biology, Department of Microbiome Sciences, Tübingen, Germany; [2]Eberhard-Karls University Tübingen, Institute for Tropical Medicine, Tübingen, Germany; [3]108 Military Central Hospital, Vietnam-German Center for Medical Research (VGCARE), Hanoi, Vietnam; [4]Centre de Recherches Médicales de Lambaréné (CERMEL), Lambaréné, Gabon

The value of milk as an energy source depends on expression of the lactose hydrolyzing enzyme lactase in the small intestine. In historically pastoral communities of Europe, Africa, and the Middle East, many people continue to express lactase after infancy and are genetically lactose tolerant, while most other humans do not and are genetically intolerant. Consumption of dairy by lactose intolerant people can lead to hydrogen and methane production in the large intestine, and digestive discomfort. Interestingly, the frequency of alleles associated with genetic tolerance is a poor predictor of actual, phenotypic tolerance. Many genetically 'intolerant' populations regularly consume lactose-containing milk and dairy products without symptoms. This poor correlation presents the hypothesis that phenotypic tolerance can arise without genetic tolerance. One hypothesized mechanism for such a phenotype is microbial processing of lactose in the large intestine, or a microbially mediated lactose tolerant phenotype. We tested this hypothesis in over 600 participants across three ethnic groups with different frequencies of genetic lactose tolerance alleles (European, Central African, and Southeast Asian). We found that nearly 25% of participants in populations with no genetic predisposition to lactose tolerance did not produce gases associated with the intolerant phenotype (hydrogen and methane) after drinking a standardized lactose dose. We also sampled the fecal microbiome of each participant to assess its role in conferring the phenotype. Microbially derived lactose tolerance in genetically intolerant populations may represent a unique dietary adaptation driven by the human microbiome, rather than the human genome.

20

Interactions of the genetic make-up and microbiota on obesity manifestations

J Alfredo Martinez[1]

[1]Centre for Nutrition Research, University of Navarra, Pamplona. Precision Nutrition and Cardiometabolic Health Program at IMDEA-Food Institute CEI UAM-CSIC and CIBEROBN, Madrid, Spain.

Obesity rates are rising dramatically around the world, causing major personal and public health costs. In this context, some research has demonstrated that dietary-induced or genetically predisposed rodent models have different microbiota composition than lean controls. However, the interactions of gut microbiota with genotype in humans has not been sufficiently examined so far, although some pioneer data have demonstrated that the expression of polymorphic genes related to obesity is conditional by fecal microbiota in intestinal cell cultures. Interestingly, other investigations have reported that some single nucleotide polymorphisms are related with the abundance of specific intestinal microorganisms in humans. Thus, genetic variants near the lactase gene have been associated with the occurrence of *Bifidobacteria*, while the genus *Akkermansia* has been linked with a polymorphism near a gene connected with adiposity traits. Researches concerning the assessment of host genetics interplay on the gut microbiome are complex since, besides to the genetic make-up, gut microbiome composition is strongly influenced by environmental factors such as the dietary intake, physical activity practice or drugs such as antibiotic administration. In this context, some studies in human beings sustain an explanatory role for host genetics in determining the gut microbiome. Actually, several genetic variants have accounted for sizeable differences in gut microbiota contents, diversity, and structure. Actually, *Bacteroides* and *Prevotella* enterotypes showed differences in intestinal microbial functional genes involved in nutrient utilization and metabolism with interactions between the host genetic make-up, gut microbiota, and dietary composition concerning the risk of obesity and metabolic syndrome manifestations. Furthermore, a metagenomic study in human feces revealed an association between an obesity-related taxon (genus *Akkermansia*) and a polymorphism near the phospholipase D1 (*PLD1*) gene (rs4894707), which has been associated with BMI. Likewise, an association was identified between the richness of *Prevotella* and the human variant rs878394 associated to lysophospholipase-like 1 (*LYPLAL1*), which is a gene related to body fat deposition and insulin resistance. Also, a genetic score composite accounting for several risk alleles implicated in obesity interacts with the *Prevotellaceae* family, which modulates obesity susceptibility. Devising approaches to manipulate the microbiota impacting on obesity, specifically those components interacting with a permissive host genetic background, may pave the way to design newer strategies of precision nutrition for more individualized, valuable and long-lasting approaches of managing obesity. This scientific field deserves renewed efforts to realize and translate the complex connections of the host genome with the intestinal microbiome in health.

Reference

1. Cuevas-Sierra A, et al. Diet, Gut Microbiota, and Obesity: Links with Host Genetics and Epigenetics and Potential Applications. Adv Nutr. 2019;10(9):S17–30.

ISNN Nutrigenetics Guidelines Working Groups

21

Precision nutrition. A nutrigenetic-based framework to establish guidelines for choline intake

Steven H Zeisel[1,2], *Mihai D Niculescu*[3,4], *Katie A Meyer*[1,2], *Olivia Dong*[5], *Agata Chmurzynska*[6], *Martin Kohlmeier*[1,2]

[1]Department of Nutrition, School of Medicine & Gillings School of Global Public Health, University of North Carolina at Chapel Hill, NC. USA.; [2]Nutrition Research Institute, University of North Carolina, Chapel Hill, NC, USA.; [3]Center for Genomic Medicine, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania; [4]Advanced Nutrigenomics, Hillsborough, NC, USA.; [5]Center for Applied Genomics and Precision Medicine, Department of Medicine, Duke University School of Medicine, Durham, NC, USA; [6]Institute of Human Nutrition and Dietetics, Poznań University of Life Sciences, Poznań, Poland

In 1998 choline was officially recognized as an essential nutrient by the Institute of Medicine, and Adequate Intake levels established based on sex, age, and pregnancy and lactation status. Subsequent nutrigenetic studies suggested, however, that genotype information could be used to further refine choline dietary recommendations. Controlled studies identified clinical manifestations of choline deficiency, as well as individuals at higher deficiency risk based on their genetic background. Both controlled animal, as well as observational studies in humans, also suggested that the roles of choline, as well as the risks derived from a choline deficient status, may be specific to certain development stages, and that transgenerational effects could be attributed to maternal choline deficiency. The aims of the ISNN 2019 inaugural working group meeting is to initiate the process of establishing the nutrigenetic bases for choline requirements, and identify the evidence-based scientific facts that can be used to further tailor current choline recommendations to the needs of each individual. The group will identify which genetic variants can be used to guide clinical practice; the levels of evidence for their association with specific choline requirements, and how such specific requirements can be met while identifying safety criteria. In addition, we will discuss the role of population science to describe distributional differences in choline consumption and relevant genetic variants to identify high-risk groups and inform an understanding of public health impact. Recognizing that establishing nutrigenetic-based choline dietary requirements is an ongoing process, this initiative will continue with the establishment of a scientific committee, under ISNN auspices, which will work further toward accomplishing these aims. If successful, this effort will result in creating guidelines on choline intakes, based on a nutrigenetic framework, and which can be used for nutritional management in health and disease.

22

Working towards genotype-specific guidelines for vitamin D intakes

Emma Beckett[1], *Patrice Jones*[1], *Inez Schoenmakers*[2], *Martin Kohlmeier*[3,4]

[1]Department of Applied Sciences, School of Environmental and Life Sciences, The University of Newcastle, Central Coast, Australia; [2]Faculty of Medicine and Health Sciences University of East Anglia, Norwich, UK; [3]Department of Nutrition, School of Medicine & Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC. USA.; [4]Nutrition Research Institute, University of North Carolina at Chapel Hill, NC, USA.

Vitamin D recommendations are centred on its role in bone health, but its importance for the prevention of many chronic diseases is increasingly apparent. This working group will consider how specific variants of Group-specific Component (*GC*, encoding vitamin D binding protein, VDBP), vitamin D hydroxylating enzymes (CYPs), and the vitamin D receptor (*VDR*) may be used in practice to estimate individual vitamin D needs. VDBP carries most 25-hydroxy vitamin D, 25(OH)D, and 1,25-dihydroxy vitamin D, $1,25(OH)_2D$. Three long-range haplotypes are commonly observed. One previously named Gc-1s, with rs4588 C and rs7041 G alleles on the same DNA strand and Gc-1f, with rs4588 C and rs7041 T alleles on the same DNA strand are most commonly observed. There are racial differences in their predominant genotype, with Gc-1s more prevalent in white people and Gc-1f in those of African descent. A third one, Gc-2, with rs4588 A and rs7041 T alleles on the same DNA strand, is less common. This haplotype is associated with lower plasma VDBP and 25OHD concentrations, although differences tend to be moderate. A recent study in post-surgery, white patients has shown more pronounced differences in 25OHD concentrations. VDR is an intracellular hormone receptor that specifically binds $1,25(OH)_2D$ and interacts with vitamin D response elements of target genes to produce a variety of biologic effects. Several common *VDR* gene variants, including rs10783219 A, rs4516035 C, rs7139166 G, and rs2228570 A have been found to increase individual risk of deficiency as well as may influence the risk of chronic conditions. Also, GWAS studies have shown that variants in the genes for hydroxylation enzymes CYP2R1 and CYP24A1 may modulate the response to vitamin D intake. Supplementation with vitamin D increases 25(OH)D concentrations in a dose-dependent curvi-linear fashion with lower increments of 25OHD per unit vitamin D at higher intakes. It is also dependent on the baseline 25OHD concentration with higher increments when a person's vitamin D status is low. The proposition to be examined is whether there is sufficient evidence that a greater-than-typical vitamin D intake target should be suggested for carriers of the risk variants; and how much greater than typical intake they should aim for.

Poster Abstracts

23

Association of rs75493593 polymorphism in *SLC16A11* gene with adiposity and metabolic markers in Chilean population.

