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Abstracts

Guest Editors

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Disclosure Statement

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Oral Presentations

O-01

The emerging contribution of mediation analysis to understand the role of nutrition and lifestyle in mediating genetic susceptibility to obesityL. Pérusse^{a,b}

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Background: The concepts of precision nutrition and precision lifestyle medicine reflect the importance of considering nutrition and lifestyle, in addition to genetics, in the next generation of personalized interventions aimed at reducing the current burden of obesity. In that context, it is important to identify nutritional and lifestyle mediators of genetic susceptibility to obesity. Mediation analysis is emerging as an alternative approach to moderation to investigate gene-nutrition/lifestyle interaction in obesity.

Objective: The objective of this presentation is to explain the differences between the concepts of mediation and moderation and provide an overview of the studies that have used mediation analysis to support the role of eating and lifestyle behaviors in mediating genetic susceptibility to obesity.

Content: Moderation analysis is used to investigate the role of nutrition/lifestyle in modifying the association between genetic susceptibility to obesity and an obesity-related trait. Mediation analysis is used to identify nutrition/lifestyle factors explaining how genetic susceptibility to obesity exerts its effect on an obesity outcome. In comparison to moderation, relatively few studies used mediation analyses to investigate gene-nutrition/lifestyle interaction in obesity. The studies published so far have identified eating behaviors, intake of specific food groups and physical activity level as putative mediators of genetic susceptibility to obesity.

Conclusion: Moderation and mediation analyses represent two complementary approaches to investigate gene-nutrition/lifestyle in obesity or the cause-effect relationship between genetic susceptibility to obesity and various obesity outcomes. Future studies relying on mediation will contribute to improve our understanding of the role of nutrition and lifestyle in explaining how genetic susceptibility to obesity impacts body weight or other obesity-related traits.

O-02

Nutrigenetics and epigenetics in precision diet interventions

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Obesity and related cardiometabolic disorders have become epidemic worldwide. Diet and lifestyle interventions are mainstream approaches to promote weight loss and health. Considerable individual variability has long been noted in response to diet and lifestyle interventions on weight loss. We have performed a series of studies to investigate the interactions between genetic variations and diet interventions on weight loss in the diet interventions trials. Our results indicate that the genetic variations related to adiposity, dietary intakes, energy metabolism, and various cardiometabolic disorders may modify the relations between diets varying in macronutrient intakes and long-term weight loss. In our recent studies, we found that, blood DNA methylation (e.g. CpG site at diabetes related TXNIP gene) and circulating microRNAs such as microRNA-122, -99/100 and -375-3p may modulate changes in body weight and cardiometabolic status in response to diet and lifestyle interventions. The evidence gathered from our studies and investigation from other groups will be the basis for constructing personalized diet and lifestyle interventions, which hold great promise to help individuals and their health care providers create precise and effective strategies to promote weight loss in the future.

O-03

Folic acid intake and methylation status of genes associated to risk of cardiopathiesL. E. Martínez^a, L.D. Campos^a, G. Calvo^a, M. D. Hernández^b, S. M. González^c, J.J. Lugo^a, M. Calzada^a

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Background: Congenital heart defects (CHD) is a complex, multifactorial disease that arises through the interaction of genetic

and environmental factors. DNA methylation epigenetic mechanism in most cases, explains the interactions between nutrients and genes involved in intrauterine growth and development programming. The folate methylation regulatory pathway is a possible contributor for genes either to confer risk or protection for CHD. The aim of this study was to determine if there is a relationship between maternal folate intake during pregnancy and methylation status (MS) of genes associated to CHDs.

Methods: Sixty-six mothers (22 cases and 44 controls) and their children were evaluated. The mothers' dietary variables were collected through a food frequency questionnaire focusing on FA and the consumption of supplements with FA. Seven SNVs of the genes AXIN1, TBX1, TBX20 and MTHFR were selected from previous literature. DNA Extraction, Genotyping and methylation analysis was performed to healthy subjects and subjects with CHDs.

Results: 15 subjects with ventricular septal defects (VSD) and 7 subjects with atrial septal defects (ASD) were selected (n = 22) and 44 healthy controls. The intake of FA supplements was higher in the control mothers with significant differences in the first trimester of pregnancy. AXIN1 and TBX20 resulted with significant OR for CHD. There was relative hypomethylation, more evident in the ventricular septal defect group compared with the atrial septal defects. Significant differences were observed in the MS of MTHFR and AXIN1 genes in VSD compared to control children. In those of the control group with risk alleles there was only difference in methylation status for MTHFR, which was higher in controls.

Conclusions: The risk variants in MTHFR are dependent of their methylation status, while AXIN1 and TBX20 are independent. MTHFR were hypomethylated in cases as compared to controls. Folate intake during the first trimester of pregnancy may explain these differences.

O-04

Nutriepigenetic signatures associated to the Mediterranean diet

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Background: The Mediterranean diet (Med-Diet) has been associated with favorable health outcomes and nutritional well-being. Clinical and epidemiological as well as experimental research support that the Med-Diet exert a protective role on cardiovascular disease and metabolic homeostasis, which may be mediated by epigenetic events. This ancillary study investigated whether adherence to Med-Diet is associated with changes in DNA methylation in peripheral blood cells, with emphasis on the role of

the consumption of nuts and extra virgin olive oil (EVOO) or folate-rich foods.

Methods: A nutriepigenomic study was performed in a Mediterranean population at high cardiovascular risk assigned to three groups of dietary intervention: Med-Diet plus EVOO; Med-Diet plus nuts; and a low-fat control group. DNA methylation status at baseline and after 5 year of follow-up was analyzed using an Infinium Human Methylation 450K bead chip as well as robust statistical tests and functional pathway classification protocols.

Results: Changes in methylation occurred in genes related to oxidative stress, adipogenesis, diabetes, and metabolic immune-inflammatory pathways. In this context, methylation changes in genes related to immunocompetence and inflammation (EEF2, COL18A1, IL4I1, LEPR, PLAGL1, IFRD1, MAPKAPK2, PPARGC1B) correlated with adherence to Med-Diet, highlighting EEF2 which also was linked to inflammatory biomarkers. In particular, nuts and EVOO induced changes in methylation of genes related to adiposity, oxidative stress, inflammation and signal transduction (i.e. CPT1B and GNAS). Moreover, methylation of a selected CpG at CPT1B gene was specifically associated with polyunsaturated fatty acids intake. Also, folate intake was found associated with methylation changes in the CAMKK2 gene, potentially modulating insulin resistance markers. Interestingly, methylation of olfactory signaling genes may contribute to energy utilization and fat accumulation, which may be eventually related with organoleptic Mediterranean food properties.

Conclusions: Overall, these findings demonstrate that the Med-Diet may produce immune and regulatory metabolic changes through epigenetic mechanisms. This knowledge concerning gene methylation signatures may contribute to define dietary/nutrient roles in health status, facilitating the implementation of precision nutrition strategies for prevention of chronic diseases targeting the methyl epigenome. Indeed, Mediterranean staple foods, such as nuts intake, good quality fats (olive oil), and fruits/vegetables rich in folate may explain some related health benefits by epigenetic phenomena.

O-05

A transcriptomic investigation of omega-3 fatty acid metabolism in mouse adipocytes uncovers a novel role for Δ-6 desaturase

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Background: The Δ-6 desaturase (D6D), encoded by the fatty acid desaturase 2 gene (*Fads2*), is critical for the synthesis of long-chain polyunsaturated fatty acids (LC-PUFA). Evidence suggests that reduced D6D activity not only disrupts LC-PUFA production, but also impacts whole body lipid handling and body weight; however, the mechanisms remain largely unexplored. The goal of this presentation is to provide an overview of our research using cell and mouse models to advance understanding of D6D in white adipose tissue (WAT).

Methods: Mouse 3T3-L1 adipocytes were differentiated with a D6D inhibitor (SC-26196) in the presence or absence of α -linolenic acid (ALA). Male C57BL/6J *Fads2* knockout (KO) and wild-type (WT) mice were fed either a lard diet (7% w/w lard) or a flax diet (7% w/w flaxseed oil) for 21 weeks prior to the collection of inguinal and epididymal WAT depots. Fatty acid composition, adipocyte size, gene expression and markers of lipogenesis, lipolysis, and insulin signaling were measured.

Results: D6D-inhibited 3T3-L1 adipocytes had reduced triacylglycerol (TAG) accumulation despite an EPA/DPA deficiency. Analyses of gene expression and cellular protein markers, as well as non-esterified fatty acids and glycerol release in medium, suggested increased lipolysis and decreased fatty acid re-esterification in D6D-inhibited cells. KO mice had reduced body weight, higher serum non-esterified fatty acids (NEFA), smaller WAT depots, and reduced adipocyte size compared to WT mice without altered caloric intake, energy expenditure, or physical activity, regardless of the diet. Markers of lipogenesis and lipolysis were higher in KO mice compared to WT mice in both WAT depots, irrespective of diet. Lastly, the increase in lipolytic markers in KO mice was accompanied by reduced basal insulin signaling in WAT.

Conclusions: Our research provides new insights showing that D6D inhibition reduces TAG accumulation and increases lipolysis independent of changes in n-3 PUFA cellular content.

O-06

Genetic variation underlying the differential response to sugar-sweetened beverage intake

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Background: Increased consumption of sugars, particularly simple sugars, has been linked to increased risk for metabolic diseases such as obesity, type 2 diabetes, hypertension and non-alcoholic fatty liver disease (NAFLD). The two most consumed simple sugars, glucose and fructose, have different adverse effects on metabolic health. In this presentation, the aim is to review data on the differential metabolic effects of simple sugars ingested in the form of sugar-sweetened beverage (SSB) and the factors affecting the variation in the response to SSB.

Methods: Data from human (RCTs, cohort and case-control), mouse and cell culture studies were reviewed.

Results: Most of the studies show that simple sugars increase fat accumulation in the liver and skeletal muscle, and increase risk for insulin resistance, hyperuricemia, obesity, type 2 diabetes, hypertension and NAFLD. Diet studies have also shown that the response is highly variable across individuals and genetic variants and ethnicity modify this response. The key genes that have been shown to affect this response include *PNPLA3*, *HNF4 γ* , *ACE*, *INHBB*, *SLC2A9*, *SLC2A2*, *GCKR* and *APOC3*.

Conclusions: Fructose and glucose have differential effects on metabolic health. The magnitude of the effect depends on genetic variants and ethnicity. Thus, studies investigating the effects of simple sugars on metabolic health need to take into account individuals' genetic and ethnic background.

O-07

Are genetic tests useful in nutrigenomics?

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Background: Genomics has made personalized medicine a reality and is a powerful tool in the field of pharmacogenetics by selecting the appropriate treatment based on genotype. The genetic variants that influence the response to nutrients and metabolism, known as nutrigenetics, is an area with the potential to provide an answer to what diet each person should have and the effect of nutrients on gene regulation, called nutrigenomics. Genotyping studies have revolutionized the diagnosis of monogenic diseases, where a change in the DNA sequence will have a phenotypic effect, such as cystic fibrosis, phenylketonuria, and galactosemia. However, the effect of multifactorial conditions where genes reflect a tendency, lifestyle, and diet, are not so easy to quantify as to its contribution to presenting a disease.

Methods: A search of the literature and review of the results of various laboratories that offer molecular tests to the general population.

Results: In seven laboratories that offer nutrigenetic studies, only one shows the polymorphic variants, the rest mention the genes they analyze but do not specify their data.

Conclusions: The results of these studies cannot be taken as diagnostic for nutrition; however, they have the potential to indicate the dietary hygiene measures of the person who has undergone the study. The results of nutrigenetic studies must be interpreted by specialists in genetics and nutrition to serve as a guide to continue understanding the variants and metabolism.