Marcelo Villagran[1], *Lorena Mardones*[1], *Fanny Petermann-Rocha*[2,3], *Maria Adela Martinez*[4], *Ana Maria Leiva*[5], *Claudia Troncoso-Pantoja*[6], *Miquel Martorell*[7], *Nicole Lasserre*[8], *Natalia Ulloa*[9], *Francisco Perez-Bravo*[10], *Carlos Celis-Morales*[2,11], *on behalf of the ELHOC group (Epidemiology of Lifestyle and Health Outcomes in Chile)*

[1]Department of Basic Science, Universidad Católica de la Santísima Concepción, Concepción, Chile; [2]BHF Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, United Kingdom; [3]Institute of Health and Wellbeing, University of Glasgow, Glasgow, United Kingdom; [4]Institute of Pharmacy, Universidad Austral de Chile, Valdivia, Chile; [5]Institute de Anatomy, Histology and Pathology, Universidad Austral de Chile, Valdivia, Chile; [6]CIEDE-UCSC, Department of Public Health, Universidad Católica de la Santísima Concepción. Concepción, Chile; [7]Department de Nutrition and Dietetics, Universidad de Concepción, Concepción, Chile; [8]School of de Nutrition and Dietetics, Universidad Santo Tomas, Sede los Ángeles. Chile; [9]Centre for Healthy Living, Department of Clinical Biochemistry and Immunology, Universidad de Concepción, Concepción, Chile; [10]Institute of Nutrition and Food Technology (INTA), Universidad de Chile, Santiago, Chile; [11]Centre for Research in Exercise Physiology (CIFE), Universidad Mayor, Santiago, Chile
Email: marcelo.villagran@ucsc.cl

Background: The *SLC16A11* gene encodes a monocarboxylate transporter. An association of the single nucleotide polymorphism (rs75493593) with type 2 diabetes (T2D) has been observed in a Mexican population. This association has not been reported in other Latin American populations with high prevalence of T2D.

Methods: We determined the presence of rs75493593 polymorphism by real-time PCR in 263 healthy individuals in Chile, assessed adiposity markers (body weight, BMI, waist perimeter, hip circumference and waist to hip ratio), metabolic markers (glucose, insulin, HOMAIR, total cholesterol, LDL-C, triglycerides, leptin, ALT, GGT, hs-CRP), and blood pressure.

Results: The minor allele (T) was found with a frequency of 29.7% in our population sample. The *SLC16A11* rs75493593 genotypes (GT and TT) were significantly associated with an increase of 1.49 mU/l in plasmatic insulin for each copy of the minor allele (95% CI 0.01, 1.40, p<0.05). This association remained significant after adjustment for socio-demographic variables, physical activity and smoking (1.36 mU/l, 95% CI 0.16, 2.58 p<0.05), but was lost when BMI was included as a confounding factor. Higher BMI was also significantly associated to polymorphic genotypes independent of socio-demographic variables.

Conclusions: This study reveals that the rs75493593 T allele in the *SLC16A11* gene is highly prevalent in a Chilean population and is associated with increased insulin and BMI in healthy individuals. These findings suggest that the rs75493593 T allele is not only associated with T2D as previously shown in a Mexican population, but that it is also related to early metabolic alterations that may lead to T2D.

#112

24

Polymorphisms in genes related to insulin metabolism are associated with insulin sensitivity in girls with obesity

Adela Chirita-Emandi[1], *Nicoleta Andreescu*[1], *Corina Paul*[2], *Alexandra Mihailescu*[1], *Paul Tutac*[1], *Cristian G. Zimbru*[1,3], *Maria Puiu*[1], *Mihai Dinu Niculescu*[1]

[1]Genetics Discipline "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania; [2]Paediatrics Department II, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania; [3]Department of Automation and Applied Informatics, Politehnica University Timisoara, Romania
Email: adela.chirita@umft.ro

Background: Polymorphisms in genes that regulate insulin metabolism, including *STAT3*, *APOC3*, *SCD*, *PNPLA3*, *MTHFR*, *FADS2*, and *CHKB*, were associated with insulin resistance. We aimed to identify children with obesity who, as carriers of various combinations of genetic polymorphisms (SNPs), may have an increased risk for insulin resistance.

Methods: 200 children with obesity (BMI>2SD using WHO reference), age 7-18 years were evaluated with anthropometric measurements, medical history, biochemical investigations and 55 relevant SNPs identified using hotspot sequencing. Linear regression modeling used HOMA-IR and genomic data.

Results: 66 girls and 71 boys (age 11.3±3 years) had complete data and were included in the linear regression model, of which 28% had HOMA-IR>2.5. Mean HOMA-IR for girls was 4.46±2.86, while for boys was 4.52+/-3.14 ($p = 0.5$). Using HOMA-IR as continuous variable and 55 SNPs, the most significant linear regression model for girls explained 52% of variability and included *SCD*-rs7849, *CHDH*-rs4563403, rs12676 and rs4687591, *PNPLA3*-rs738409, *PEMT*-rs6502603, *ABCB4*-rs1202283 and rs1149222. Except for rs4563403, rs738409 and rs1202283, all other SNPs were inversely correlated with HOMA-IR, suggesting a protective effect. In a separate regression model, age explained 0 out of 45.4% percent of the variability in girls (n = 57) and 9 out of 17.6% of variability in boys (n = 68).

Conclusions: The prediction model involving the selected SNPs had a good predictive value for insulin response in girls but not in boys. *ABCB4*, *PEMT*, and *CHDH* were not previously involved in insulin metabolism. The genetic score could be used to characterize the risk and to justify preventive strategies in metabolic syndrome.

Acknowledgements: This work was performed at The Center of Genomic Medicine, "Victor Babes" University of Medicine and Pharmacy in Timisoara, and funded by POSCCE Project ID:1854, SMIS:48749, 677/09.04.2015, and POC Project Use of nutrigenomic models for the personalized treatment with medical foods in obese people (NutriGen)2016-2019, SMIS:104852, 91/09.09.2016, ID P_37-684.

25

Vitamin D Deficiency, Diet and Physical Activity and Development of Gestational Diabetes in Emirati Women

Sharifa AlBlooshi[1] *and Abderrahim Oulhaj*[1]

[1]Department of Public Health, UAE University, United Arab Emirates
Email: sharifa.albooshi@zu.ac.ae

Background: Vitamin D deficiency and Gestational Diabetes Mellitus (GDM) are common health problems among pregnant women in the Middle East region including the United Arab Emirates. We examined the association of vitamin D status, diet, physical activity and other covariates with the risk of GDM in early pregnancy.

Methods: We conducted a prospective cohort study on 563 Emirati pregnant women. The primary exposure was vitamin D deficiency (25(OH) <12 ng/mL) and vitamin D insufficiency (25(OH) 12-20 ng/L). The outcome variable was GDM.

Results: Overall, 58.3% of pregnant women had vitamin D deficiency and 26.4% had insufficiency. The overall incidence of GDM was 15.2%. The incidence of GDM was 16% in vitamin D deficient women, 16.1% in vitamin D insufficient women and 10.7% in women with normal vitamin D. Adjusted logistic regression analysis showed that vitamin D concentration, vitamin D insufficiency (2.11, 95% CI: 0.81 – 5.64, $p = 0.101$) and deficiency (1.94, 95% CI: 0.88 – 5.32, $p = 0.118$) were not associated with GDM. Low and moderate physical activity levels were not significantly associated with increased odds of GDM. The Daily consumption of red meat (AOR: 6.16, 95% CI: 1.31 - 28.92, $p = 0.021$) and dates (AOR: 1.86, 95% CI: 1.03 - 6.49, $p = 0.043$), family history of diabetes (AOR: 1.93, 95% CI: 1.02 - 3.62, $p = 0.043$) and Body Mass index (BMI) before pregnancy (AOR: 1.07, 95% CI: 1.02 - 1.11, $p = 0.003$) were significantly associated with GDM.

Discussion: The study demonstrated a high prevalence of vitamin D insufficiency (26.4%) and deficiency (58.3%) in pregnant Emirati women according to Institute of Medicine criteria. Total of 15.2% (95% CI: 12.4% - 18.5%) of Emirati women developed GDM as per World Health Organization (2013) criteria in late pregnancy and the association between vitamin D deficiency in early pregnancy and GDM was not significant.

Conclusions: Vitamin D deficiency and physical activity were not associated with GDM, while daily intake of red meat and dates, increasing BMI before pregnancy and positive family history were positively associated with GDM.

26

Association between energy adjusted fat intake and presence of rs1149222, rs4846048, rs1557503, rs470117 in obese children: A cross-sectional study

Costela Lăcrimioara Şerban[1], *Nicoleta Andreescu*[2], *Vlad Serafim*[2], *Diana Tiugan*[2], *Alexandra Mihăilescu*[2], *Corina Paul*[3], *Salomeia Putnoky*[4], *Maria Puiu*[2], *Mihai Dinu Niculescu*[2]

[1]Functional Sciences Department, "Victor Babes" University of Medicine and Pharmacy, Timişoara, Romania; [2]Genetics Discipline, Center of Genomic Medicine "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania; [3]Department of Pediatrics, "Victor Babes" University of Medicine and Pharmacy, Timişoara, Romania; [4]Microbiology Department, "Victor Babes" University of Medicine and Pharmacy, Timişoara, Romania
Email: costela.serban@umft.ro

Background: Studies in obese adults indicated that genetic polymorphisms may play a role in associated metabolic disorders. Less it is known about the role of genetic variations in obese children. This study investigated the potential role of several genetic variations on energy-adjusted lipid intakes in children.

Methods: A cross-sectional study was conducted with 200 obese children and adolescents (age 12.6±8.1 years and zBMI 3.38±1.2) recruited for NutriGen study (ClinicalTrials.gov NCT02837367). Using initial dietary information collected using four 24-hour recalls, then converted to macro- and micronutrients, and genotypes, several models were created for the prediction of energy-adjusted fat intakes.