O-08

Clinical, metabolomic and proteomic data integration to accurately diagnose diabetic kidney disease

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Currently, creatinine and albuminuria are used to diagnose diabetes kidney disease (DKD). However, functional and histological renal abnormalities are present before creatinine and

albumin become abnormal. In addition, their concentrations depend not only on glomerular filtration rate (GFR), but also on many additional factors. Based on that, various metabolites and proteins have been proposed as DKD diagnostic biomarkers. The aim of this study was to search for models with high diagnostic precision for DKD built on clinical, protein and metabolomic markers. We analyzed a cohort of individuals that included healthy individuals and patients with type 2 diabetes with or without DKD. The glomerular filtration rate was calculated by standard tests (i.e. 24-hour urine collection for creatinine clearance and albuminuria). In addition, we quantified 42 metabolites in plasma and urine samples and 9 serum proteins. Diagnostic accuracy was calculated by vector machine models in order to do an integrative analysis of metabolic, proteomic and clinical variables. A total of 200 individuals were analyzed, 43 healthy subjects, 102 without DKD and 55 with DKD. We develop 13 models, in which some have a 100% accuracy for DKD diagnosis (specificity 100%, sensitivity 100%). The results of this study suggest that the use of the serum-based models could improve the diagnosis of DKD in clinical practice, and this strategy facilitates the diagnosis by using a single serum sample.

O-09

Gut metagenomic information in the implementation of precision nutrition

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Background: Alterations in gut microbiota composition, called dysbiosis, is one of the factors that can contribute to the development of obesity, insulin resistance, non-alcoholic fatty liver disease and other clinical manifestations in humans. For this reason, it is necessary to have a precise view of the state of dysbiosis, which opens the door to the use of metagenomic tests based on genomic technologies at an increasingly affordable price.

Methods: Spanish volunteers from the Obekit study (n = 361) were classified according to different metabolic variables including body mass index (BMI), insulin levels/resistance, and inflammatory markers. Sequencing of the V3-V4 region of the 16S rRNA gene was performed in fecal samples from all participants.

Results: Individuals with the different metabolic alterations showed a significant decrease in alpha-diversity and richness indexes, such as Shannon and Chao-1. Several bacterial families, genera and species presented significant differences between the individuals with high and low levels of the different metabolic

biomarkers. Particularly, Ruminococaceae, Christenellaceae and Coriobacteriaceae were more abundant in those individuals with less disease risk biomarkers whereas Prevotellaceae was more abundant in those subjects with more metabolic complications.

Conclusions: Microbiota information is able to discriminate individuals with diverse metabolic alterations. These results open the door to the design of metagenomic tests that can detect dysbiosis and help to early identify individuals at more microbiota-related metabolic risk. Also, as gut microbiota composition and diversity can be modulated by diet and other lifestyle factors, this information may also be used in precision nutrition to personalize the intervention and optimize the restoration of gut eubiosis.

O-10

Gut microbiome and metabolic health in school age children: perspectives for dietary interventions

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Background: Pediatric obesity is a major health problem worldwide and it is commonly associated with metabolic alterations such as dyslipidemia, insulin resistance and metabolic syndrome (MetS). A number of studies have described that alterations in metabolites such as branched chained amino acids (BCAA) or bile acids (BA) are implicated in the pathophysiology of obesity and metabolic alterations, and that gut microbial metabolism could have a significant role. Thus, we aimed to explore whether in early adolescents, circulating levels of BCAA and serum bile acids were associated with the gut microbiome and this way to metabolic health.

Methods: Targeted metabolomic analysis was performed in serum samples of early adolescents (10-12 years old) by LC-MS/MS. Gut microbial characterization was performed by 16S rRNA gene and shotgun sequencing.

Results: We found that children with MetS showed a significant increase in total BA (36.48%), secondary (26.79%) and 12 α -hydroxylated (34.40%) and these were associated with dyslipidemia and insulin resistance markers. Interestingly, serum total BA levels were negatively correlated with gut microbial diversity (P = 0.035) while, 12 α -hydroxylated, secondary BAs and

deoxycholic acid showed negative correlations with a number of genera known for its bile acids sensitivity or potential health effects, including *Bifidobacterium*, *Akkermansia*, *Veillonella* and *Faecalibacterium*. On the other hand, BCAA were associated with insulin resistance markers and correlated negatively with genes encoding bacterial BCAA inward transporters. Particularly we identified that *Faecalibacterium prausnitzii* contributed to approximately ~70% BCAA transporters gene count and was also negatively correlated with BCAA levels and insulin resistance markers ($P < 0.05$).

Conclusions: The findings from the current study suggest that the bile acids dysregulation observed in MetS could predispose to gut microbial dysbiosis. Reciprocally the gut microbiome by modulating serum BCAA levels, could influence the presence of insulin resistance. This underscores that preventive or therapeutic interventions for metabolic alterations should target both metabolites as well as the gut microbiome.

O-11

miRNAs and extracellular vesicles from diet as novel players for personalization

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Epidemiological evidence suggests that adherence to diets rich in vegetables and fruits have a preventive effect against the risk of developing chronic non-communicable diseases (NCD), such as cardiovascular and cancer. This effect has been traditionally associated with the bioactive molecules that these foods contain. Cell communication is essential for organism development. To facilitate communication, both plant and animal cells can release nanoparticles, known as extracellular vesicles (EVs), that transport bioactive molecules including nucleic acids, such as microRNAs (miRNAs). miRNAs are small non-coding RNAs that regulate essential biological processes in plants and animals.

Food-derived miRNAs (exog-miRNAs) can be transported in EVs that contribute to partially increase their resistance against the adverse conditions of the digestion process and be absorbed. This can facilitate their possible regulatory (or bioactive) effect on consumer gene expression when they are consumed through diet. This phenomenon of interaction between living beings from different kingdoms through miRNAs (cross-kingdom regulation) has opened a new research paradigm questioning whether dietary miRNAs could act as bioactive components. Characterization methods have shown that plant EVs have similar structures to mammalian EVs which may facilitate their uptake, tissue distribution and ability to produce biological effects in mammalian cells. Given that the quantity of miRNAs that might reach tissues may not be sufficient to be able to exert the bioactive effect, different strategies are being developed (i.e., usage of EVs) for enhancing miRNA stability.

Advances in the knowledge of how dietary miRNAs could influence the regulation of our genes will expand the possibility of being able to develop or consume new foods or fortify traditional ones (i.e., infant formula milk, functional foods) for future personalization and combat our rampant NCD.

O-12

Calafate (*Berberis microphylla*), a Chilean native berry: is it suitable to consider it for personalized nutritional approaches regarding obesity?

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Background: Obesity is a serious (and continuously growing) public health problem present in both developed and developing countries. Being the white adipose tissue (WAT) the main storage of lipids when there is an excess of energy, its pathological growth is the process that defines this pathology, and also it is the hallmark for co-morbidities appearances. In this scenario, it becomes imperative to develop new approaches for the treatment and prevention of obesity and its co-morbidities, supporting the currently existing strategies. In this sense, there is an intense search for bioactive compounds with anti-obesity properties, with the ability to counteract this condition through different flanks: by blocking oxidative stress or inflammation, increasing energy expenditure, inducing browning of WAT, etc. One of the matrixes with the most promising bioactive compounds in this regard is the Chilean native fruit Calafate.

Methods: The properties of treatments with Calafate aqueous extracts over in vitro and in vivo obesity models were tested regarding antioxidant and anti-inflammatory capacity, brown adipose tissue (BAT) thermogenesis induction, WAT-browning ability, adipose tissue weight gain prevention, energy expenditure induction, restoration of mitochondrial function, among others.

Results: A Calafate extract reduced the expression of iNOS and TNF- α , and increased IL-10, when applied to an adipocyte/macrophage co-culture. Moreover, it was reported that this extract inhibits the inflammatory response and stimulates glucose uptake in 3T3-L1 cells treated with conditioned media from activated macrophages. It was also observed that it inhibits inflammation and apoptosis in activated human macrophages, suppresses inflammation and apoptosis, and improves the antioxidant response of activated human adipocytes. Then, this in vitro approach was confirmed in vivo. It was described anti-inflammatory (blunted TNF- α and F4/80 WAT expression) and insulin-sensitizing (AKT phosphorylation restoration) characteristics of the administration of a polyphenol-pure Calafate extract in HFD-fed mice. Finally, Calafate extract administration was able to prevent HFD-weaken activation of UCP-1, PGC1 α , PRDM16, (among others), at mRNA and protein level, and mitochondrial activity in BAT and WAT, in direct correlation with higher energy expenditure, lower respiratory quotient, lower body weight gain, and restored mitochondrial function in mice. Moreover, it was observed that microbiota has a major role in these reported in vivo effects.

Conclusions: Certainly, it has been gathered a promising amount of evidence regarding Calafate treatment potential over obesity and obesity-related outcomes. Though efforts regarding food engineering, deeper molecular mechanism, and specially, clinical validation are still needed, we are convinced that sooner than later this approach can be surely accounted as one of the precision and personalized complementary nutrition tools.

O-13

Biological age and diet: measuring the impact of lifestyle on a 6CpG-epigenetic clock

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Background: Changes in DNA methylation along the life have been documented, and environmental exposures (i.e. diet, physical activity and smoking) can accelerate or decelerate this process. The epigenetic clock estimates the biological age of an individual measuring the methylation pattern in specific areas of its genome. Recently, a new epigenetic clock based on 6 CpGs has been proposed, with high potential to become an easy accessible tool able to measure the epigenetic age (EA) of an individual. The aim of this study is to validate the 6 CpG epigenetic clock comparing it with other biomarkers of aging such as telomere length (TL) and methylation in the long interspersed nuclear elements (LINE-1). Moreover, the impact of life-style associated factors on these molecular marks has been evaluated.

Methods: 200 healthy participants having extreme dietary patterns (healthy vs western diet) were selected. Dietary intakes, body composition, physical activity level and smoking has been assessed. DNA extracted from whole blood was used to measure the 6CpG-EA, TL and LINE-1 methylation levels.

Results: 6CpG-EA was positively correlated with chronological age and negatively with TL and LINE-1 methylation. Despite no significant associations were detected with the overall diet quality (HEI), 6CpG-EA was correlated with dietary intakes of nutrients involved in the one-carbon (1C) metabolism, especially in the western diet group.

Conclusions: These outcomes support the 6CpG epigenetic clock as an easy accessible tool to estimate biological age, in accordance with other molecular markers of aging, and suggest that EA can be modulated by diet, especially through micronutrients involved in the 1C metabolism.

O-14

Machine learning in nutrition research

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Background: Nutrition data analysis is usually performed by statistics approaches. Nevertheless, data analysis is difficult to do given the data size and complexity. Machine learning algorithms may improve the correct patterns identification and data classification. However, machine learning is hardly utilized by experts in nutrition, so in this talk we present some application of machine learning to problems related with nutrition with the aim to motivate experts to use new machine learning technology.

Methods: A deep search of machine learning applied to the nutrition field is done and we present an introduction to machine learning and its use in the found applications.

Results: The search results showed that machine learning is rarely used in the nutrition field.

Conclusions: Machine learning is largely used in many fields, usually experts in machine learning perform the data analysis, however, the technology of machine learning allows one to use it without being an expert in machine learning. This talk aims to motivate experts in nutrition to use this new technology for data analysis.

O-15

Genetics and epigenetics of olfaction in nutrition and obesity

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Background: Sensorial modalities, including olfaction, may influence food preferences, appetite, and eating behaviors. Besides physiological issues (such as age, circadian rhythmicity, and hormone secretions), the interindividual variability in odor perception may be driven by genetic and epigenetic marks, which in turn can impact food consumption and metabolic/health status.

Methods: On the one hand, a review was performed concerning genetic variants in olfaction genes and associations with nutrition features and obesity. On the other hand, an ancillary nutriepigenomic analysis was conducted using data from the Methyl Epigenome Network Association (MENA) project. Clinical and nutritional data were obtained from structured databases of the MENA cohorts. DNA methylation was measured in peripheral white blood cells by microarray (Infinium Human Methylation 450 K BeadChips). Pathway analyses were fitted using KEGG and pathDIP reference platforms.