Results: Using stepwise method, four nutrients (total saturated fatty acids, iron, α-linolenic acid and eicosapentaenoic acid) and four genetic polymorphisms (rs1149222, rs4846048, rs1557503, rs470117) explained 47.5% of the variance of energy-adjusted fat intake. All predictors, except for iron ($\beta = -0.309$), had a positive association with energy-adjusted fat intake. The contributions to variance for rs1149222, rs4846048, rs1557503 and rs470117 were 12.0%, 16.4% 17.0%, and 16.9%, respectively. Almost half of variance (49.5%) was explained by total saturated fatty acid intake ($\beta = 0.572$).

Conclusions: Genetic variations could contribute to food choices in children with obesity. Therefore, identifying the carriers of variations that predispose to obesogenic eating habits, could help in identifying those individuals at risk for such habits, and adequately tailor their dietary counseling.

Acknowledgements: This work was performed at The Center of Genomic Medicine, POSCCE Project, SMIS:48749, and funded by POC Project NutriGen, SMIS:104852.

27

Single nucleotide polymorphisms in PEMT gene associate with different omega 3 and 6 fatty acid levels in red blood cells in overweight children

Vlad Serafim[1], *Adela Chirita-Emandi*[1,2], *Diana-Andreea Tiugan*[1,2], *Nicoleta Andreescu*[1,2], *Alexandra Mihailescu*[1], *Iulian Velea*[3], *Maria Puiu*[1,2] , *Mihai Dinu Niculescu* [1]

[1]Genetics Discipline, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania; [2]"Louis Turcanu" Clinical Emergency Hospital for Children, Timisoara, Romania; [3]Paediatric Department, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

Background: Phosphatidylcholine (PtdCho) is the most common phospholipid in cell membranes. Polyunsaturated fatty acids (PUFA) from PtdCho, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), were suggested to have protective roles against obesity-induced metabolic disorders, cardiovascular diseases, and Alzheimer's disease. PtdCho can be synthetized through two different metabolic pathways: CDP-choline pathway and phosphatidylethanolamine N-methyltransferase (PEMT) pathway.

Objective: Considering the importance of the fatty acid composition of cell membrane, this study concentrated on the impact of single nucleotide polymorphisms in PEMT gene on PUFA composition of red blood cells.

Methods: The investigated cohort consisted of 197 overweight children, aged 7-18, (95 males, 103 females) with BMI two standard deviations above the World Health Organization reference mean, and abdominal circumference above the 90th percentile. The selected PUFA were extracted from red blood cells and measured using high performance liquid chromatography coupled with tandem mass spectrometry. Next generation sequencing was used for identification of 11 single nucleotides variations within the *PEMT* gene.

Results: 66 children (33%) were heterozygous and 12 (6%) were homozygous for the rs1109859 variant allele. By comparing PUFA levels between the major and minor allele groups, we found statistically significant differences in EPA and DHA levels, and similarly in linoleic, alpha-linolenic and arachidonic acids levels. The group with the minor allele had higher membrane concentrations of these fatty acids.

Conclusions: *PEMT* rs1109859 genetic variations are associated with PUFA composition of the red blood cell membrane and may constitute a potentially protective factor against obesity-related diseases and metabolic disorders.

Acknowledgements: This work was performed at The Centre of Genomic Medicine, POSCCE Project, SMIS:48749, and funded by POC Project NutriGen, SMIS:104852.

28

The nutrigenetics of Choline Kinase Beta in overweight children

Diana-Andreea Tiugan[1,2], *Vlad Serafim*[1], *Nicoleta Andreescu*[1,2], *Costela Lăcrămioara Șerban*[4], *Alexandra Mihăilescu*[1], *Corina Paul*[1,3], *Adela Chiriță-Emandi*[1,2], *Maria Puiu*[1,2] , *Mihai Dinu Niculescu*[1]

[1]Center of Genomic Medicine Timișoara, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania; [2]"Louis Țurcanu" Clinical Emergency Hospital for Children, Timișoara, Romania; [3]Paediatrics Section II, "Pius Brînzeu" Clinical Emergency Hospital, Timișoara, Romania; [4]Functional Sciences Department, "Victor Babeș" University of Medicine and Pharmacy Timișoara, Romania
Email: tiugandiana@gmail.com

Background: CDP-choline pathway or Kennedy pathway is the main mechanism in which phosphatidylcholine is synthesized by all animal cells. It involves choline kinase/ethanolamine kinase that catalyzes the phosphorylation of choline/ethanolamine producing phosphocholine/phosphoethanolamine. Presence of *CHKB* gene polymorphisms in an overweight population were correlated with alterations in choline metabolism. Less is known about whether choline intakes alter this correlation.

Objective: This study focused on the relationship between choline intakes, its plasma levels and *CHKB* genotypes.

Methods: 196 overweight children (96 males and 100 females) were included. Plasma choline, choline intakes and *CHKB* rs1557503 were determined and correlations between these three variables were analyzed by logistic or linear regression.

Results: Linear regression indicated that the correlation between choline intakes and plasma levels is genotype dependent. Further logistical regression suggested that choline intakes may be correlated with *CHKB* rs1557503 genotypes.

Conclusions: *CHKB* rs1557503 polymorphism may play an important role in both choline metabolism and dietary intakes. Further investigations are requested for a better understanding of these mechanisms.

Acknowledgements: This work was performed at The Centre of Genomic Medicine, POSCCE Project, SMIS:48749, and funded by POC Project NutriGen, SMIS:104852.

29

Daily fat intake and polymorphism in PCYT1B rs4898190: A cross-sectional study

Costela Lăcrimioara Şerban[1], *Meda Bugi*[2], *Nicoleta Andreescu*[2], *Alexandra Sima*[3], *Iulia Perva*[2], *Paul Tuţac*[2], *Vlad Serafim*[2], *Diana Tiugan*[2], *Salomeia Putnoky*[4], *Mihai Dinu Niculescu*[2], *Maria Puiu*[2]

[1]Functional Sciences Department, "Victor Babes" University of Medicine and Pharmacy, Timişoara, Romania; [2]Genetics Discipline, Center of Genomic Medicine Timişoara, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania; [3]Department of Internal Medicine - Diabetes, Nutrition and Metabolic Diseases, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania; [4]Microbiology Department," Victor Babes" University of Medicine and Pharmacy, Timişoara, Romania

Email: costela.serban@umft.ro

Background: Genetic variations were previously reported to predict susceptibility for specific patterns of dietary habits. Here we identified the *PCYT1B* rs4898190 as a partial predictor for the daily lipid intake in obese adults.

Methods: Using a cross-sectional design, 197 males and 212 females, with mean age 53.4±12.1 years and BMI 36.6±5.8 kg/m^2 were recruited for the NutriGen study (ClinicalTrials.gov NCT02837367). Dietary information was collected using four 24-hour recalls, and then converted to macro- and micronutrients daily intakes. Genotyping was performed for 55 variant polymorphisms. Using stepwise multiple regression method, the best model for predicting daily fat intake included rs4898190, total saturated fat, calcium, potassium, iron, thiamine, manganese, copper, linoleic acid (LA), alpha-linolenic acid (ALA) and vitamin E, when controlling for energy intake.

Results: The model explained 94.7% of the variability on lipid intake. Calcium, potassium, ALA, iron and manganese had small contributions, with Betas within -0.14 for ALA and -0.053 for manganese. The strongest contributor was total saturated fatty acid intake (β = 0.505), explaining alone 25.1% of the lipids intake variance. rs4898190 correlated negatively with lipid intake, explaining alone 3.3% of its variance. The presence of one allele versus two alleles associated with significantly lower calorie (-467.5±198.3), lipids (-22.9±10.0), total saturated fatty acids (-8.2±3.8) and thiamine intakes (-0.39±0.19). Subjects carrying at least one allele had significantly lower LA (-5.5±1.28) and ALA intakes (0.7±0.15) versus non-carriers.

Conclusions: The inclusion of the *PCYT1B* rs4898190 in a multivariate predicting model could improve the prediction sensitivity for estimating daily total fat intake in obese adults.

30

Effect of TMAO on the expression of microRNAs and genes related to cardiovascular disease

Laura Diez-Ricote[1], *Víctor Micó*[1], *Britt Blokker*[2], *José M Ordovás*[1,3], *Lidia Daimiel*[1]

[1]Nutritional Genomics and Epigenomics Group, IMDEA Food, CEI UAM + CSIC, 28049 Madrid, Spain; [2]Nutrigenomics and Systems Nutrition Group, Norwich Medical School, University of East Anglia, Norfolk, Norwich, UK; [3]Nutrition and Genomics Laboratory, JM-USDA Human Nutrition Research Center on Aging at Tufts University, Boston, Massachusetts, MA, -02111, USA

Email: lidia.daimiel@imdea.org

Background: Cardiovascular diseases (CVD) are the first causes of death, mainly due to lifestyle, with diet playing a key role. Dietary metabolites modulate microRNAs, which in turn, regulate gene expression related to metabolism and CVD. Choline and L-carnitine are food components found in animal products and are metabolized into trimethylamine (TMA) by gut microbiota. TMA is then oxidized in the liver to TMAO, a metabolite that has been associated with CVD.

Objective: We wanted to investigate TMAO modulation of the expression of CVD-related microRNAs and genes in human cells.

Methods: HEPG2 and THP-1 were treated with (6μM) TMAO for 4h, 8h 12h and 24h. RNA enriched in microRNAs and proteins were isolated. Previously selected microRNAs and their target genes were amplified by q-PCR. Proteins were analyzed by western blot.

Results: We found that TMAO increased expression of miR-92a after 8h and miR-30c after 8h and 24h of incubation with HEPG-2 cells. We selected putative target genes for these microRNAs and analyzed their expression in the same conditions. We found that *PER2*, a target gene of miR-92a and miR-30c, significantly decreased its relative expression at 8h and 24h treatment in HepG2 cells. Chemokine *CXCL16*, a target of miR-30c, showed a significant decrease at 8h and a slight decrease at 24h. miR-21 was significantly upregulated at 24h in THP-1 and showed a trend towards the upregulation in HEPG-2 cells after 8 h of treatment. *STAT3*, a target gene of miR-21, showed a slight decrease at 8h and 24h in HepG2. Chemokine *IL12A* target gene of miR-21, showed a slight decrease at 24h. Further analysis of target genes indicated that selected microRNAs are involved in lipid metabolism and inflammation.