Results: Copy number variable regions in olfactory receptor (ORs) genes (*OR4P4*, *OR4S2*, *OR4C6*, *OR4D1*, and *OR52K1*) have been associated with obesity predisposition. Similarly, single nucleotide polymorphisms in ORs genes (*OR7D4*, *OR7E24*, and *OR7G3*) were also found to be associated with adiposity and eating behaviors. In addition, 15 CpG sites at olfactory pathway genes were associated with BMI, including ORs (*OR4D2*, *OR51A7*, *OR2T34*, and *OR2Y1*) and downstream transducing molecules (*SLC8A1*, *ANO2*, *PDE2A*, *CALML3*, *GNG7*, *CALML6*, *PRKG1*, and *CAMK2D*). Furthermore, methylation levels at *OR4D2* and *OR2Y1* genes correlated with daily macronutrient intakes.

Conclusions: Sequence variants in ORs genes appeared to contribute to the predisposition to obesity and related eating behaviors. Moreover, relationships between olfactory pathway gene methylation signatures, obesity markers, and dietary intakes were found. This knowledge may contribute to identify genetic/epigenetic biomarkers to predict obesity risk as well as implement genome-based dietary strategies for prevention, prognosis, and management of excessive adiposity within a precision nutrition scope.

O-16

Comparison of weighted and unweighted genetic risk scores predicting the plasma triglyceride responsiveness to an omega-3 fatty acid supplementation

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Background: We previously identified single nucleotide polymorphisms (SNPs) affecting the plasma triglyceride (TG) responsiveness to an omega-3 fatty acid (FA) supplementation in the Fatty Acid Sensor (FAS) Study. From these SNPs, 31 were computed into a genetic risk score (GRS) predicting the plasma TG response. Recently, a genome wide association study (GWAS) on participants of the UK Biobank identified 14 new SNPs interacting with omega-3 FA supplementation and influencing plasma lipid levels, 7 of which were specifically influencing TG levels. The objectives were: 1- to verify whether the addition of these new SNPs allows to refine our initial GRS; and 2- to compare the predictive capacity of a weighted and unweighted version of both the initial and the new GRS.

Methods: A total of 141 participants of the FAS Study received 5g fish oil/day (1.9-2.2g EPA and 1.1g DHA) for 6 weeks. Plasma TG levels were measured before and after the supplementation. A total of 7 SNPs interacting with omega-3 FA supplementation and influencing TG levels in the UK Biobank were genotyped in the FAS Study and used to compute a new 38-SNP GRS (31 SNPs + 7 new SNPs) by summing the number of at-risk alleles. A weighted version of both GRS31 and GRS38, in which each SNP is given a score based on its odds ratio, was also calculated.

Results: The initial, unweighted GRS31 explained 50.5% of the variance in the plasma TG response to an omega-3 FA supplementation and its weighted version (wGRS31) 34.1%. Similarly, the new GRS composed of 38 SNPs (GRS38) explained 49.5% of the variance in the plasma TG response whereas the wGRS38 explained 39.5%.

Conclusions: Neither the addition of the 7 SNPs interacting with omega-3 FA supplementation and influencing plasma TG levels in the UK Biobank nor GRS weighting improved the predicting capacity of the initial GRS31. Replications in independent study cohorts are necessary to confirm these findings.

O-17

The pro-thermogenic effects of *Berberis Microphylla* (Calafate) extract in mice fed a high-fat diet are dependent on the presence of gut microbiota

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Background: the metabolism of polyphenols carried out by the gut microbiota (GM) can influence their bioactivity/bioavailability. The aim of the present study was to evaluate whether the pro-thermogenic effect of a polyphenol-rich *Berberis-microphylla* extract (Calafate) depends on GM in obese mice.

Methods: 8-week-old C57BL6 mice (n=30) were divided into 4 diets/treatments. Control Diet (C), High-Fat-Diet (HF), High-Fat-Diet/Calafate (HFC) and High-Fat-Diet/Calafate/Antibiotics (HFCAB). At 19 weeks, animals of HFCAB were treated with a broad-spectrum antibiotic in the drink for 2 weeks. Then, HFC and HFCAB were treated with a daily dose of 50mg of total-polyphenols/kg-animal-weight, of the Calafate extract for 3 weeks. At 24 weeks, animals were euthanized and interscapular brown-adipose-tissue (BAT) and epididymal (eWAT) and inguinal (iWAT) white-adipose-tissue were obtained. Gene expression of thermogenic markers (Ucp-1, Pgc1- α , Ppara/ γ , Prdm16, Sirt1 and Dio2) and beige adipose tissue marker (Tbx1) were analyzed. Transmission-electron-microscopy was used to evaluate mitochondrial morphology and mitochondrial cristae density in BAT. Further, cecal content was extracted to analyze the GM by mass sequencing with MiSeq-Illumina and Short-chain fatty acids (SCFAs) by Gas chromatography-mass spectrometry (GC-MS). α -diversity of GM was calculated using Shannon index and β -diversity values using principal coordinate analysis. One-way ANOVA and Tukey post hoc was used for comparison between groups.

Results: we observed higher expression of Dio2 in BAT and in iWAT of HFC versus C and HFCAB, in addition to higher expression of Tbx1 in eWAT of HFC versus HFCAB. HFC presented higher density of mitochondrial cristae versus HF and HFCAB. HFCAB presented lower α -diversity versus C, HF and HFCAB. There were no differences in β -diversity nor in the production of SCFA between the groups.

Conclusions: a polyphenol-rich Calafate extract promotes thermogenesis and browning in mice with diet induced obesity. The effects of Calafate disappear when animals are treated with antibiotics.

O-18

***Moringa oleifera* improves maflD by inducing epigenetic modifications in a murine model of non-alcoholic steatohepatitis**

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Background: Metabolism-associated fatty liver disease (MAFLD) encompasses a spectrum of diseases from simple steatosis to nonalcoholic steatohepatitis (NASH). Several studies have reported therapeutic effects of *Moringa oleifera* leaf extracts due to their antioxidant, anti-inflammatory and lipid-lowering effects. We evaluated the hepatoprotective effect of the aqueous extract of *Moringa oleifera* on the expression of hepatic miRNAs, genes and proteins involved in lipid metabolism, as well as histological and biochemical parameters in a murine model of non-alcoholic steatohepatitis.

Material and Methods: Aqueous extract was characterized by means of DPPH and ABTS spectrophotometric assays. Male C57BL/6J mice were randomized into two groups. 1) Standard diet (ND) (n = 5) (18% lipids) and 2) High-fat diet (HF) (n = 10) (60% lipids and 42 g/L sugar in drinking water), for 16 weeks. At week 9, five animals from the HF group were divided into a subgroup, 3) *Moringa oleifera* (HF + MO), 290 mg/kg/day p.o. for eight weeks. Expression of miRNAs involved in liver disease and SIRT1, AMPK α and SREBP1c proteins were determined in liver homogenate. Liver transcriptome was studied by microarray. Alpha-SMA immunohistochemistry and hematoxylin-eosin, Masson and Sirius red staining were performed. Statistical differences between groups were determined using ANOVA/Kruskal-Wallis test.

Results: The group treated with *Moringa* extract showed decrease in SREBP1c, while SIRT1 increased. Also, hepatic expression of miR-21a-5p, miR-103-3p and miR-122-5p, miR-34a-5p was downregulated. Histological analysis showed a significant decrease in liver inflammation, steatosis, collagen, and alpha-SMA reactivity in the *Moringa* group (HF+MO). Liver transcriptome analysis showed negative expression of mRNAs involved in DNA damage response, endoplasmic reticulum stress, lipid biosynthesis, and insulin resistance in *Moringa* animals.

Conclusion: Treatment with *Moringa oleifera* is a therapeutic alternative for the NASH spectrum of liver disorders.

O-19

SNPs of ABCA1 (rs9282541) and PPAR GAMMA (rs1801282) genes are related with serum lipid profile in adult women from Mexico

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Background: Genetic polymorphisms can be used as biomarkers for the early diagnosis of cardiovascular diseases (CVD). Among the polymorphisms related to these alterations, some described in the ABCA1 and PPAR gamma genes, are associated with different conditions: high serum lipid levels, adipogenesis, obesity and insulin sensitivity. Such associations are described today, for European populations. The aim of this study was to evaluate the association between rs9282541-ABCA1 and rs1801282-PPAR gamma polymorphisms with serum lipid levels in a population of adult Mexican women.

Methods: 242 women (18 to 50 years of age), residents of Monterrey, Nuevo León, México, were included in this study. After signing an informed consent, the women underwent anthropometric and body composition measurements; fasting blood was also used to determine the serum lipid profile and DNA extraction, following standardized protocols. Genotyping was performed by Real-Time PCR using TaqMan probes. Linear regression was used to analyze the association between the mentioned variables.

Results: The median age of total population was 25 years old; median of fat mass expressed as percentage was 39.4%; also 50.8% of participants had decreased serum HDL levels (<50 mg/dL). With respect to genetic analysis we found that minor allele frequency was 0.059 and 0.098 for rs1801282-G and rs9282541-A polymorphisms, respectively. The linear regression analysis shown negative associations of rs9282541-ABCA1 with weight (p = 0.041), percentage of fat (p = 0.020), triglycerides (p = 0.045), HDL (p = 0.028) and VLDL (p = 0.045). No statistically significant associations were observed with rs1805192-PPAR gamma.

Conclusions: In women from northeastern Mexico there is a high proportion of subjects with metabolic alterations. The rs9282541-ABCA1 could be used as a biomarker of alterations related to the lipid profile; however, studies that replicate these findings are required.

O-20

Plant-based dietary patterns, genetic susceptibility and cardiometabolic traits in the CARTaGENE Biobank

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Background: Plant-based dietary patterns (PBDP) have been associated with a lower risk of obesity and cardiovascular disease. Additionally, PBDP have been reported to modulate the genetic susceptibility to obesity in adults. However, it is still unknown whether PBDP may partly explain the mechanisms by which obesity genes express themselves. Hence, the aim of this study was to examine whether adherence to three PB-scores mediated or moderated the associations between a polygenic risk score for body mass index (PRS-BMI) and cardiometabolic traits.

Methods: This cross-sectional study included 3,976 participants (56% women, aged 55.2±7.6) from the Quebec CARTaGENE cohort. A 97-SNP PRS-BMI and three PB-scores based on 18 food groups were calculated (overall, healthy, and unhealthy PBDP). General linear models were conducted to assess main effect associations between the PRS-BMI and PB-scores on anthropometry and cardiometabolic traits. Causal mediation analyses (CMA) were used to evaluate mediation and interaction models. All models were adjusted for age, sex, genetic ancestry, energy intake, physical activity, anxiety, and sociodemographic characteristics.

Results: Five outcomes were significantly associated with the PRS-BMI (β [95%CI]): BMI (0.10 [0.07, 0.13]), waist circumference (WC) (0.08 [0.05, 0.11]), waist-to-hip-ratio (WHR) (0.03 [0.01, 0.05]), fat mass (0.07 [0.04, 0.09]) and diastolic blood pressure (0.03 [0.00, 0.06]). Among PBDP, only the unhealthy-PB-score was associated with the PRS-BMI (-0.04 [-0.06, -0.01]). Results from CMA showed inconsistent mediation for the unhealthy-PB-score on the association between the PRS-BMI and WC (β -total effect = 1.47 [0.95, 2.00]; β -indirect effect: -0.04 [-0.07, -0.01]). The consumption of legumes inconsistently mediated the association between the PRS-BMI and BMI, WC, WHR and fat mass.

Conclusions: A 97-SNP PRS-BMI is associated with cardiometabolic traits and higher adherence to an unhealthy-PBDP. These findings suggests that a PBDP characterized by the consumption of low-quality food items might be involved in the obesity genetic susceptibility pathway.

Poster Presentations

P-01

Effect of cocoa supplementation on gene expression in mononuclear circulating cells in smokers and non-smokers.

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Background: Cocoa polyphenols regulate the expression of genes and exert effects such as inflammation decrease, blood pressure regulation and improvement of other cardiovascular disease (CVD) risk factors. Cigarette smoking increases oxidative stress, and is a risk factor for CVD, among others. The present study explored the effect of consumption of a cocoa supplement with high polyphenol content on circulating mononuclear cells composition and gene expression between apparently healthy male smokers and non-smokers.

Methods: The present study consisted of two visits and recruited 16 participants, (n = 8 smokers and 8 non-smokers), who fulfilled the inclusion criteria and received a cocoa supplement (375 mg of flavanols, containing 80 mg of epicatechin/d) during 2 weeks. Compliance to the treatment was controlled by capsule collection and registration. Blood was collected under fasting conditions and 2 h after the intake of the supplement, at baseline and after two weeks of consumption of the supplement. Mononuclear cells were isolated, and counted by cell cytometry. The mRNA expression of genes involved in inflammation and antioxidant activity (*SENS2*, *SOD2*, *IL-10*, *IL-8*, *FPR1*, and subfraction p50 of *NFkB*) was measured using RT-PCR.

Results: At baseline there was no difference between the two groups in age, BMI, metabolic parameters and expression of the analyzed genes. Smokers had a significantly higher percentage of monocytes ($p < 0.05$). After 2 h of polyphenol consumption (peak of concentration of metabolized derivatives in plasma), differences were observed in the expression of *IL-10* and *FPR1* in mononuclear cells in both groups. After two weeks of supplementation, a significant decrease in blood pressure was found in the compared groups. Significant increase was observed in the expression of *FPR1* and *SOD2* in both groups, with a higher expression in smokers and the analyzed *NFkB* subunit decreased significantly in smokers only.

Conclusions: The findings from the present study suggest that supplementation with a high-polyphenol cocoa supplement modify expression of genes involved in the inflammatory response and antioxidant pathways in circulating mononuclear cells. The response in the inflammatory pathways may differ between smokers and non-smokers.

P-02

Protein intake modifies associations between *FTO* gene polymorphism rs9939609 and adiposity outcomes in the CARTaGENE biobank

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Background: The *FTO* gene has the most consistent association with obesity. Implicated in appetite regulation, it is mainly expressed in the central nervous system and has been observed to interact with protein intake on body mass index (BMI). The aim of this study was to investigate whether protein intake modifies BMI and other adiposity outcomes according to variation in the *FTO* gene (rs9939609).

Methods: This cross-sectional analysis considered genome-wide genotyping, dietary, sociodemographic, and anthropometric data from the CARTaGENE cohort ($n = 7,792$). General linear models were conducted to test interactions between *FTO* genotypes (TT wild-type and AA/AT increased risk allele carriers) and protein intake (g/kg/d) in relation to adiposity outcomes of BMI (kg/m²), waist circumference (WC) (cm), and fat mass (kg). Statistical models were adjusted for principal components of ancestry, age, sex, marital status, household income, education, energy intake, physical activity, and smoking. Regions of Significance (RoS) analysis was performed for probing significant interactions.

Results: Compared to TT genotype participants, those carrying the risk allele for *FTO* had higher (mean \pm SD) BMI (27.5 ± 3.5 vs. 27.0 ± 4.9 , $p < 0.001$), WC (93.3 ± 14.4 vs. 92.1 ± 13.5 , $p < 0.001$), and fat mass (24.4 ± 10.3 vs. 23.6 ± 9.8 , $p = 0.001$). Significant interactions between protein intake and *FTO* genotypes were observed for all adiposity outcomes (β [95% CI]): BMI -0.56 [$-1.01, -0.10$], WC -1.72 [$-2.86, -0.06$], and fat mass -1.08 [$-1.97, -0.20$]. RoS showed that the differences in all adiposity outcomes between *FTO* genotype groups were attenuated when protein intake was above ~ 1.1 g/kg/d.

Conclusions: Protein intake interacts with *FTO* rs9939609 on adiposity outcomes. The results of this study support a higher recommended dietary allowance for protein intake, especially in a population with a high genetic risk of obesity. Precision nutrition interventions for obesity may benefit from evaluating *FTO* genotypes.

P-03

The maternal metabolic status modifies offspring's telomere length after maternal bariatric surgery

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Background: Obesity is a complex chronic disorder involving different factors such as education, eating habits and physical activity, as well as genetic and epigenetic factors and their interactions. As the prevalence of obesity increases, the number of bariatric surgeries is growing. However, the impact of bariatric surgery on epigenetic factors are not yet fully understood. The present study aims to compare the effect of maternal bariatric surgery on telomere length (TL) of children and its interaction with adiposity and metabolic markers.

Methods: Blood and saliva samples from 27 children born before ($n = 13$) and after ($n = 14$) their mothers' bariatric surgery ($n = 11$) were collected. TL was estimated in blood and saliva with data from the Methylation-EPIC BeadChip array. Linear mixed model regressions with random effects for family and adjusted for age of the children, sex, presence of twins, time from the bariatric surgery and age of the mother at the time of the delivery were used to evaluate the modifying effect of adiposity on TL and its interaction with the metabolic status of mothers before and after the bariatric surgery.

Results: In comparison to children born before, children born after the maternal bariatric surgery exhibited higher TL after adjusting by chronological age in both blood ($p = 0.04$) and saliva ($p = 0.08$). Significant interactions with modifying effects on TL were exhibited between the children's body fat percentage and markers of the maternal metabolic status: the triglyceride-glucose (TyG) index ($p = 0.01$), the triglyceride:high-density cholesterol (HDL) ratio (Tg:HDLr) ($p = 0.03$) and the non-HDL:HDL ratio ($p = 0.01$).

Conclusions: These results suggest that there is a maternal modulatory effect on the TL of the offspring born after the maternal surgery that may be modified by the metabolic status of the mother after the bariatric surgery.

P-04

Association between visceral adipocyte hypertrophy and circulating amino acids

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Background: In the context of a positive energy imbalance, triglycerides will preferentially accumulate in subcutaneous adipose tissue. As the expansion capacity of this organ saturates, fat can accumulate in ectopic locations such as the visceral adipose tissue (VAT) compartment and liver. Previous metabolomic studies have shown that circulating levels of the amino acid glutamate were significantly associated with visceral fat accumulation. In this study, we aimed to determine the association between circulating glutamate and the pattern of adipocyte growth (hypertrophy vs hyperplasia).

Methods: We studied a sample of 149 non-diabetic bariatric surgery patients. The mean size of visceral and subcutaneous adipocytes was measured histologically. Targeted metabolomic was used to measure plasma levels of glutamate and other amino acids. Liver surgical biopsy samples were characterized by trained pathologists. We computed the linear regression between body mass index (BMI) and visceral adipocyte size to identify participants with VAT adipocytes larger than expected according to their BMI (hypertrophic, n=80) and those with smaller adipocytes than expected (hyperplastic, n=69). We compared cardiometabolic variables, circulating amino acids levels and liver pathology report variables between groups.

Results: Mean (\pm SD) age of the sample was 37.6 \pm 8.9 years, mean BMI was 48.7 \pm 7.6 kg/m² and 75% of participants were females. Individuals with hypertrophic visceral adipocytes had a larger waist circumference (p = 0.01), higher HOMA-IR index (p = 2.6E-05), higher triglyceride (p = 0.05) and lower HDL-cholesterol (p = 0.01) concentrations compared to the hyperplastic group. In terms of circulating amino acids, hypertrophic patients had significantly higher levels of glutamate (p = 0.0002) and cysteine (p = 0.01) as well as lower levels of asparagine (p = 0.03). Finally, hypertrophic participants had a greater prevalence of liver steatosis (p = 0.04) and non-alcoholic steatohepatitis (NASH, p = 0.01) than hyperplastic patients.

Conclusions: The higher levels of glutamate in individuals presenting larger-than-predicted visceral adipocytes confirm previously reported observations of a positive association between this metabolite and VAT accumulation.

P-05

Association of epigenetic aging acceleration with obesity phenotypes in blood and saliva of offspring born before versus after maternal bariatric surgery

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Background: The rise in obesity rates worldwide is prompting an increase in bariatric surgery for body weight management and reduction of adiposity excess. These procedures are expanding also in women of childbearing age and have effects on the metabolic homeostasis of mothers and children. Likewise, the growing adiposity phenotypes have an impact on metabolic and biological aging. In this respect, the use of epigenetic clocks allows the prediction of the biological age of individuals. The aim of this study was to compare the acceleration of biological age in children born before versus after the maternal bariatric surgery.

Methods: Children born from mothers with severe obesity undergoing bariatric surgery and after the mothers' bariatric surgery participated in the present study (n = 27). Blood and saliva samples were collected to measure methylation levels. Methylation age (MethAge) and telomere length (TL) were estimated using the MethylationEPIC BeadChip array. Estimated mean acceleration values for MethAge and TL were computed using linear mixed model regression analysis with random effects for family.

Results: A significant decrease of MethAge acceleration (p = 0.03) and an increment on TL estimates (p = 0.04) were observed in blood samples from children born after versus before the maternal bariatric surgery. A reduction of MethAge acceleration in blood of children born after the bariatric surgery was significantly associated with body mass index (-1.74, p < 0.001), waist-to-height ratio (-1.46, p = 0.02), conicity index (-1.13, p = 0.03) and body fat percentage (-1.24, p = 0.04). Likewise, a significant association between TL estimates and waist-to height ratio was observed in both blood (1.13, p = 0.03) and body fat percentage in saliva (0.18, p = 0.05).

Conclusions: These results suggest that maternal bariatric surgery may have a potential impact on age-associated methylation profiles and with the development of chronic metabolic diseases in the offspring.

P-06

Weight loss surgery induced changes in adipose tissue expression and methylation profiles of clock genes

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Background: The circadian clock is a set of genes that controls daily biological rhythms and is associated with metabolic health. This molecular clock is sensitive to light and dark cycles, and to other factors such as changes in body weight. Significant weight loss is achieved as a result of bariatric surgery. Examining the molecular profiles of clock genes following bariatric surgery may help in unveiling their impact on the remission of obesity-associated comorbidities.

Methods: A total of 21 participants with severe obesity undergoing biliopancreatic diversion with duodenal switch (BPD-DS, n=7), Roux-en-Y gastric bypass or sleeve gastrectomy (RYGB+SG, n=14) were included in the study. Gene expression and methylation levels of 13 clock genes (*ARNTL*, *CIART*, *CLOCK*, *CRY1*, *CRY2*, *DBP*, *NPAS2*, *NR1D1*, *NR1D2*, *PER1*, *PER2*, *PER3*, *TEF*) were measured in whole subcutaneous adipose tissue biopsy samples obtained during the surgery and 12 months later in the morning hours. Body weight loss, as well as type 2 diabetes and dyslipidemia remission rates were measured 12 months after the intervention.

Results: Participants undergoing BPD-DS showed greater body weight loss than those in the RYGB+SG group (41.7 ± 4.6 vs $28.2 \pm 6.8\%$; $p = 5 \times 10^{-5}$), and were also more prone to achieve both type 2 diabetes and dyslipidemia remission (OR = 0.75; 95%CI = 0.51-0.91; $p = 0.03$). A total of 6 genes (*NR1D1*, *CIART*, *DBP*, *NR1D2*, *PER3*, *TEF*) were found to be significantly upregulated 12 months after BPD-DS surgery, from which *NR1D1* and *CIART* were also upregulated after RYGB+SG. From these, *NR1D1*, *NR1D2*, *PER3* and *TEF* were also significantly hypomethylated. The change in *PER3* expression levels correlated positively with the percentage of body weight loss ($r = 0.53$, $p = 5 \times 10^{-3}$), and was associated with a combined type 2 diabetes and dyslipidemia remission rate (OR = 1.23; 95%CI = 1.01-1.51; $p = 0.04$).