Conclusions: TMAO affects the expression of microRNAs associated with CVD and such modulation affects target genes.

31

Effect of a caloric restriction based on Mediterranean diet in macrophage microRNAs related to nutrient sensing pathways

Víctor Micó[1], Laura Diez[1], María Tanarro[1], Laura Berninches[1], José María Ordovás[2, 3], Lidia Daimiel[1]

[1]Nutritional Control of Epigenome Group, IMDEA Food, CEI UAM + CSIC, 28049 Madrid, Spain; [2]Nutritional Genomics and Epigenomics Group, IMDEA Food, CEI UAM + CSIC, 28049 Madrid, Spain; [3]JM-USDA Human Nutrition Research Center on Aging at Tufts University, Boston, Massachusetts, MA 02111, USA.

Background: Mediterranean Diet (MD) and Caloric Restriction (CR) have been postulated as healthy dietary patterns that promote greater life expectancy and quality of life. Despite these health associations, the mechanisms related to these beneficial effects of CR have not been studied in depth.

Objective: To describe if CR based on MD modifies macrophages microRNAs levels after 1 year of treatment.

Material and Methods: We selected 40 patients from PREDIMED-PLUS Study (20 from control group and 20 from intervention group) according to the weight loss of the participants to ensure that each sub-sample was representative of the whole cohort. We selected Monocyte-Derived Macrophages and analyzed microRNAs and gene expression by Real Time q-PCR.

Results: MiR-30c and miR-130a were differentially downregulated after 1 year of intervention but not modulated in the control group. Then, we searched for putative target genes of these microRNAs and selected 3: *AKAP10*, *PRKAA2* and *LDLR* and we analyzed the expression changes after one year of intervention in intervention group identifying 3 different patterns of expression. Group 1 (n = 3) included samples where miR-130a was down-regulated but genes did not change. Group 2 (n = 4) included samples were miR-130a was down-regulated and genes were strongly up-regulated. Group 3 (n = 4) included samples were miR-30c and target genes were down-regulated. We observed that participants from the control group reduced less their triglyceride levels and slightly increased total cholesterol, LDL and HDL levels.

Discussion: One year of intervention with a CR based on MD down-regulated macrophage miR-130a and miR-30c levels. They are involved in lipid metabolism and mTOR signaling. The three different patterns of genes regulation and their possible association with lipid profile suggest that the microRNAs modulation of these genes could be associated with the individual response to the intervention.

32

Does fat sensitivity determine fat preference and high-fat food intake?

A Chmurzynska[1], MA Młodzik-Czyżewska[1], G Galiński[1], J Mikołajczyk-Stecyna[1], A Radziejewska[1], E Bulczak[1], AM Malinowska[1]

[1]Institute of Human Nutrition and Dietetics, Poznań University of Life Sciences, Poland

Background: The associations between fatty acid (FA) sensitivity, fat preference, and high-fat food intake have not been fully recognized.

Method: For this reason, we enrolled 421 people aged 20–40. The frequency of consumption of high-fat foods was analyzed using an application for mobile devices, based on the ecological momentary assessment approach. Self-reported fat preference was analyzed using the Fat Preference Questionnaire. Salad dressings with varying concentrations of canola oil (from 2.5% to 40.0%) were used as stimuli to test fatty acid sensitivity. Genotyping of rs1761667 (*CD36*) rs1573611 (*FFAR1*), rs17108973 (*FFAR4*), and rs2274333 (*CA6*) was performed with using TaqMan probes.

Results: People of normal and increased body weight did not differ in their general frequency of eating high-fat foods. People with body mass index (BMI) ≥ 25 more often preferred high-fat foods over their low-fat counterparts and showed lower dietary fat restraint than did people with normal BMI ($p < 0.01$ for both associations). Fat preference and frequency of eating high-fat foods does not depend on polymorphisms of the genes involved in signal transduction. People with *CA6* AA genotype more frequently stated that they prefer high-fat foods over low-fat foods and more frequently ate high-fat products ($p < 0.05$) than people with at least one minor allele.

Conclusions: FA sensitivity was not associated with fat preference parameters or with fat intake or frequency of eating high-fat foods.

Acknowledgement: This study was supported by the Polish National Science Centre (grant no. 2014/15/B/NZ9/02134).

33

Interaction between gut microbiota and host genetics in women body mass index

Amanda Cuevas-Sierra[1], José Ignacio Riezu-Boj[1,2,3], Fermín Ignacio Milagro[1,2,3], J Alfredo Martínez[1,2,3,4]

[1]Department of Nutrition, Food Science and Physiology, Center for Nutrition Research, University of Navarra, Pamplona, Spain; [2]IdiSNA, Navarra Institute for Health Research, Pamplona, Spain; [3]CIBERobn, Fisiopatología de la Obesidad y la Nutrición, Carlos III Health Institute, Madrid, Spain; [4]Institute IMDEA Food, Madrid 28049, Spain

Background: Gut microbiome has been recognized to have a fundamental role in human metabolism and health, where implications with host genetics in relation to body weight regulation are still unclear.

Objective: The purpose of this study was to evaluate the interactions between gut microbiota composition and a set of selected obesity-related SNPs on body mass index (BMI).

Methods: Fecal and saliva samples were collected from 64 normal weight, 110 overweight and 186 obese Spanish volunteers. Microbiota composition was determined following the Illumina 16S Metagenomics Sequencing Protocol, based on specific primers targeting the V3/V4 region of the 16S rRNA gene. Genetic risk score (GRS) was constructed with 10 SNPs statistically or marginally associated with BMI in the reference population. The interactions between BMI, microbiota and host genetics were analyzed by multiple linear regressions models.

Results: Sixty-two bacterial families were analyzed to feature associations with BMI, where 14 were significantly related to BMI. Only *Prevotellaceae* family interacted significantly with GRS in women ($p<0.001$; $R^2 = 0.21$). The interaction between gut microbes and human genetics were analyzed by multiple linear regressions resulting that the *Prevotellaceae* family interacted with the GRS in women. While female subjects with higher abundance of *Prevotellaceae* and higher GRS were more obese, women with the same genetic risk but lower abundance of Prevotellaceae presented a lower BMI.

Conclusions: These findings suggest interrelationships between the *Prevotellaceae* family and the genetic background, which may be a key factor in determining BMI, particularly in women.

34

Unravelling the crosstalk between microRNAs and DNA methylation in obesity

Francisca Salas-Pérez[1], Taís Silveira Assmann[1], Amanda Cuevas-Sierra[1], José Ignacio Riezu-Boj[1,2,3], María L Mansego[4], J Alfredo Martínez[1,2,3,5], Fermín Ignacio Milagro[1,2,3].

[1]Department of Nutrition, Food Science and Physiology, Center for Nutrition Research, University of Navarra, Pamplona, Spain; [2]IdiSNA, Navarra Institute for Health Research, Pamplona, Spain; [3]CIBERobn, Fisiopatología de la Obesidad y la Nutrición, Carlos III Health Institute, Madrid, Spain; [4]Department of Bioinformatics, Making Genetics S.L, Pamplona 31002, Spain; [5]Institute IMDEA Food, Madrid 28049, Spain

Background: Inadequate dietary intake is considered a major contributor to obesity prevalence, where epigenetic modifications are thought to play a role in the onset and development of diseases. MicroRNA (miRNA) expression and DNA methylation (DNAmet) are two epigenetic mechanisms, which play a pivotal role in physiological processes that can vary due to environmental factors and metabolic disturbances.

Objective: To analyze the interactions between circulating miRNA expression and DNAmet levels of genes involved in metabolic pathways in obesity.

Methods: A total of 103 subjects were grouped in obese and non-obese according to BMI (30–40 kg/m^2, n = 78; £ 25 kg/m^2; n = 25). DNAmet profiles were measured in white blood cells using arrays and 96 miRNAs were quantified in plasma using miRNA panels. Potential target genes of miRNAs were identified in miRWalk 3.0 database. Pathway analyses were performed using PathDIP. Statistical significance was reported as FDR <0.05 (q-value).

Results: Twenty-six miRNAs were differentially expressed in obese subjects compared to non-obese individuals. Bioinformatic analysis showed that these 26 miRNAs target 1,001 validated genes. Moreover, 4,231 CpG sites located at 2,411 known genes were associated with BMI (q-value <0.001). The comparison between these two analyses showed 173 common genes that participate in pathways of metabolic relevance, including sphingolipid, insulin resistance, type 2 diabetes, lipolysis, and longevity signalling pathways.

Conclusions: These analyses evidenced differential miRNA expression profile and DNAmet pattern of genes involved in relevant metabolic pathways, suggesting a tight regulation in obese subjects, and appears as an interesting approach to find new potential candidate genes.

35

Bacteroides eggerthii abundance interacts with circulating microRNA expression and BMI levels in a cohort of obese individuals

Taís Silveira Assmann[1], *Amanda Cuevas-Sierra*[1], *José Ignacio Riezu-Boj*[1,2,3], *Fermín Ignacio Milagro*[1,2,3], *J Alfredo Martínez*[1,2,3,4]

[1]Department of Nutrition, Food Science and Physiology, Center for Nutrition Research, University of Navarra, Pamplona, Spain; [2]IdiSNA, Navarra Institute for Health Research, Pamplona, Spain; [3]CIBERobn, Fisiopatología de la Obesidad y la Nutrición, Carlos III Health Institute, Madrid, Spain; [4]Institute IMDEA Food, Madrid, Spain

Background: Obesity is a global epidemic and an independent risk factor for several metabolic disorders. Variations in gut microbiota composition and in circulating microRNA (miRNA) have been proposed as playing important roles in the onset and development of obesity and other metabolic diseases. However, the determinants that mediate the interactions between miRNAs and the microbiome in a context of obesity are scarcely understood. The present work aims to investigate interactions between circulating miRNA patterns and gut microbiome composition in obesity.