Conclusions: These findings suggest that bariatric surgery induces significant changes in both adipose tissue expression and methylation profiles of clock genes. These changes are mainly observed after BPD-DS and possibly attributable to a more pronounced weight loss. A potentially relevant role of *PER3* in metabolic recovery merits further investigation.

P-07

Genetic Risk Score as predictor of changes in serum lipid traits and body fat in healthy Brazilian young adults

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Background: Lipid profile disturbances and unhealthy body fat distribution and percentage are risk factors for cardiometabolic diseases. This risk factors closely linked to a complex interplay between genetic and dietary factors. In this context, nutrigenetics approach is being used to study the influence of single nucleotide polymorphisms (SNPs) on the circulating lipids in response to foods, nutrients or bioactive food compounds intake. The aim of this study was to assess the interaction between lipid genetic risk score (L-GRS) on circulant lipids profile as well L-GRS interactions with dietary factors on lipidic and body composition traits.

Methods: We used data collected from the Brazilian Obesity, Lifestyle and Diabetes study (BOLD) performed with healthy young adults (n = 200; 19–24 years). Blood samples were collected for lipids profile analysis and DNA genotyping. An unweighted L-GRS was calculated according to the number of lipids-associated risk alleles from eight SNPs on *SCARB1*, *APOB*, *LIPC*, *LDLR* and *FABP2* genes. The Generalized Linear Model (GzLM) adjusted by age, sex, and physical activity level was performed to test the associations.

Results: There was association between L-GRS and LDL cholesterol ($p = 0.01$), non-HDL cholesterol ($p = 0.01$), ApoB ($p = 0.04$), Castelli indexes I and II ($p = 0.02$ and $p = 0.01$), and total body fat mass % ($p = 0.04$), with these traits values being higher in the group with L-GRS ≥ 6 than in the group with L-GRS < 6 . There were no interactions ($p > 0.05$) between the L-GRS with dietary intake on lipids traits or on body fat distribution.

Conclusions: The findings from the current study suggest that the calculated L-GRS can be a predictor of higher serum levels of LDL-cholesterol, N-HDL-cholesterol, ApoB, Castelli I and II indexes and higher total body fat mass %. However, there was no interaction of L-GRS with dietary intake.

P-08**Gene-diet interactions and obesity outcomes:
A systematic review of observational studies**H.Y. Han^a, G. Masip^{a,b}, T. Meng^a, D.E. Nielsen^a^aSchool of Human Nutrition, McGill University, Sainte-Anne-de-Bellevue, Canada; ^bInstitute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland

Background: Genetic susceptibility to obesity has been characterized through the development of polygenic risk scores (PRS), and growing evidence suggests interactions between diet and PRS on obesity outcomes. This systematic review summarizes the available evidence on PRS-diet interactions in obesity outcomes.

Methods: MEDLINE, EMBASE, Web of Science, and Cochrane Library were systematically searched until 1st April, 2022 (PROSPERO CRD: 42022312289). MESH terms and keywords related to obesity, PRS, dietary patterns, food/beverages, and nutrient intakes were used in the search strategy. Inclusion criteria for article screening included studies that were 1) observational in design; 2) reported obesity-related outcome(s) (anthropometry); 3) included dietary exposure(s); 4) evaluated an obesity PRS; 5) assessed PRS and diet interaction.

Results: Of 5,966 identified records, 4,251 remained after de-duplication, 97 were eligible for full-text screening, and 40 articles were included in the review. Eight of 13 studies (61%) that investigated dietary patterns reported that higher diet quality attenuated associations between a PRS and anthropometric outcomes. Fourteen of 19 studies (73%) that assessed food/beverage consumption reported significant interactions. Higher intake of fruit and/or vegetables, and lower intake of fried foods and soft drinks, attenuated associations between a PRS and anthropometric outcomes. Findings for alcohol-PRS interactions were mixed in terms of significance and directionality. Sixteen of 22 studies (73%) that assessed macro- and micronutrient intakes reported significant interactions, with the most consistent observations that lower total fat/fatty acid intake attenuated associations between a PRS and anthropometric outcomes. Most studies were conducted among samples of European ancestry.

Conclusions: The majority of studies conducted to date report significant interactions between diet and polygenic risk of obesity on obesity outcomes, with food/beverage and macronutrient intakes having the most consistent evidence. Greater effort is needed to assess the replicability of gene-diet interactions and obesity among different ethnicities.

P-09**MTNR1B rs10830963 interacts with dietary fiber to influence glucose and insulin-related traits in Brazilian young adults**N.T. Cruvine^a, A.C.S. Lima^a, A.C.S. Duarte^a, C.S. Seguro^a, N.R. Silva^a, K.S. Vimalaswaran^b, M.A. Horst^a^aNutritional Genomics Research Group, Faculty of Nutrition, Federal University of Goiás, Goiânia, Goiás, Brazil; ^bHugh Sinclair Unit of Human Nutrition, Department of Food and Nutritional Sciences, University of Reading, Reading, UK

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic and progressive disease with is closely related to lifestyle, especially diet. Single Nucleotide Polymorphisms (SNP) in genes related to glycemic metabolism, such as *MTNR1B*, appear to be associated with an increased risk of developing T2MD. In this context, nutrigenetics studies have been performed to investigate the effect of SNP in response to the intake of foods, nutrients or bioactive food compounds, on the pathways enrolled in glycemic metabolism. Therefore, the aim of this study was to verify whether the SNP *MTNR1B*-SNP (rs10830963) interacts with dietary intake, and glucose and insulin-related traits.

Methods: data were obtained from Brazilian Obesity, Lifestyle and Diabetes study (BOLD) performed with healthy young adults (n=200; 19–24 years). We collected blood samples to analyse serum levels of glucose and insulin-related traits and DNA genotyping. Food intake was assessed by trained nutritionists using non-consecutive 3-day food records. To test the associations, we performed multiple linear regression with backward strategy, in a dominant model.

Results: G allele for *MTNR1B* rs10830963 was associated with higher serum levels of insulin (B = 1.57; p = 0.002), insulin/glucose ratio (B = 0.02; p = 0.003), HOMA-B (B = 0.35; p = 0.003), and HOMA-IR (B = 22.8; p=0.01), but not with fast glucose and glycated hemoglobin. In carriers of the G risk allele, insulin values and insulin/glucose ratio were inversely associated (B = -0.2; B = 0.05; p = 0.01, respectively), and HOMA-IR was directly (B = 0.002; p = 0.01) associated with dietary fiber intake, but not with carbohydrates, lipids, proteins or energy intake.

Conclusions: The findings from the present study suggest that the presence of the G allele for *MTNR1B* rs10830963 can predict higher serum levels of insulin, insulin/glucose ratio, HOMA-B, and HOMA-IR. The dietary fiber can influence the glycemic metabolism in G carriers when compared with CC carriers. Large intervention and follow-up studies with an objective assessment of dietary factors are needed to confirm our findings.

P-10

TAS2R38 haplotype is associated with serum HDL-cholesterol in the Canadian Longitudinal Study of Aging

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Background: TAS2R38 is the most widely studied bitter taste gene. Variation in a common TAS2R38 haplotype has been associated with bitter taste sensitivity, consumption of bitter tasting foods, and risk factors for chronic disease. The objective of this present investigation was to determine whether a common TAS2R38 haplotype is associated with risk factors for chronic diseases in the Canadian Longitudinal Study on Aging (CLSA).

Methods: Genetic (rs1726866 and rs10246939), anthropometric, and sociodemographic data were obtained from the CLSA, a large-scale representative cohort comprised of middle- and older-aged men and women (n = 26,090). The primary outcome measure was visceral adiposity index (VAI), a sex-specific measure of metabolic health comprised of waist circumference, body mass index, serum triglycerides, and HDL-cholesterol. The individual components of VAI were assessed as secondary outcomes. Participants with TAS2R38 rare haplotypes, being pregnant or missing data for individual components of VAI were excluded. A TAS2R38 common haplotype was categorized into AV/AV (conventionally recognized as supertasters) (n = 5,655), AV/VI (tasters) (n = 12,821) and VI/VI (non-tasters) (n = 7,614). Generalized linear models adjusted for sex, age, recruitment province, the first five principal components of ancestry, income, education, smoking status, marital status, and physical activity level were used to assess associations between TAS2R38 haplotype and the outcome variables. VAI is a sex-specific measure, therefore, all analyses were stratified by sex.

Results: VAI values were highest among supertasters, but no significant associations were observed between TAS2R38 haplotype (supertasters, tasters, and non-tasters, respectively) and VAI (males (mean±standard deviation): 4.42±8.95, 4.28±14.38, 4.37±10.37; p = 0.85; females: 4.15±8.26, 3.86±13.31, 3.89±9.40; p = 0.14). Among the individual components of VAI, HDL-cholesterol (mmol/L) was significantly different between haplotype group (supertasters, tasters, and non-tasters, respectively), with supertasters having the lowest HDL level (mean±standard deviation: 1.44±0.75, 1.45±0.90, 1.45±0.54; p = 0.04). No significant differences were observed for the other components of VAI.

Conclusions: TAS2R38 haplotype was not significantly associated with VAI in the CLSA, but was associated with serum HDL-cholesterol level.

P-11

Agavins from *Agave tequilana* Weber var. azul induce a bifidogenic effect on overweight subjects

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Background: Although agavins from *Agave tequilana* spp. and cranberry polyphenols are recognized to have prebiotic effects, their impact on human metabolic health and the microbial species linked to their consumption remain to be elucidated. The aim of this study was to identify the metabolic health effects and gut microbiota signatures after the intervention.

Methods: A double-blind, randomised, four-arm parallel group, controlled trial was undertaken in overweight adults (n=85). Participants were randomized into groups consuming either 5 g of agavins from *Agave tequilana* Weber var. azul, 120 mg of cranberry polyphenols, a combination of both prebiotics or maltodextrin as placebo for 10 weeks. Clinical and metabolic data from participants was collected before and after the intervention, as well as fecal samples, which were subjected to DNA extraction and microbial 16S sequencing (Illumina). Linear mixed models were used to compare clinical and metabolic parameters among groups. Metagenomic data was used to classify participants upon their assigned group by partial least-squares discriminant analysis (sPLS-DA).

Results: Although we did not observe significant changes in metabolic parameters among study groups, sPLS-DA results allowed to identify distinct gut microbiota signatures following the Intervention. The classification of participants in the agavins group showed the highest accuracy of 0.70, with *Bifidobacterium longum* being the microbial species more strongly associated to agavins consumption. The combination of two prebiotics slightly decreased the accuracy of classification to 0.64 and was also mostly associated with an increase in *B. longum* along with *B. adolescentis*. Finally, with the lowest accuracy rate of 0.50, the classification of cranberry polyphenols was mainly driven by changes in the abundance of *Oscillibacter* spp. and *Ruminococcus lactaris*.

Conclusions: The impact of agavins or cranberry polyphenols on metabolic health could not be brought to light in the present study. However, exploratory metagenomic analyses suggest a stronger impact of agavins on gut microbiota, possibly linked to a bifidogenic effect.

P-12

Pregestational consumption of cafeteria diet induces serum fatty acid changes mediated by gut microbiota in adult male offspring

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Background: Maternal diet can modulate gut microbiota in offspring due to intrauterine environment. Moreover, shifts in gut microbiota play a role in the development of obesity by changes in the host-microbiome lipid co-metabolism. Therefore, this study aimed to examine the influence of a maternal cafeteria diet during pregestational period on gut microbiota and its correlation with serum fatty acid profiles in adult male offspring.

Methods: Ten male pups from dams fed standard diet (C-C, n = 5) or cafeteria diet (Caf-C, n = 5) during pregestational period, were fed standard diet after weaning, and body weight was recorded once a week for 26 weeks. Fresh fecal samples were collected, and gut microbiota was analyzed by sequencing the V3-V4 region of 16S rRNA gene. At the end of the study, serum samples were obtained to analyze glucose levels and fatty acid profiles.

Results: *Firmicutes/Bacteroidetes* index and, at the class level, the relative abundance of *Elusimicrobia* and *Alphaproteobacteria*, were increased in the Caf-C group ($p < 0.05$). Likewise, serum glucose, caprylic (C8:0) and myristic (C14:0) acids levels were increased in pups from dams fed cafeteria diet ($p < 0.05$). Conversely, serum lignoceric acid (C24:0) levels were decreased in the Caf-C group ($p < 0.05$). Of note, the relative abundance of *Elusimicrobia* was negatively correlated with serum lignoceric acid (C24:0) levels. In contrast, serum glucose and caprylic acid (C8:0) levels were positively correlated with *Firmicutes/Bacteroidetes* index.

Conclusions: These results suggest that maternal pregestational consumption of cafeteria diet influenced serum fatty acid profiles through shifts in gut microbiota in adult male offspring rats. Our results indicate the impact of the maternal diet on offspring metabolism in later adulthood. More studies need to be done to understand the metabolism of these gut bacterial species and the involvement of these metabolites in health and disease.

P-13

Dietary intake associated with the TCF7L2 rs7903146 polymorphism in Mexican obese scholar-age children

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Background: Studies in adults have associated TCF7L2 rs7903146 polymorphism (SNP) with the risk of obesity, dietary intake (DI), metabolic syndrome, and type 2 diabetes. There is a lack of information on these interactions in children. This study identifies the association between DI and TCF7L2 rs7903146 polymorphism (SNP) in obese children.

Methods: This is a transversal and correlational study ($n = 257$ children; 128 girls and 119 boys) aged 6 to 12 years. Data were collected from the UANL Childhood Obesity Program. Anthropometric measurements were obtained with internationally standardized techniques. The homeostasis model assessment insulin resistance (HOMA-IR) index was calculated (Mathews, 1985). DI (energy and macronutrients) was evaluated by food frequency and 24-hours recall questionnaires using the Food Processor Nutrition Analysis ESHA Research 10.12.0[®]. Genotyping of TCF7L2 rs7903146 SNP was performed by TaqMan[®] OpenArray[™] Genotyping System[®]. Schoolchildren were classified by BMI Z-score (OMS, 2007) and rs7903146 SNP genotype frequencies (CC, CT, TT), as well as non-/low consumers or moderate/high consumers by food type to analyze the gene-diet interaction.

Results: 122 (47.5%) school-age children were obese. The genotype frequency of CC, CT, and TT of rs7903146 SNP was 0.63, 0.32, and 0.05, respectively. 70% of TT carriers (genotype risk) had obesity and a higher HOMA-IR; There was no association between macronutrient intakes and genotypes in obese and normal-weight children. Multinomial logistic regression model adjusted for age, BMI and sex showed a significant association between non/low milk consumers with TT genotype (OR=4.855[1.412-16.691], $p = 0.012$) and non/low cream consumers with CT genotype (OR = 3.84[1.109-13.347], $p = 0.034$).

Conclusions: T allele of TCF7L2 rs7903146 SNP is associated with a significantly higher risk of obesity and HOMA-IR in our study population. Further research is required to determine interactions between DI with TT genotype and if a specific nutritional treatment can attenuate the genetic predisposition to childhood obesity.

P-14**The impact of a maternal cafeteria diet on nutritional status and gut microbiota in male offspring**

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Background: Maternal overnutrition during pregnancy and lactation can lead to defects in the offspring's metabolic profile and microbiota changes. Maternal programming involves new peripheral and central pathways, including energy expenditure and inflammatory response. Diet is a critical determinant of gut microbiota diversity. An unhealthy maternal diet affects offspring gut health, with common species identified in mother and offspring microbial communities.

Methods: Female C57BL/6 mice were randomized into two dietary groups: standard control chow diet (control) and cafeteria diet. The animals were exposed to this diet for nine weeks, including pre-gestation (before and during mating), gestation, and lactation. Male offspring were culled to 10 pups per dietary group and housed in cages after weaning at lactation day 21, then were exposed to a control diet until eight weeks of age. Weight gain and food intake were registered weekly. At week 8, fecal samples were collected for gut microbiota analysis.

Results: The cafeteria offspring showed significantly lower body weight than the control group at weeks 4 to 8 ($p < 0.01$). Regarding the food intake, the cafeteria group presented significantly less intake at weeks 3 to 8 than the control group ($p < 0.01$) (Mann-Whitney U test). In addition, found no significant difference between the control and cafeteria groups concerning bacterial diversity (alpha diversity; Shannon index).

Conclusions: Maternal cafeteria diet offspring had less weight and food intake than the control group. This diet high in fat tends to be low in protein, a fundamental nutrient for lowering the risk of restriction in intrauterine growth. A cafeteria diet also contains low-key micronutrients needed for fetal growth. Otherwise, maternal exposure to a cafeteria diet does not lead to changes in alpha diversity; some effects at the bacterial species level could be generated.

P-15**A *Berberis microphylla* (Calafate) extract prevents obesity, promotes thermogenesis and modulates the production of short-chain fatty acids in mice fed on a high-fat**

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Background: Foods rich in polyphenols can promote thermogenesis and modulate both gut microbiota (GM) and production of short-chain fatty acids (SCFAs). We aim to evaluate the effect of a polyphenol-rich *Berberis microphylla* (Calafate) extract in obese mice.

Methods: 8-week old C57BL6 mice were divided ($n = 10$ each) in 4 treatments for 4 months: Control diet (C), Control diet/Calafate (CC), High fat diet (HF), and High fat diet/Calafate (HFC). CC and HFC were treated with 50 mg total polyphenols/kg weight/day of Calafate extract. At month 4, animals were euthanized and final body weight were recorded. Samples of interscapular brown (BAT), epididymal white (eWAT) and inguinal white (iWAT) adipose tissues were obtained. Expression of thermogenic markers (ucp-1, pgc1 α , sirt1, prdm16, ppara/ γ , dio2) on BAT and iWAT were analyzed. In cecal content was analyzed GM by mass sequencing and SCFAs by gas chromatography–mass spectrometry. α -diversity of GM was calculated using Shannon index and β -diversity using PCA analysis. Two and one-way ANOVA, and Tukey post-hoc was used.

Results: HF presented higher body weight than HFC mice. BAT ucp-1, pgc1 α , ppara and sirt1 expression were higher in HFC than HF. iWAT expression of PGC1 α , PPAR α , PRDM16, SIRT1, and DIO2 were also increased. No significant differences were observed in α -diversity. PCA analysis showed that the differences in GM composition between the groups (β -diversity) was given by diet and not by Calafate treatment. Regarding SCFAs, HF presented a lower total amount of SCFAs and SCFAs from fiber fermentation (acetic acid, propionic acid, butyric acid) than C, CC and HFC. Beside, Calafate treatment favored higher production of total SCFAs and SCFAs from fiber fermentation in HFC.

Conclusions: a polyphenol-rich Calafate extract decrease body weight, promote expression of thermogenic genes and increase of total SCFAs and SCFAs from fiber fermentation in obese mice.

P-16**The decrease in risk of hypertriglyceridemia mediated by the intake of alpha-linolenic acid is associated with the rs3812316 polymorphism of the *MLXIPL* gene**

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Background: The *MLXIPL* gene codes for the protein that binds the consensus sequence of the carbohydrate response element named ChREBP. This transcriptional factor is activated in response to a high-carbohydrate diet; therefore it is key to understand the gene-nutrient interaction that leads to metabolic diseases.

Methods: The present study analyze the interaction of the SNPs (single nucleotide polymorphisms) rs3812316 and rs17145750 in the *MLXIPL* gene with the dietary, anthropometric, and biochemical parameters in a cross-sectional study in 587 Mexican Mestizo subjects without chronic non-communicable diseases. We also analyzed the expression of the *MLXIPL* mRNA levels in liver and adipose tissues according to the SNP's genotypes, and finally, an *in-silico* test of the ChREBP protein stability and the allelic imbalance was also performed.

Results: The minor allelic frequency G of rs3812316 was associated with a lower risk of hypertriglyceridemia (OR = -0.070 ± 0.027, 95% CI = -0.124 to -0.016, $p < 0.011$) in women, a more unstable protein ($\Delta\Delta G = -0.83$ kcal/mol), and probably lower tissue mRNA levels. We found other independent factors that influence and determine triglyceride levels, such as insulin resistance and HDL-c in women ($p < 0.05$).

Conclusions: Our data suggest that fatty acid alpha-linolenic acid-rich diet would prevent the risk of hypertriglyceridemia associated with the rs3812316 SNP (1.97 ± 0.03 vs 2.11 ± 0.01 mg/dL, $p < 0.001$).

P-17**DHA and exercise synergistically counteract obesity-related gene expression alterations in visceral adipose tissue in mice**

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Background: Obesity is a chronic disease with a high worldwide incidence rate, in which metabolic and inflammation disruption of adipose tissue homeostasis plays a major role in their onset and progression¹. Therapeutic strategies based on omega-3 fatty acids supplementation and/or physical exercise could ameliorate obesity-related symptoms and counteract associated comorbidities. However, the direct impact of omega-3 docosahexaenoic acid (DHA) and exercise, separately or in combination, on adipose tissue has not been explored yet. The main objectives were to study the effects of DHA and/or exercise interventions in obese mice and evaluate the transcriptional response of key genes involved in inflammation and metabolism in visceral fat.

Methods: C57BL/6J female mice were fed a high fat diet for 4 months to induce obesity. Mice were distributed in five groups: normal-weight (control), obese (DIO), obese subjected to aerobic physical exercise (DIOEX), obese dietary supplemented with DHA (DIOMEG), and obese subjected to both exercise and DHA supplementation (DIOEGEX). After the interventions (18 months), the retroperitoneal fat depot was isolated, and gene expression was evaluated by RT-PCR.

Results: Both, DHA and exercise decreased the expression of the inflammation-related adipokine *Ccl2* and upregulated the expression of the anti-inflammatory cytokines *Il4* and *Il10*. These effects were potentiated by a simultaneous intervention with both DHA and exercise. In addition, DHA in combination with exercise modulated the expression of key metabolic genes of the FGF21 axis (*Fgf21*, *Fgfr1*, *bklotho*).

Conclusions: DHA and exercise elicit synergistic effects that can modulate the expression of adipose factors related to immune system response and metabolism. These effects could potentially reduce inflammation and stimulate adipose metabolism to prevent metabolic dysfunctions. Therapeutic strategies based on the combination of long-term DHA supplementation and physical exercise could be beneficial to alleviate metabolic and inflammatory alterations associated with obesity.

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P-18

Description of the microbiome fingerprint associated with obesity in a Spanish population

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Background: Gut microbiota plays a role in the homeostatic regulation of energy metabolism, so aberrations in its composition (dysbiosis) may be involved in the development of metabolic diseases, including obesity. Here, we investigate the specific microbiome fingerprint associated with obesity.

Methods: An obesity (OB) index was designed to classify a population of 361 Spanish individuals (Obekit trial: 65 normal-weight, 110 overweight and 186 obese subjects) in LOW or HIGH level of obesity, according to three variables: body mass index, fat mass and waist circumference. Sequencing of the V3-V4 region of the 16S rRNA gene from fecal samples was performed, and differential abundance for families, genera and species was analysed using ALDEx2 R package.