Methods: The analyzed sample comprised 78 subjects with obesity (cases, BMI 30–40 kg/m^2) and 25 eutrophic individuals with normal weight (controls, BMI 25 kg/m^2). The expression of 96 miRNAs was investigated in plasma of all individual using miRCURY LNA miRNA Custom PCR Panels (Exiqon). Microbiota composition was determined following the Illumina 16S rRNA protocol. The FDR (Benjamini-Hochberg test, q-value) correction was used for multiple comparison analyses.

Results: Twenty-six miRNAs were found differentially expressed in plasma of obese subjects compared to normal weight individuals and the abundance of 12 bacterial species were different between cases and controls. Furthermore, an interaction among miRNAs (miR-130b-3p, miR-185-5p, and miR-21-5p), *B. eggerthi* and BMI levels was evidenced ($r^2 = 0.148$, $p = 0.004$). Moreover, those miRNAs that correlated with *B. eggerthi* abundance are known to regulate target genes that participate in metabolism-related pathways.

Conclusions: Our research featured an interaction between *B. eggerthi* abundance and several circulating miRNA expressions involving the control of body adiposity.

36

Lignan phytocomplexes extracted from legumes act as anti-inflammatory agents in a model of adipocyte metaflammation: antioxidant properties and nutriepigenomic effects

R Gabbianelli[1], *G Sagratini*[2], *E Merelli*[3], *M Wabitsch*[4], *M Piangerelli*[3], *F Giusti*[2*], *L Bordoni*[1*]

[1]Unit of Molecular Biology, School of Pharmacy, University of Camerino, Camerino, Italy; [2]Food Chemistry Division, School of Pharmacy, University of Camerino, Camerino, Italy; [3]Computer Science Division, School of Science and Technology, University of Camerino, Camerino, Italy; [4]Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, Ulm University Medical Center, Ulm, Germany;
*equally contributed to the work

Background: Metaflammation, a state of metabolically driven inflammation also referred to as 'low-grade' inflammation, is a key contributor to the development of obesity complications such as type 2 diabetes and cardiovascular diseases. Among numerous phytochemicals, lignans are secondary metabolites whose biological properties have not been properly characterized yet. This study aims to investigate the effect on metaflammation of natural mix of lignans isolated from legumes and their synthetic equivalents and to evaluate the possible intermediating role of epigenetic on this process.

Methods: An *in vitro* model of inflamed adipocytes was used. Cytotoxicity of phytocomplexes was evaluated through MTT assay. Antioxidant properties were assessed by chemiluminescence assay. Gene expression of genes involved in inflammation (*MCP1*, *IL6*, *IL1B*, *NFKB1*) or epigenetic regulation (*DNMT1*, *DNMT3A*, *DNMT3B*, *HDAC*1, *HDAC*2, *HDAC3*) were analyzed and global DNA methylation and H3 histone acetylation were measured.

Results: A protective effect of the selected mix of lignans against metaflammation in this model was measured. In particular, reduced levels of inflammatory genes and altered expression of genes that regulate epigenetic pathways suggest a potential involvement of epigenetic mechanism as responsible for the measured anti-inflammatory effect. This was observed for both natural and synthetic mixtures, despite a limited antioxidant activity was measured in the second ones.

Conclusions: This study suggests that not only antioxidant activity but also nutriepigenomic effects could be responsible for the measured anti-inflammatory properties of the selected mixtures of lignans extracted from legumes. Further studies are needed to elucidate the underlying epigenetic molecular mechanisms.

37

A conceptual framework to implement nutritional decision support integrated within the Electronic Health Record

Don Roosan[1]

[1]College of Pharmacy, Western University of Health Sciences, Pomona, California, USA.

Background: Gestational diabetes Mellitus (GDM) is a complication of pregnancy affecting approximately one out of seven pregnancies and is characterized by glucose intolerance.[1] Genomics and gut microbiome data has the potential to identify patients at risk of developing Type 2 Diabetes Mellitus and intervene early with diet and lifestyle modification. We plan to develop a model based on supervised learning using clinical indicators, microbiomics, and genomics to predict and individualize patients' responses to dietary options.[2] To develop a sustainable and scalable predictive algorithm, it is imperative to create a framework to operationalize the omics data from multiple disparate sources for a successful implementation with the electronic health record (EHR).

Method: We created a conceptual framework model using a multi-step process that facilitates data management and information flow. This model may serve as the foundation framework to integrate and implement the web-based predictive decision support.

Results: The proposed model represents omics and clinical data flow for a specific patient. The model explains the information flow from the laboratory to EHR along with a traditional narrative summary of result interpretation for clinicians. In addition, the model will be made discrete and computable data for predictive analytics on Amazon Web Services based and integrated within the EHR as a clickable function.

Conclusions: The proposed model may serve as a framework for implementing complex patient health data that will help clinicians predict best available diet for improved glucose management in GDM patients.

References

1. Kolu P, Raitanen J, Rissanen P, Luoto R. Health care costs associated with gestational diabetes mellitus among high-risk women–results from a randomised trial. BMC Pregnancy Childbirth. 2012;12(1):71.
2. Kim M, Rai N, Zorraquino V, Tagkopoulos I. Multi-omics integration accurately predicts cellular state in unexplored conditions for Escherichia coli. Nat Commun. 2016;7:13090.

38

Does personalised nutrition advice based on *APOE* and *MTHFR* genotype affect dietary behaviour?

Alexandra King[1], S Saifi[1], J Smith[1], L Pilic[1], C Graham[1], M Glaister[1], Y Mavrommatis[1]

[1]Faculty of Health and Applied Science, St Mary's University, Twickenham, TW1 4SX, UK.
Email: alexandra.king@stmarys.ac.uk

Background: Cardiovascular disease (CVD) is the most common cause of death worldwide and dietary intake is linked to numerous modifiable risk factors of CVD. Current dietary recommendations in the UK to reduce the risk of CVD are not being met. A genotype-based personalised approach to dietary recommendations may motivate individuals to make positive changes in their dietary behaviour, although studies to date have reported mixed findings. The aim of the present study was to determine whether personalised nutrition advice, based on *apolipoprotein E* (*APOE,* rs7412; rs429358) and *methylenetetrahydrofolate reductase (MTHFR*, rs1801133) genotype, affect reported dietary intake of saturated fat and folate.

Methods: Baseline data (n = 99) was collected to determine genotype, dietary intake and cardiovascular risk. Participants were provided with personalised nutrition advice via email based on their *APOE* and *MTHFR* genotype and reported intake of folate and saturated fat. After one-week, dietary intake was collected for a second time.

Results: There was a statistically significant two-way interaction between time and fat recommendations ($p < 0.001$) and time and folic acid recommendations ($p = 0.002$). Personalised nutrition advice led to favorable dietary changes in participants that were not meeting dietary recommendations, irrespective of genotype. In participants not meeting dietary recommendations, only those with a risk associated *APOE* genotype met saturated fat recommendations following personalised nutrition advice.

Conclusions: The incorporation of genotype-based personalised nutrition advice in a diet behaviour intervention may elicit more favourable changes in dietary behaviour than the current 'one size fits all' approach.

39

Common variants in the *CD36* gene are associated with dietary fat intake and high fat food consumption in a cohort of Quebec adults

Tongzhu Meng[1], *Stan Kubow*[1], *Daiva E Nielsen*[1]

[1]School of Human Nutrition, McGill University, 21111 Lakeshore Road, Ste. Anne de Bellevue, Quebec City, Canada
Email: daiva.nielsen@mcgill.ca

Background: The *CD36* gene is a candidate for sensory detection of fatty acids and has been associated with individual differences in fat preferences and consumption. Excess adiposity may compromise sensory detection, but no previous study has examined whether Body Mass Index (BMI) modulates associations between *CD36* and fat consumption.

Objective: To evaluate associations between *CD36* variants and habitual fat consumption amongst normal weight (NW) and overweight/obese (OW) individuals.

Methods: Dietary, genetic (10 variants), anthropometric, and lifestyle data were obtained from the CARTaGENE biobank (n = 12,069), a Quebec cohort of middle-aged adults. Diet was assessed with a 12-month food frequency questionnaire. Outcome variables included intakes (% kcal/day) of total, saturated, monounsaturated (MUFA), and polyunsaturated fat (PUFA) and consumption of three food categories (servings/day): added fats and oils, high-fat foods, and desserts. General linear models adjusted for demographic, dietary, and lifestyle covariates were used to assess associations between *CD36* variants and outcome variables.

Results: Significant *CD36* by BMI interactions on dietary fat intakes were observed for three variants. Amongst OW, rs1054516 minor allele homozygotes consumed less saturated fat than major allele carriers (10.3% vs. 10.5%, p = 0.037). Amongst NW, rs10499859 minor allele carriers consumed more PUFA than non-carriers (6.1% vs. 5.0%, p = 0.002) and rs1527483 minor allele carriers consumed more saturated fat (12.0% vs. 10.8%, p = 0.030). The latter group also had significantly higher consumption (servings/day) of high-fat foods and desserts, respectively, compared to non-carriers (1.24 vs. 0.93, p = 0.018, 0.70 vs. 0.55, p = 0.021).

Conclusions: *CD36* variants are associated with habitual fat consumption. Associations are more pronounced amongst NW individuals.

40

UVR levels and folate gene variants independently predict folate levels in an elderly Australian cohort

Patrice Jones [1,2], *Mark Lucock*[1], *Christopher Scarlett*[1], *Martin Veysey*[3], *Emma Beckett*[1,2]

[1]School of Environmental & Life Sciences, University of Newcastle, Ourimbah, NSW, Australia; [2]Hunter Medical Research Institute, New Lambton Heights, NSW, Australia; [3]Hull-York Medical School, University of York, Heslington, York, UK
Email: emma.beckett@newcastle.edu.au

Background: Ultraviolet radiation (UVR) may adversely affect folate status, with increases in UVR exposure associated with decreased folate levels. Variance within folate-associated genes also reflect UVR environment, with frequency of several variants linked to latitude. Such variants may have a role in modulating the influence of UVR exposure on folate levels. This study examined independent and interactive influences of UVR and folate variants on red blood cell (RBC) and serum folate levels in an elderly Australian cohort (n=487).

Methods: Variants within *MTHFR* (-C677T, -A1298C) *MTHFD1* (-G1958A, -T401C), *TYMS* (-1494del6, -28bp 2R/3R,) *SHMT* (-C1420T), *MSR* (-A66G), *MS* (-A2756G), *RFC1* (-G80A), and *DHFR* (-19bp del) were genotyped via RFLP/allele-specific PCR. UVR exposure of participants was assessed as the accumulated erythemal dose rate in the study area, over a 120-day period prior to blood sampling, accessed via NASA's Total Ozone Mapping program. Least squares regression was used to model these factors with age, sex, and B vitamin intake (folate, vitamin B_{12}, vitamin B_6).

Results: Erythemal dose rate ($p < 0.0001$, $\beta = -0.18$) and carriage of the *MTHFD1*-G1958A variant ($p = 0.034$, $\beta = 0.09$) predicted RBC folate levels. Intake of folate ($p<0.0001$, $\beta = 0.19$) and vitamin B12 ($p = 0.025$, $\beta = 0.14$), as well as carriage of *SHMT*-C1240T ($p = 0.040$, $\beta = 0.09$) and *TYMS* 1494del6 variants ($p = 0.005$, $\beta = 0.13$) were significant predictors of serum folate levels. No interactions between genetic factors and UVR levels were observed.

Conclusions: These findings indicate both genetic and environmental factors (intake & UVR) as potential predictors of folate status with notable differences between how these factors influence RBC and serum folate levels.

41

Interaction between dietary choline intake during pregnancy and choline-metabolising genetic polymorphisms on risk of preterm birth

Jie Zhu[1,2,3], *Bei Wang*[4], *Yuhong Liu*[5], *Qingya Tang*[1], *Wei Cai*[1,2,3]

[1]Department of Clinical Nutrition, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine; [2]Department of Nutrition, Shanghai Jiao Tong University School of Medicine; [3]Shanghai Key Laboratory of Pediatric Gastroenterology and Nutrition; [4]Department of Obstetrics, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine; [5]Department of Gynaecology and Obstetrics, Shanghai Seventh People's Hospital.

Objectives: This case-control study aims to investigate the interaction between choline intake during pregnancy and genetic polymorphisms in choline dehydrogenase (*CHDH*) and betaine-homocysteine methyltransferase (*BHMT*) on preterm birth risk among Chinese women.

Methods: 129 women with preterm delivery and 141 women with full-term delivery were recruited at Xinhua Hospital, Shanghai. Dietary choline intake during pregnancy was assessed by a validated food frequency questionnaire, genotyping was conducted for *CHDH* (G233C, rs12676) and *BHMT* (G742A, rs3733890), and plasma homocysteine (Hcy) level was assayed.

Results: *CHDH* rs12676 or *BHMT* rs3733890 alone was not correlated with the incident preterm birth. However, significant interactions were observed between maternal choline intake during pregnancy and *CHDH* rs12676 ($p = 0.023$) or *BHMT* rs373389 ($p = 0.045$) on preterm delivery risk after adjusting for multiple confounding variables. Plasma Hcy level was about 38 % higher in the case women carrying CC genotype of *CHDH* rs12676 who consumed less choline than the median, compared to the control women with GG genotype who had more choline intake than the median level ($p = 0.006$). Similarly, the case women carrying AA genotype of *BHMT* rs373389 who consumed less choline than the median showed about 21% higher Hcy levels, compared with the control women with GG genotype who had more choline intake than the median level ($p = 0.015$).

Conclusions: Genetic polymorphism of *CHDH* rs12676 or *BHMT* rs3733890 may interact with maternal choline intake, which may modify preterm birth risk among Chinese women partially through the disturbance in choline metabolism.

Acknowledgement: This study was registered at ClinicalTrials.gov. (N°. NCT02841813).

42

Analysis of nutrigenomic effects of flavanols: a systematic bioinformatic evaluation of flavanol-modulated gene expressions in cell models of cardiometabolic disease

Marika Massaro, Tatjana Ruskovska, Sonia de Pascual-Teresa, Irena Krga, Wim Vanden Berghe, Elena Kistanova, Pedro Mena, Marie-Paule Gonthier, Claudia Nunes dos Santos, Andreia Gomes, Egeria Scoditti, Maria Annunziata Carluccio, Emilie Combet Aspray, Nadia Calabriso, Anna Arola Arnal, Maria Begoña Muguerza Marquínez, Manuel Suárez Recio, Francisca Isabel Bravo Vázquez, Eileen R Gibney, Ana Rodriguez-Mateos, Christine Morand, Dragan Milenkovic[1*]

[*1]POSITIVe working group. Université Clermont Auvergne, INRA, UNH, CRNH Auvergne, F-63000 Clermont-Ferrand, France and Department of Internal Medicine, Division of Cardiovascular Medicine, School of Medicine, University of California Davis, Davis, California, 95616, United States of America

[*]This abstract is based upon work from COST Action on "Interindividual variation in response to consumption of plant food bioactives and determinants involved (POSITIVe), supported by COST (European Cooperation in Science and Technology)

Email: marika.massaro@ifc.cnr.it

Background: The role of flavanols in terms of gene regulation in various cell models relevant to cardiometabolic disease has never been systematically addressed. Therefore, we conducted a systematic literature search and comprehensive bioinformatic analysis of the genes which expression has been reported as affected by flavanols in the cells defining the cardiometabolic health (hepatocytes, adipocytes, endothelial, smooth muscle and immune cells), to decipher molecular mechanisms of action underlying their cardiometabolic health properties.

Methods: Literature search was performed in PubMed and Web of Science using pre-defined criteria (pure compounds and metabolites, no extracts, physiologically relevant concentrations). Identified differentially expressed genes were analyzed by several bioinformatic tools including: MetaCore, GeneTrail2 (for access to KEGG and BioCarta databases), Metascape and OmicsNet.

Results: Analysis of extracted data from the literature identified 54 differentially expressed genes at mRNA level. Gene network analysis revealed that these genes are involved in inflammation, immune response, cell adhesion, apoptosis and cell signaling. Deeper analysis of their functional roles revealed the pathways such as *TNF signaling pathway, NF-kappa B signaling pathway, Leukocyte transendothelial migration and Cell adhesion molecules.* Studied cell types respond differently on the flavanol exposure, but inflammatory response is a common mechanism. Transcriptional factors, such as PPARG, NFKB1, CREB1 or STAT3, and miRNAs such as mir-335-5p, mir-16-5p, mir-124-3p or mir-26b-5p have been identified as regulators of gene expression by flavanols.

Conclusions: The results of this systematic analysis of nutrigenomic effects of flavanols will support the future setup of nutrigenetic studies to pave the way for individualized dietary recommendations.

43

Deciphering the effect of increased PUFA metabolism and arachidonic acid on transgenerational risk of type-2 diabetes risk

Michael A Zulyniak[1]

[1]School of Food Science and Nutrition, University of Leeds, Leeds, UK.
Email: m.a.zulyniak@leeds.ac.uk

Background: Globally, 1 in 11 adults have diabetes mellitus, most of whom are type-2 diabetic (T2D). Risk of T2D is influenced by many factors, including diet. Polyunsaturated fatty acids, namely arachidonic acid (ARA), has been proposed as a risk factor for T2D; however, its causal role is uncertain.

Aim: To infer the effect of blood arachidonic acid levels on insulin resistance and transgenerational T2D risk in two large cohorts of British men and women.

Methods: Two-sample Mendelian randomization (MR) was applied to evaluate the effect of low or high levels of ARA on glycaemia and development of T2D in the UK Biobank (n = 463,010) and MAGIC (n = 5,130) cohorts. Inherited predisposition to low or high ARA levels and risk of T2D was also investigated in siblings and parents. In MR-base, six genetic variants were significantly associated with arachidonic acid concentration (P<10-8). After pruning, one variant (rs174547) on the *FADS1* gene was retained (-1.69 ± 0.02% ARA per effect allele; $P<10^{-971}$).

Results: Lower blood ARA was associated with lower insulin disposition index (-0.038 ± 0.012 per % unit ARA; P = 0.002) within MAGIC. In UK Biobank, lower ARA was associated with <1% increased risk of participant T2D (P<0.05), per % ARA decrease. Similarly, parents of UK Biobank participants with lower ARA levels, were also at < 1% increased risk of T2D (PM<0.05; PF = 0.05). No effect was observed on siblings of participants or BMI.

Conclusions: This MR approach infers that persistent exposure to elevated synthesis of ARA and blood ARA levels is not a risk factor forT2D or insulin resistance.

44

Extra-virgin olive oil polyphenols modulate the expression of key inflammatory genes and miRNAs in human adipocytes

E Scoditti[1], *S Carpi*[2], *M Massaro*[1], *B Polini*[2], *M Digiacomo*[3], *C Manera*[3], *M Macchia*[3], *MA Carluccio*[1], *R De Caterina*[4], *P Nieri*[2]

[1]Laboratory of Vascular Biology and Nutrigenomics, CNR-Institute of Clinical Physiology (IFC), Lecce, Italy [2]Laboratory of Molecular Pharmacology, Department of Pharmacy, University of Pisa, Pisa, Italy [3]Laboratory of Medicinal Chemistry, Department of Pharmacy, University of Pisa, Pisa, Italy [4]Institute of Cardiology, University of Pisa, Pisa, Italy
Email: egeria.scoditti@ifc.cnr.it

Background: Adipose tissue inflammation plays a pathophysiological role in the cardiometabolic risk associated with obesity. Underlying regulatory networks involve inflammatory gene products and microRNAs (miRNAs). Antioxidant polyphenols are integral components of the healthful Mediterranean diet and are endowed with anti-inflammatory activities. Polyphenols typical of extra virgin olive oil (EVOO) including secoiridoids, oleocanthal (OC) and oleacein (OA), and simple phenols, such as hydroxytyrosol (HT), are putative active ingredients of EVOO. However, their role in obesity-associated adipocyte inflammation and related miRNAs deregulation has not been completely elucidated. We investigated the effect of OC, OA and HT on the expression of gene transcripts and miRNAs associated with inflammatory and dysmetabolic responses in human adipocytes.