Results: Individuals with HIGH OB index exhibited a significant reduction in the families Coriobacteriaceae, Christensenellaceae, Bifidobacteriaceae and Ruminococcaceae, and in the genera *Anaerofilum*, *Anaerovibrio*, *Acetivibrio*, *Eggerthella* and *Gemmiger*. On the contrary, the species *Prevotella micans*, *Prevotella brevis* and *Parabacteroides helcogenes* were significantly more abundant in those individuals with HIGH OB index.

Conclusions: Our study suggests the involvement of gut microbiota dysbiosis in the onset and development of obesity and might help to develop nutritional precision strategies targeting microbiota against this metabolic disease.

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P-19

Relationship between single nucleotide polymorphisms in SULT1A1 and SULT1C4, and ABCC2 genes and excretion of phase II flavanone metabolites after orange juice intake

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Background: Citrus juices are source of dietary flavanones and the regular consumption of these compounds is inversely associated with the development of cardiometabolic diseases. However, the biological benefits depend on their bioavailability, and a high heterogeneity in citrus-flavanones bioavailability has been observed. Several factors such as age, diet, lifestyle, health status, and genetic background may affect the absorption, metabolism and excretion, contributing to the interindividual variation observed. Thus, this study aimed to assess the association between the single nucleotide polymorphism of sulfotransferases SULT1A1, and SULT1C4, and ABCC2 transporter genes and the excretion of phase II flavanone metabolites 24 hours urine after of orange juice intake.

Methods: In the present study four candidate single nucleotide polymorphisms (SNPs) in genes in SULT1A1(rs3760091, rs4788068), SULT1C4 (rs1402467), and ABCC2 (rs8187710) genes, involved in flavanone bioavailability were genotyped. Forty-six volunteers ingested a single dose of 500 mL of orange juice and 24-hour urine was collected. The flavanones hesperetin and naringenin phase II metabolites were quantified by LC-qToF-MS/MS in urine and volunteers were grouped in high, medium and low metabolites excretors.

Results: Using five genetic models (codominant, dominant, recessive, over dominant and log-additive), a significant association ($p < 0.05$) between SULT1A1(rs4788068) and SULT1C4_rs1402467 polymorphism and excretion of phase II flavanone metabolites in urine of volunteers after 24 h of orange juice intake was observed. The GGCC and GCTG haplotypes for ABCC2, SULT1A1, SULT1A1, and SULT1C4 was associated with high excretor phenotype.

Conclusions: These findings suggest that polymorphism on these genes can significantly affect absorption and excretion of citrus flavanones and explain the high and low excretors profiles of these metabolites. In addition, these results may provide bases for future personalized nutritional guideline to consume flavanone-rich foods.

P-20**Dietary supplementation with methyl donors improves pathophysiological and molecular conditions in a murine model of NAFLD**

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Background: Metabolic associated liver disease (MAFLD) is the most common cause of chronic liver damage worldwide. Differential methylation in genes and histones has been correlated with metabolic alterations present in MAFLD. Supplementation with methyl group donor molecules could work as a therapeutic strategy to reverse the progression of the disease.

Methods: Male mice of the C57BL/6J strain with an initial weight of 20–25g were fed with a conventional diet (ND n = 8); or a diet high in fat and sugar (HF n = 8) for 18 weeks; or a diet rich in fat and sugar for 10 weeks, plus 8 weeks of HF diet + supplementation with methyl group donors *ie*; methionine, betaine, choline, B12 and folate (HFMS n = 8). At 18 weeks, ITT was performed. At sacrifice, sample from liver, epididymal and visceral fat and serum was collected. Biochemical analysis was performed, as well as hepatic histological staining's and analysis. Global DNA methylation was quantified in liver. Transcriptome was analyzed using double-channel microarrays for mouse genome.

Results: The supplemented animals (HFMS) exhibited a decrease in body weight, liver weight and epididymal and visceral fat ($p < 0.001$). Adipocyte's area in HFMS group decreased significantly compared to HF group. HFMS group showed reduced serum levels of triglycerides and glucose and greater sensitivity to insulin activity. Histological analysis of livers from ND and HFMS animals showed no damage characteristic of NAFLD, such as, lipid infiltration and inflammation. Global-DNA methylation was increased in HFMS animals. Transcriptome analysis in HFMS group showed a decrease in mRNAs pathways associated with inflammation and liver disease and an increase in transcripts associated with lipid and cholesterol metabolism.

Conclusions: Supplementation with methyl donors has beneficial effects in a murine model of NAFLD, even in an obesogenic diet consumption.

P-21**Determinants of satiety sensation: Sex, fat-free mass, body fat percentage, and resting metabolic rate differentiate individuals with low or high satiety phenotype**

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Background: The satiety sensation is regulated by internal and external signals. Among the internal signal the adipose tissue secretes the hormone leptin that is involved in satiety. Contrary, ghrelin plays a fundamental role in hunger, the opposite to satiety. Genes of these hormones or their receptors including Leu72Met of *ghrelin* (*GHRL*) gene and Gln223Arg of *leptin receptor* (*LEPR*) gene, could have an effect on the regulation of this process. Besides, anthropometric variables such as fat free mass and basal metabolic rate, have been little discussed about their effect on satiety. The aim of this study was to know the variables that explain satiety sensation in normal weight subjects.

Methods: Quasi-experimental study design with 132 participants, BMI 18.5–24.9 kg/m², mean age 20.6 ± 1.9 years. Anthropometric measurements were done with the InBody 370. Ghrelin and leptin were determined by ELISA assay. Genotype analysis of the two single nucleotide variants were determined by allelic discrimination using TaqMan[®] probes. The subjective sensations of appetite were reported with visual analogue scales. The appetite score was calculated considering 4 appetite sensations, the higher the score, the higher the appetite. The satiety quotient was used to classify the subjects as low or high satiety quotient. Linear regression model and discriminant analysis were performed using the SPSS software (v.20.0).

Results: A multivariable regression model was built, to know which variables were predictors of the appetite score; but only the body fat percentage was associated with greater satiety. In the discriminant analysis, it was found that sex, fat-free mass, body fat percentage, and resting metabolic rate differentiate individuals with low or high satiety phenotype. Nevertheless, single nucleotide variants and appetite hormones did not have any effect on satiety sensation in this population.

Conclusions: Our findings suggest that sex, body composition and resting metabolic rate were the main determinants of satiety sensation and genetic variants were not involved.

P-22

The antiobesogenic effect of 10-gingerol is related to downregulation of *Fabp4* and *Acaca* expression

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Background: The progressive increase in obesity prevalence has generated the need to develop new therapeutic alternatives that can be used as complement in the treatment of obesity. Ginger and its components, gingerols, exert protective effects on obesity. 10-gingerol has shown greater anti-cancer, neuroprotective and antioxidant capacity compared to other gingerols present in ginger. However, 10-gingerol effect on adipose tissue has been scarcely explored. Therefore, the aim of this study was to investigate the antiobesogenic effect of 10-gingerol and its proadipogenic gene expression regulation in 3T3-L1 cell line.

Methods: *In vitro* experimental study in the 3T3-L1 preadipocyte cell line. Four study groups were formed: negative control (preadipocytes), positive control (adipocytes), gingerol-pre (preadipocytes stimulated with 15 mg/mL of 10-gingerol during adipogenic differentiation), and gingerol-post (adipocytes stimulated with 15 mg/mL of 10-gingerol). Cell viability was determined by MTT assay. The percentage of lipid content in adipocytes was estimated by Oil Red O staining. The expression of proadipogenic genes was determined by real-time PCR and with the $2^{-\Delta\Delta Ct}$ method. Data were analyzed with the SPSS v25 program; $p < 0.05$ was considered as statistically significant.

Results: In the gingerol-pre group, the lipid content decreased 28.17% versus the positive control group ($p < 0.001$). Similarly, in the gingerol-post group, the lipid content decreased 47.25% versus the positive control group ($p < 0.001$). No significant differences in cell viability were observed between the groups ($p = 0.177$). Regarding gene expression, 10-gingerol significantly decreased *Acaca* levels ($p < 0.001$) in the gingerol-pre group. In the gingerol-post group, *Fabp4* and *Acaca* genes were significantly downregulated ($p < 0.05$), while *C/Ebpa* and *Fasn* genes increased their expression levels ($p < 0.001$).

Conclusions: 10-gingerol suppresses lipid droplet accumulation and decreases *Acaca* and *Fabp4* levels in 3T3-L1 cells. It suggests the antiobesogenic effect of 10-gingerol could be oriented towards the decrease in the levels and activity of key lipogenic enzymes, as well as fatty acid transport proteins.

P-23

Dietary supplementation with Mexican foods, *Optuna ficus indica*, *Theobroma cacao* and *Acheta domesticus* improves gut-liver axis in high fat/sucrose/fructose diet-fed mice

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Background: Metabolic associated fatty liver disease (MAFLD) is the most common liver disease worldwide. Excessive caloric intake from fats and sugar is the major risk factor for MAFLD's development. The aim of the study was to evaluate the effect of HF-diet supplementation with a mixture of Mexican functional foods (MexMix): Nopal (*Optuna ficus indica*), *Theobroma cacao* and edible crickets (*Acheta domesticus*) on the gut-liver axis in a MAFLD mice model.

Methods: Twenty-four male C57BL/6J mice were divided into three groups: 1) control group: Normal diet. 2) HF Group: High-fat diet (45%) and *ad libitum* fructose-sucrose water and 3) therapeutic group (MexTHER): HF-diet up to week teen and switched for 8 additional weeks to HF-diet supplemented with 6.7% nopal, 8.7% cocoa and 8.7% cricket. The animals were sacrificed at week 18th. Histological and molecular analysis were performed in liver tissue and biochemical tests in serum.

Results: Mice treated with MexMix-supplemented diet showed body weight, visceral fat, and epididymal fat decrease compared to HF animals. Serum levels of triglycerides, insulin, leptin and PAI-1 were also clearly reduced, while adiponectin was significantly increased. MexMix diet improved intestinal health, seen as, augmented short fatty acids (SFCs) production and increased crypt depth and reduced mucosal inflammatory infiltrate. In liver, MexMix diet significantly reduced steatosis. Hepatic transcriptome analysis showed differential gene expression in MexTHER group compared to HF animals. Down-regulated genes were mainly involved in inflammatory pathways, and up-regulated genes were implicated in fatty acid transport and oxidation, and antioxidant activity. Using real time qPCR, we confirmed increased expression of *Cat*, *Sod* and decreased expression of *Tnfa* and *Pparg*. Also, MexMix diet down-regulated hepatic miRNA-34a associated to triglyceride accumulation and progression of MAFLD.

Conclusion: MexMix food supplementation is a potential strategy for the treatment of MAFLD and other diseases associated to excessive consumption of fat and sugars.

P-24**Polymorphism of rs3801387-WNT16 and rs7108738-SOX6 genes are associated with osteopenia/osteoporosis in women postmenopausal from Northern Mexico**

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Background: The osteopenia/osteoporosis (OPE / OP) phenotype is a condition characterized by low bone mineral density (BMD) that results in the microarchitectural risk of bone. It is estimated that to 2050, 1 in 12 postmenopausal Mexican women will present osteoporosis, increasing the risk of fracture and consequently morbidity and mortality. Variations in BMD are attributed to environmental and genetic factors (50 to 80%). Single nucleotide polymorphisms (SNPs) rs3801387 of the WNT16 gene and rs7108738 of the SOX6 gene have been associated with decreased BMD in hip and spine regions in Asian and European women. The aim in this study was to analyze the association of these polymorphisms in postmenopausal women with OPE / OP de Monterrey, N.L.

Methods: 256 MPP underwent dual X-ray absorptiometry (DXA) to determine BMD in dual of femur (DMOdf). DNA Genotyping was performed by Real-Time PCR using TaqMan probes. The data obtained was analyzed using simple linear regression, odds ratio and chi square.