Methods: Differentiated Simpson-Golabi-Behmel syndrome (SGBS) adipocytes were pre-treated with EVOO polyphenols (1-25 μmol/L) before tumor necrosis factor(TNF)-α stimulation. Levels of mRNA gene expression as well as cell and exosomal miRNAs were measured by real-time PCR.

Results: We found that 3 inflammation-related miRNAs (miR-155-5p, miR-34a-5p and let-7c-5p) were deregulated by TNF-α in both cells and exosomes. The TNF-α deregulated miRNAs were significantly counteracted by EVOO polyphenols. Concordantly, EVOO polyphenols significantly reduced mRNA expression of genes implicated in adipocyte inflammation (*IL1B*, *COX2*), angiogenesis (*VEGF*, *MMP2*), oxidative stress (NADPH oxidase), leukocyte chemotaxis and activation (*MCP1*, *CXCL10*, *MCSF*).

Conclusions: This study demonstrates that EVOO polyphenols counteract the adipocyte expression and secretion of inflammatory miRNAs and the expression of related genes toward a protective profile. These effects may contribute to the preventive effects of a Mediterranean diet toward inflammatory diseases associated with obesity, including atherosclerosis.

45

Predicting 1-year outcome to a personalized lifestyle intervention for Canadians with MetS

Dana E Lowry[1], *Zeny Feng*[2], *Khursheed Jeejeebhoy*[3], *Rupinder Dhaliwal*[4], *Paula Brauer*[5], *Dawna Royall*[5], *Angelo Tremblay*[6], *Doug Klein*[7], *David M Mutch*[1]

[1]Department of Human Health and Nutritional Sciences, University of Guelph, Guelph, Ontario, Canada; [2]Department of Mathematics and Statistics, University of Guelph, Guelph, Ontario, Canada; [3]Emeritus Professor of Medicine and Physician, St. Michael's Hospital, Toronto, Ontario, Canada; [4]Metabolic Syndrome Canada; [5]Department of Family Relations and Applied Nutrition, University of Guelph, Guelph, Ontario, Canada; [6]Department of Kinesiology, Faculty of Medicine, Université Laval, Québec City, Québec, Canada; [7]Department of Family Medicine, University of Alberta, Edmonton, Alberta, Canada
Email: dmutch@uoguelph.ca

Background: Metabolic syndrome (MetS) comprises a cluster of risk factors that includes central obesity, hypertension, dyslipidemia and impaired glucose homeostasis. Although lifestyle interventions reduce MetS risk, not everyone responds to the same extent. The primary objective of this study was to identify baseline variables (i.e., genetics, diet scores, aerobic fitness, and bioclinical

measurements) that could predict 1-year changes in cMetS score in individuals participating in the Canadian Health Advanced by Nutrition and Graded Exercise (CHANGE) program.

Methods: Participants were randomly allocated into training (n = 157) and test (n = 29) datasets. First, a linear mixed-effect model revealed that age, medication use, fasting glucose, triglycerides, HDL-C, waist circumference, systolic blood pressure (SBP) and fibre intake were significantly associated with cMetS score across all time points. Next, we used multiple linear regression to develop two predictive models using 1-year cMetS score as the outcome variable.

Results: Model 1 included only baseline variables and was 38% accurate (within one standard deviation) for predicting cMetS score. Model 2 included both baseline variables and the 3-month change in cMetS score, and was 86% accurate (within one standard deviation) for predicting cMetS score. As a secondary objective, we also examined if we could predict a person's categorical response bin (*i.e.*, positive responder, non-responder, or adverse responder) at 1-year using the same variables (Model 3). We found 72% concordance between predicted and observed response bins.

Conclusions: These various predictive models need to be further tested in independent cohorts, but provide a potentially promising new tool to project patient outcomes during lifestyle interventions for MetS.

46

Meals, Microbiota & Mental Health of Children and Adolescents

Birna Ásbjörnsdóttir[1,2], *Bertrand Lauth*[2,3], *Magnús Gottfreðsson*[2,4], *Ingibjörg Karlsdóttir*[3], *Lárus S. Guðmundsson*[5], *Orri Smárason*[3,6], *Bryndís Eva Birgisdóttir*[1]

[1]Unit for Nutrition Research, Faculty of Food Science and Nutrition, University of Iceland and Landspitali University Hospital, Reykjavík, Iceland; [2] Faculty of Medicine, University of Iceland, Reykjavík, Iceland; [3]BUGL, Children & Adolescents Psychiatric Department, Landspitali University Hospital, Reykjavík, Iceland; [4]Landspitali, University Hospital, Reykjavik, Iceland; [5]Faculty of Pharmaceutical Sciences, University of Iceland, Reykjavik, Iceland; [6]Faculty of Psychology, University of Iceland
Email: beb@hi.is

Background: Recent studies indicate an interaction between diet, intestinal microbiota, gut permeability and mental health in relation to factors such as chronic low-grade inflammation.

Objectives: The aim of this novel observational longitudinal case-control study is to investigate associations between dietary factors, genetic variants, intestinal microbiota, intestinal permeability and mental health among children and adolescents diagnosed with mental health disorders and compare with healthy controls and siblings.

Methods: All children and adolescents referred to the only outpatient psychiatric clinic in Iceland, over a one-year period, will be offered to participate (N = 150) (5-15y). Two control groups will be used; same parent siblings close in age (N<150) as well as age and sex-matched children from the same postal area (N = 150). A three-day food diary, rating scales for mental health and multiple questionnaires will be completed and biological samples (blood, saliva, urine, faeces, buccal swap) collected. Measurements include nutritional status, inflammatory factors, and oral and faecal microbiota composition but also nutrimetabolomics, nutrigenomics and how host gene anchors might predict particular microbiota.

Conclusions: The scientific value is based on a good quality study design and longitudinal approach. A strength of the study is in the simultaneous use of categorical and dimensional assessments, in order to identify patterns between food and supplements, genetic variants, intestinal microbiota, measurements of intestinal permeability and mental health. This kind of approach has been called for as a basis for lifestyle treatment options for improving mental health and fits well with priorities recently put forward in the Roadmap for Mental Health Research in Europe.

47

Effect modification by the gut microbiota on metabolic response to resistant starch (RS) wheat supplementation

Riley L. Hughes[1] *and Nancy L. Keim*[1,2]

[1]Department of Nutrition, University of California, Davis, CA, USA. [2]USDA-ARS Western Human Nutrition Research Center, Davis, CA, USA.

Objective: To determine whether features of individuals' baseline gut microbiota modify the effect of a resistant starch (RS) intervention on post-prandial glycemic response and other metabolic markers that have been linked to gut microbial action (e.g. short-chain fatty acids).

Methods: Metabolic responses and 16S rRNA gene data generated from a double-blind, placebo controlled, crossover clinical trial of RS and regular wheat will be used to investigate whether baseline features of the microbiota are correlated with inter-individual differences in the effect of RS supplementation. Women and men consumed 3 or 4 rolls per day, respectively, made from RS (14-18g RS) or conventional wheat (4-5.5g RS) for 7 days during each arm of the trial. Linear mixed models of glycemic response and gut microbiota features as well as covariates (e.g. habitual fiber intake) will be used to determine microbiota features associated with improvement in glycemic response as a result of RS supplementation.

Results: RS wheat reduced post prandial insulin and glucose compared to regular wheat consumption ($p_{ins} = 0.004$, $p_{glu} = 0.01$). However, there is a significant amount of inter-individual variability in the magnitude and direction of postprandial glycemia responses to RS wheat supplementation (intra-class correlations (ICC) of post-prandial glucose and insulin area under the curve (AUC) were high, 42.07% and 52.86%, respectively).

Conclusions: The results of this study show a high degree of inter-individual variability in metabolic response to fiber (RS) supplementation, suggesting the presence of individual factors that modify the effect of the intervention.

48

Prioritization of deleterious variations in Glutathione S-transferases potentially impacting circulating ascorbic acid levels

Magnolia Astrid Pretell-Bocangel[1] *and Peter Eck*[1]

[1]Human Nutritional Science, University of Manitoba, Manitoba, Canada

Background: Copy number variations of the Glutathione S-transferases genes are associated with circulating ascorbic acid. However, other variations as Single Nucleotide Variations have not ever been tested, both rare and common. Assuming that rare Single Nucleotide Variations show higher penetrance on a given phenotype, a strategy to prioritize them for impact sizes is presented. The study aims at prioritize non-synonymous variants in Glutathione S-transferases based on the potential impact on circulating ascorbic acid levels.

Methods: 1339 non-synonymous variants (nsSNVs) were included in the analysis. The variants were annotated using Combined Annotation Dependent Depletion (CADD), Annotate Variation (ANNOVAR). Allele frequency was sourced and combined from the 1000 Genomes, NHLBI-ESP 6500 exomes, and Genome Aggregation Database. The degree of deleteriousness was scored based on Polyphen2, SIFT, MutationAssessor, LRT, FATHMM, PROVEAN, MutationTaster, MetaSVM, M-CAP. The degree of genetic conservation was determined with GERP++_RS, phyloP100way, phastCon, SiPhy_29way. A combined score of above parameters is used to prioritize variations for functional testing and association studies.

Results: We identified 43 ns-SNVs that could have damaging functional and/or structural effects in *GSTM1, GSTT1*, and *GSTTP1*.

Conclusions: The described novel approach was used to prioritize the potentially most deleterious variations. These could be applied to functional tests and a population-based study.