Results: The median BMDdf for the BMD group without OPE/OP was 1.000 g/cm² and for the OPE/OP group it was 0.820 g/cm². The minor allele of frequencies (MAF) for rs3801387 was G (25.0%) for the OPE/OP group. The rs7108738 of the SOX6 gene the MAF in the OPE/OP group was 22.0%. Significant associations were found with the dual regions of the femur, Wards triangle and column.

Conclusion: The single nucleotide polymorphisms that were analyzed may be markers of low BMD, but not of an increased risk of OPE / OP by having these risk alleles. The association of polymorphisms rs3801387 of the WNT16 gene and rs7108738 of the SOX6 gene in MPP from Northern Mexico should continue to be investigated.

P-25**Effect of the genetic variants rs5275 and rs689466 of PTGS2 on inflammatory markers in obese subjects treated with a dietary plan supplemented with omega-3 fatty acids**

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Background: Obesity is linked to multiple pathologies among which low-grade chronic inflammation is considered a hallmark. It has been reported that omega-3 fatty acids exert a key role on inflammatory processes. In this regard, PTGS2 is an enzyme that synthesizes major lipid mediators. Some genetic variants of the PTGS2 gene such as -1195 G>A (rs689466) and 8,473 T>C (rs5275) are associated with chronic diseases; however, these have not been investigated in the field of obesity. The aim of this study was to evaluate the effect of these genetic variants on the inflammatory profile of obese subjects treated with a dietary plan supplemented with omega-3 fatty acids.

Methods: 52 obese subjects were enrolled in a clinical trial for a 12-week dietary intervention including 1.8 g/d of omega-3 fatty acids as supplementation or placebo. Anthropometric and biochemical variables were assessed as well as serum hs-CRP (Getein1100) and IL-10 (ProQuantum Immunoassay Thermofisher). Genotyping was performed through allelic discrimination using TaqMan probes. Statistical analysis was evaluated with SPSS V.20 using the Hardy-Weinberg equation and the Mann Whitney U test. Statistical significance was set at $p < 0.05$.

Results: Both groups Omega-3 (n = 25) and Placebo (n = 27) displayed a significant reduction in anthropometric parameters and serum triglycerides. The genotype frequency of both variants was in Hardy-Weinberg equilibrium: rs5275 ($p = 0.520$) and rs689466 ($p = 0.753$). We found no significant differences between both groups in hs-CRP and IL-10. Notwithstanding homozygous TT (rs5275) and AA subjects (rs689466) displayed higher serum levels of IL-10 ($p = 0.034$ and $p = 0.028$) in the Omega-3 group compared to Placebo group.

Conclusions: Homozygous subjects, TT (rs5275) and AA (rs689466), might obtain higher health benefits through the consumption of 1.8 g/d of omega-3 fatty acids alongside with a dietary plan. Further *in silico* and *in vitro* studies are required to evaluate a mechanistic connection between these genetic variants and serum IL-10.

P-26**Assessment of GPR120 activation through immunoprecipitation in peripheral blood mononuclear cells in healthy subjects after acute and chronic consumption of omega-3 fatty acids: A comparison of different protein extraction protocols**

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Background: GPR120 is a receptor that mediates remarkable anti-inflammatory actions of omega-3 fatty acids. It is expressed in adipocytes, macrophages, and monocytes. Previous research has assessed the activation of GPR120 on *in vivo* models. Notwithstanding, the activation of this receptor is poorly understood in peripheral blood mononuclear cells (PBMCs) as a non-invasive approach. Remarkably, cell-lysis buffers for protein extraction gain special relevance for down-stream procedures such as Immunoprecipitation (IP) and Western Blot (WB). Thus, the aim of this study was to evaluate the activation of GPR120 in PBMCs of individuals consuming omega-3 fatty acids from three different protein extraction protocols.

Methods: A total of 10 subjects were enrolled in this study. Five individuals had a chronic supplementation of omega-3 fatty acids (2 g/d for at least 30 days) and the rest of the subjects had no previous supplementation, but they were given 5 g the night prior evaluation. Then, blood was collected after an 8-12 hour fasting period and PBMCs were isolated using a density gradient medium. After cell isolation, a total of 5-7x10⁶ cells were lysed using three different reagents: TRIzol, RIPA, and modified RIPA. Following, IP of Beta-arrestin protein was performed using SureBeads (Biorad); afterwards GPR120 was identified through a standard WB technique.

Results: Among the three cell-lysis methodologies, GPR120 was found to be present in samples of individuals with both chronic and acute consumption. There were no significant differences between the RIPA and modified RIPA buffers. However, the extracted proteins with the TRIzol method did not display any presence of GPR120.

Conclusions: The activation of GPR120 can be assessed in PBMCs of individuals with chronic and acute exposure to Omega-3 fatty acids supplementation through RIPA buffer lysis with or without modification, but not when using TRIzol as protein extraction reagent.

P-27**Plasma levels of adipocytokines are associated with targeted lipidomic profile in Mexican pediatric patients with type 2 diabetes mellitus and metabolic syndrome**

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Background: Chronic plasma fatty acid (PFA) profiles are modulated by nutrition, metabolism and have been associated with low-grade inflammation. The decrease in fat oxidation in muscle and liver prompts insulin resistance (IR) and impairs glucose uptake, which results in type-2 diabetes mellitus (T2DM) and metabolic syndrome (MetS). T2DM and MetS incidence is impacting the pediatric population. Therefore, this study aimed to determine the association between plasma levels of adipocytokines and fatty acid profiles in Mexican pediatric patients with T2DM and MetS.

Methods: Cross-sectional comparative study with sixty patients aged 7-17 years divided into three groups: healthy control (HC, n = 21), T2DM (n = 20), and MetS (n = 19). Anthropometric, biochemical, and clinical data were determined. PFAs were fractionated and quantified by gas chromatography and adipocytokines by flow cytometry.

Results: HC group had significantly lower BMI (p<0.001), central obesity markers (WC%, W/ht) (p<0.001), and HOMA-IR (p<0.001) compared to T2DM and MetS groups. Saturated fatty acids (SFA) plasma levels, including PL-octanoic acid (C8:0) and PL-heptadecanoic acid (C17:0), were associated with HOMA-IR. Furthermore, plasma levels of MCP-1 and IL-8 were higher in T2DM group (p<0.05), while IL-18 levels were increased in both MetS (p<0.05) and T2DM (p<0.001) groups. IL-18 levels were positively associated with PL-palmitic acid (C16:0). Total omega-3 PFA levels were significantly different (p<0.001) between the three groups (HC>T2DM>MetS).

Conclusions: In this study, HOMA-IR was associated with PL-C8:0 and PL-C17:0, which are not routinely monitored in most PFA profiles. PL-C16:0 was confirmed as a lipotoxicity biomarker related to inflammatory state (IL-18) in T2DM and MetS groups with IR. Chronic inflammation and IR were evident in metabolically unhealthy patients (T2DM and MetS). However, omega-3 PFAs profiles were significantly higher in the HC and T2DM groups, which characterizes healthier lipidomes. Although multiple factors can affect PFAs, MetS patients seem at risk of advancing their metabolic disorders because of the unknown diagnosis of their IR and inflammatory state.

P-28

Dietary intake of micronutrients by IL10 -592 C>A polymorphism genotypes in COVID-19 outpatients from Western Mexico

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Background: COVID-19 is the disease caused by the SARS-CoV-2 virus, which can cause systemic and mainly pulmonary affectations. Several factors can influence disease progression, including diet and genome (IL10 -592 C>A polymorphism). The aim of this study is to describe the dietary intake of micronutrients by IL10-592 C/A polymorphism genotypes in COVID-19 outpatients from Western Mexico.

Methods: Study group: COVID-19 outpatients who attended the rapid testing module of the University Center of Health Sciences of the University of Guadalajara and were diagnosed by antigen test (n = 243). Genotyping was performed by the PCR-RFLP technique and dietary intake was assessed by a 24-h recall to determine the percentage adequacy of micronutrient intake, using the software *nutritionist pro*.

Results: Variations were found in the percentages of insufficiency (< 90%), for carriers of the mutated genotypes (AA) the micronutrients Zinc (CC = 33 %; AA = 17.1 %), iron (CC = 72.3 %; AA = 65.7 %), calcium (CC = 59.6 %; AA = 51.4 %), riboflavin (CC = 8.5 %; AA = 5.7 %), vitamin D (CC = 75.5 %; AA = 71.4 %) and A (CC = 43.6 %; AA = 37.1 %), had lower percentages compared to carriers of the wild genotypes (CC), which showed lower insufficiency percentages of vitamin C (CC = 35.1 %; AA = 45.7 %) and K (CC = 66 %; AA = 71.4 %), while there are no relevant variations between the recessive and dominant models.

Conclusion: The intake of some micronutrients is lower than the recommended daily allowance in both wild and mutated genotypes, which alongside with the presence of the polymorphism could be associated with the intra-individual variation observed in the course of the disease.

P-29

TCF7L2 rs11196175 polymorphism associated to insulin resistance in mexican obese scholar-age children

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Background: Several studies have shown the importance of insulin resistance (IR) as the major factor for obesity and type 2 diabetes mellitus. Some genes, such as TCF7L2, have been associated with IR. There is a lack of information on Mexican children. The aim of the study was to identify the association between the TCF7L2 rs11196175 polymorphism (SNP) with IR, as early markers, in obese scholar-age children 6 to 12 years.

Methods: It is a descriptive, correlational, and cross-sectional study of 352 scholar-age children. Body mass index (BMI) was calculated to classify obesity (WHO, 2007), and the homeostasis model assessment insulin resistance index (HOMA-IR) was calculated according to Mathews, 1985. Genotyping of TCF7L2 rs11196175 SNP was performed by TaqMan® OpenArray™ Genotyping System®.

Results: 42% (148 of the scholar-age children) were obese; from these 78.3% (126) have a HOMA-IR of ≥ 3.16 . The higher frequency of the allele was the homozygous T of the TCF7L2 gene (rs11196175 SNP) with 75.6% (266 of the scholar-age children). The correlation by Chi² showed a significant association (p < 0.00001) between insulin resistance with the T allele of the TCF7L2 gene rs11196175 SNP in obese scholar-age children.

Conclusions: The strong relationship between the allele homozygous T of the TCF7L2 gene (rs11196175 SNP) with insulin resistance in obese scholar-age children 6 to 12 years evidence its importance as a risk factor in metabolic alterations at early ages. More research is needed to contribute to the prevention and personalized nutrition.

Metabolic Syndrome associated with FTO rs3751812 and TCF7L2 rs7903146 polymorphisms in Mexican scholar-age children 6-12 years

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Background: Recent studies have analyzed the participation of single nucleotide polymorphisms (SNPs) of the FTO and TCF7L2 genes in metabolic syndrome (MS). Despite the increase of MS in children, there are few studies in Mexico. To analyze the role of the FTO rs3751812 and TCF7L2 rs7903146 polymorphisms (SNPs) in

MS we performed a study based on the data from the UANL Childhood Obesity Program.

Methods: Descriptive and cross-sectional study that met the ethical criteria in 231 scholar-age children 6 to 12 years. Children were classified as normal weight, overweight and obesity (WHO, 2007). MS diagnosis was according to International Diabetes Federation (IDF, 2017). Genotyping of FTO rs3751812 and TCF7L2 rs7903146 SNPs were performed by TaqMan® OpenArray™ Genotyping System®.

Results: 45% (103 of the scholar-age children) were overweight and obese; from these, 40.4% (42) were diagnosed with MS. The association analysis (χ^2 test and Cramer's V coefficient) of the FTO rs3751812 and TCF7L2 rs7903146 SNPs in children with and without MS were both statistically significant ($p = 0.027$ and $p = 0.041$, respectively).

Conclusions: The study suggests the influence of the genetic variants: FTO rs3751812 and TCF7L2 rs7903146 SNPs and their association with MS in children. These variations affect individual responses, so they could be considered to establish personalized nutritional recommendations based on evidence. More studies are needed on the Mexican population.