49

Lessons from the research within the Food4me project

R San Cristobal[1,2], *S Navas-Carretero*[2], *JA Martínez*[1,2] *on behalf of the Food4Me consortium.*

[1]Precision Nutrition and Cardiometabolic Health. IMDEA-Food Institute (Madrid Institute for Advanced Studies), CEI UAM + CSIC, Madrid, Spain; [2]Centre for Nutrition Research, University of Navarra, Pamplona, Spain. Centro de Investigacion Biomedica en Red Area de Fisiologia de la Obesidad y la Nutricion (CIBEROBN), Madrid, Spain. IdisNA Institute for Health Research, Pamplona, Spain

Background: Precision Nutrition involves a wide array of personal information aiming to tailor individual nutritional requirements for health promotion. However, the integration of this individual information is still a conundrum.

Objectives: For these reason, the Food4Me project aimed to deliver new scientific tools for the exploitation of dietary, phenotypic and genotypic data in the prescription of personalised nutrition; and to demonstrate the validity of individualized nutrition in an online intervention across seven European countries.

Methods: Self-reported socioeconomic, psychological, anthropometric, phenotypic and genetic information were collected through online standardised procedures to develop research to promote the interpretation of the scientific knowledge to be translated into public health services.

Results: Outcomes of the Food4Me study evidenced the validity of using web-based technologies for the dietary intake estimation to record nutrition information, as well as the reliability of anthropometric data, phenotypic and genetic characterisation by dried blood spot and buccal swab sampling. Additionally, the application of behaviour change techniques through validated operating procedures and algorithms achieved suitable behavioural changes on dietary habits [1]. Further analyses were carried out to characterize clusters of population based on specific dietary, metabolic or genetic information associated to an increased risk of metabolic complications. These analyses evidenced the need to emphasize the role of education to fight against deleterious dietary habits that impact on obesity and cardiometabolic health [2].

Conclusions: These results evidenced the need of qualified health counsellors who have the ability to translate technical information into understandable language to the general population in order to deliver personalised nutritional advise based on individual's information [3].

References

1. Celis-Morales, C., et al., Effect of personalized nutrition on health-related behaviour change: evidence from the Food4Me European randomized controlled trial. Int J Epidemiol, 2017. 46(2): p. 578-588.
2. San-Cristobal, R., et al., Capturing health and eating status through a nutritional perception screening questionnaire (NPSQ9) in a randomised internet-based personalised nutrition intervention: the Food4Me study. Int J Behav Nutr Phys Act, 2017. 14(1): p. 168.
3. Kohlmeier M, De Caterina R, Ferguson LR, Görman U, Allayee H, Prasad C, Kang JX, Nicoletti CF, Martinez JA. Guide and Position of the International Society of Nutrigenetics/Nutrigenomics on Personalized Nutrition: Part 2 - Ethics, Challenges and Endeavors of Precision Nutrition. J Nutrigenet Nutrigenomics. 2016;9(1):28-46

50

Effect of *GC* genotypes and haplotypes on vitamin D sufficiency

Martin Kohlmeier[1], *Karina Fischer*[2], *Heike Bischoff-Ferrari*[2]

[1]UNC Nutrition Research Institute, University of North Carolina at Chapel Hill, Kannapolis, NC, USA; [2]UniversitätsSpital Zurich, University of Zurich, Switzerland

Background: The main transporter of vitamin D metabolites in blood is vitamin D-binding protein (VDBP), encoded by the group-specific component (*GC*) gene. Several common GC variants have been found to strongly influence 25-hydroxyvitamin D (25(OH)D) concentration in blood.

Objective: To determine which common genotypes or haplotypes in the *GC* region best predict vitamin D sufficiency.

Methods: 273 older adults were recruited from two large hospital centers in Zurich after recovering from unilateral knee replacement surgery. Of those, concentrations of 25(OH)D were measured in 271 participants using HPLC-MS/MS. Genotypes were determined with a customized microarray (Illumina MEGA-EX).

Results: Out of 140 variants across 115 kb, exonic variant rs4588 gave the greatest separation between 25(OH)D concentrations by genotype (30.33 vs. 25.42 vs. 19.38 ng/mL for CC vs. CA vs. AA). The other commonly investigated exonic variant rs7041 gave a distinctly smaller spread (30.22 vs. 26.70 vs. 23.69 ng/mL for GG vs. GT vs. TT). The three diplotypes arising from the two most common long-range haplotypes A and B (similar to previously reported Gc1s and Gc2), which were present in about 60% of the participants, resulted in slightly greater 25(OH)D concentration differences than any variants on their own (30.91 vs. 25.87 vs. 18.72 ng/mL for AA vs. AB vs. BB). Haplotype B was unambiguously predicted by the rs2282679 C allele. The uncommon haplotype C (similar to Gc1f) with 25(OH)D concentrations like haplotype A was consistently predicted by the rs222042 G allele.

Conclusions: The 8% carriers of the rs4588 AA genotype had 36% lower 25(OH)D concentrations than the 23% with the CC genotype. The observations in this relatively homogeneous group of older Swiss adults will help to genetically identify individuals most likely to be at risk for low 25(OH)D concentration.

51

Modulation of phosphodiesterase 5A expression by docosahexaenoic acid in human vascular cells and in peripheral blood mononuclear cells isolated from pulmonary arterial hypertension patients

Massaro Marika[1], *Scoditti Egeria*[1], *Santarpino Giuseppe*[3], *Calabriso Nadia*[1], *Mundi Santa*[2], *Carluccio Maria*[1], *De Caterina Raffaele*[4]

[1]C.N.R. Institute of Clinical Physiology, Lecce, Italy; [2]Department of Biological and Environmental Science and Technology (DISTEBA), University of Salento, Lecce, Italy; [3]Department of Cardiac Surgery, Città di Lecce Hospital, GVM Care & Research, Lecce, Italy; [4]Institute of Cardiology, University of Pisa, Pisa, Italy
Email: marika.massaro@ifc.cnr.it

Background: Phosphodiesterase5A (PDE5A) catalyzes the hydrolysis of cGMP to GMP, thus curtailing nitric oxide (NO) signaling and favoring inflammation and vasoconstriction. The ω-3 fatty acid docosahexaenoic acid (DHA) has long been considered a cardioprotective nutrient. Recent experimental findings also suggest protective roles for DHA in the prevention and treatment of inflammatory pulmonary dysfunction, including pulmonary arterial hypertension (PAH). However, molecular mechanisms underlying their effects remain incompletely understood. We therefore investigated whether and how DHA affects the expression of inflammatory genes, including *PDE5A*, in endothelial and smooth muscle cell cultures and in peripheral blood mononuclear cells (PBMCs) isolated from PAH patients.

Methods: Human endothelial and smooth muscle cells were exposed to DHA before challenge with inflammatory stimuli. After this time, PDE5A protein and mRNA expression were assessed by Western blot and qPCR, while the activation of the pro-inflammatory transcription factors nuclear factor-κB (NF-κB) and Activator Protein-1 (AP-1) were assessed by trans-activation assays. PBMCs isolated from PAH subjects were incubated with DHA before evaluating the expression of a pro-inflammatory gene set, including *PDE5A* by qPCR.

Results: In both endothelial and smooth muscle cells, DHA treatment administered before inflammatory stimulation reduced *PDE5A* induction and, correspondently, the activation of AP-1 and NF-κB. Concordantly, ex-vivo exposure of PAH PBMCs to DHA curbed the expression of several pro-inflammatory genes including *PDE5A*, tumor necrosis factor α (*TNF*) and vascular endothelial growth factor (*VEGF*).

Conclusions: DHA downregulates inflammation-mediated expression of *PDE5A*, as well as *TNF* and *VEGF*. The final result of such effects may mimic – and perhaps cooperate with – properties of PDE5A inhibitors, now approved for use in PAH.

52

Slow Intestinal Transit Associated Mechanisms in Goto-Kakizaki rats

Joice Naiara Bertaglia Pereira[1], *Gilson Masahiro Murata*[2], *Fabio Takeo Sato*[3], *Aline Rosa Marosti*[4], *Carla Roberta de Oliveira Carvalho*[2], *Rui Curi*[1]

[1]Interdisciplinary Post-Graduate Program in Health Science, Cruzeiro do Sul University, São Paulo, Brazil; [2]Deparment of Physiology and Biophysics, Institute of Biomedical Sciences, University of São Paulo, São Paulo, Brazil; [3]Department of Genetics, Evolution, and Bioagents, Institute of Biology, State University of Campinas, Campinas, Brazil; [4]Department of Medicine, University Center of Maringa, Maringá, Brazil

Background: Genetics may be a critical factor in the development of type-2 diabetes mellitus (T2DM). The Goto-Kakizaki (GK) rat is an experimental model of spontaneous and non-obese T2DM used to study the genetic influence on the pathophysiology of this disease. The intestinal contribution to the development of insulin resistance (IR) in these animals is still unknown.

Objective: The present study aimed to investigate the morphology and the inflammatory state of the small and large intestines and intestinal motility in the GK rats.

Methods: The study used 4-month-age Wistar (control) and GK rats. The following parameters measured in the small and large intestines: histomorphometry of the villi, muscle and mucosa tunics, goblet cells abundance (proportion of acid and neutral mucin-secreting cells), the total population of myenteric neurons, expression of inflammatory and anti-inflammatory markers, and intestinal motility.

Results: In the small intestine, the GK rats exhibited decreased intestinal area, increased crypt depth, villi, and muscle thickness, increased the content of IL-1β and NFkB P65, and myenteric neuronal hypertrophy. In the large intestine, GK rats had altered distribution of the different mucin types-producing cells in both proximal and distal colons and the presence of infiltrating inflammatory cells in the distal colon; however, no differences existed in the content of pro- and anti-inflammatory cytokines. GK rats also had slower intestinal transit.

Conclusions: The altered intestinal morphology, local inflammation, and decreased intestinal motility collectively might play a role for the systemic inflammation and the development of IR and T2DM in GK rats.