ERA-NET Cofund ERA-HDHL:
ERA-NET Biomarkers
funded projects

The mail objective of the cofunded call for Joint Transnational Research Proposals on "Biomarkers for Nutrition and Health" was the identification and validation of biomarkers that are modulated by diet and that are modulated by diet and that indicate a change in health status and/or the risk of developing diet-related diseases.

This Joint Action funded 12 projects for a total amount of about 11.2 M€.

ALPHABET

Early life programming of childhood health: a nutritional and epigenetic investigation of adiposity and bone cardiometabolic, neurodevelopmental and respiratory health

WHAT

The ALPHABET project aims to improve understanding of nutritional and epigenetic biomarkers of offspring health with a view to refining dietary exposure measures and to aid development of more effective evidence-based public health strategies with an emphasis on advocating a healthy diet in pre-pregnancy, pregnancy and early postna-tal life, to reduce obesity, improve health and attenuate development of a range of adverse health outcomes in future generations.

WHO

The consortium includes 7 partners from 6 countries (Ireland, UK, France, The Nether-lands, Poland and the US).

HOW

Utilising biological samples and data from existing European longitudinal birth cohorts at the international forefront of lifecourse epidemiology the consortium will investigate the complex relationships between maternal diet (defined by dietary quality and inflam-matory potential), offspring health outcomes (including adiposity, bone, cardiometabolic, respiratory and neurodevelopmental health) and epigenetic patterns (DNA methylation) from birth throughout childhood.

FUNDING

ALPHABET receives approximately 1.2M€.
Project coordinator: **Dr. Catherine Phillips** (University college Dublin, Ireland)

BioFN

Biomarkers for Infant Fat Mass Development and Nutrition

WHAT

Childhood obesity is a rapidly growing problem. Weight loss programs have limited effects and prevention is our only hope to stem this new epidemie. Infant fat mass development in particular, has long-term effects on later body fat mass and thus metabolic health. Lipid profiles may be used as biomarkers for fat mass development and

provide predictive biomarkers for later childhood obesity.

WHO

BioFN brings together experts on lipidomics, paediatric endocrinology, systems biology and lipid metabolism from United Kingdom, The Netherlands and Denmark.

HOW

BioFN will use lipid profiling in samples from two birth cohort studies, Sophia-Pluto (Rotterdam, NL) and Cambridge Baby Growth Study (UK) that bath have very precise body composition data. This will allow to develop predictive biomarkers for fat distribution. By quantifying the dietary effect on lipid metabolism, gut microbiome meta-bolism and fat distribution BioFN will provide tools to prevent childhood obesity.

FUNDING

BioFN receives approximately 1.1M€.

Project coordinator: **Dr. Albert Koulman** (Univercity of Cambridge, UK)

BioNUGUT

Gut Metabotypes as Biomarkers for Nutrition and Health

WHAT

Health reflects a balanced condition of all eukaryontic cells and all the microbes living in and on human body. In contrast, for many different disease entities it has been shown that the host-microbiome axis is dysregulated. Since the gut microbiome is known to be heavily influenced by diet, a balanced and symbiotic interplay between gut bacteria and the human organism might be a promising indicator for nutrition and health.

WHO

The consortium combines two groups with access to large and well characterized human cohorts and two well established groups in Metabolomics experienced in liquid chromatography, mass spectrometry (LC-MS) and matrix assisted laser desorption ionization-time of flight (MALDI-TOF) based approaches. Those groups are from Germany, Canada and Austria.

HOW

Identification of bacterial metabolites in the human serum as markers for nutrition and health using a three step program:

1. Identification of biopatterns of gut bacterial metabolites in the human serum,
2. Validation of the identified biopatterns in two independent international cohorts and in the same cohort at different time points, and
3. Verification of the eligibility of the bio-patterns as indicators for nutrition and health in two human intervention studies.

FUNDING

BioNUGUT receives approximately 1.1M€.

Project coordinator: **Matthias Laudes** (UKSH, Germany)

CABALA_Diet&Health

CirculAting Bile Acids as biomarkers of metabolic health - Linking microbiotA, Diet and Health

WHAT

Bile acids (BA) through TGRS and FXR regulate mammalian inflammation, lipid, glucose, and energy metabolism, and are in turn regulated by diet-microbiome interactions in the gut. CABALA_Diet&Health aims to establish circulating BA profiles as biomarkers of health, modulated by diet which reflect a change in metabolic health.

WHO

In this project researchers from Italy, Ireland, the UK and Israel work together.

HOW

Using existing data and new mechanistic studies the consortium will provide direct evidence in hu mans that diet-gut microbiota interactions modulate plasma BA profiles and modulate host health. The aim is to

identify plasma BAprofiles as health biomar-kers and establish microbiota modulation of BA signalling as a unifying molecular basis for efficacious probiotic, prebiotic and polyphenol functional foods.

FUNDING

CABALA_Diet&Health receives approximately 1.04M€.

Project coordinator: **Kieran Tuohy** (Fondazione Edmund Mach, Italy)

DERIVE

DEvelopment of Riboflavin biomarkers to relate dietary sources with status, gene-nu-trient Interactions and Validated health Effects in adult cohorts

WHAT

Sub-optimal riboflavin status may be more widespread than is generally recognised across the developed world, because ofthe reliance on dietary data only in nutrition surveys, without biomarker evidence.
DERIVE will address this gap by developing accessible riboflavin biomarkers for use in population surveys globally, and by demonstrating important functional, gene-nutrient and health effects of optimal riboflavin status in Canadian, Irish and UKcohorts.

WHO

This unique partnership ofscientists from three jurisdictions brings together Canadian, Irish and UKpopulation cohorts to study navel nutrient factors, and related gene-nutrient interactions, and functional effects that influence health, including hypertension, a leading cause of mortality. The project will lead to enhancements in health and disease prevention that can be marketed as a global strategy rather than one that is population specific.

HOW

The proposed study will access bio-banked blood samples (collected under the JINGO initiative http://www.ucd.ie/jingo/) and data from one ofthe most comprehensive dietary surveys in the EU, the Irish National Adult Nutrition Survey (www.iuna.net) as well as bio-banked specimens and data from the BC Generations Project (www.bcgeneration-sproject.ca), part ofthe Canadian Partnership forTomorrow Project, a major research platform forthe study ofdisease causation.

FUNDING

DERIVE receives approximately 0.6M€.

Project coordinator: **Mary Ward** (Ulster University, Ireland)

FAME

Fatty Acid Metabolism - Interlinking Diet with Cardiometabolic Health

WHAT

FAMEaims to: a) identify novel lipidomics biomarkers as biomarkers of fatty acid status and of future cardiometabolic clinical events, b) establish relationships between whole diets and specific foods with tissue status of fatty acids as explanatory factors for diet relationships with cardiometabolic health, and c) to investigate genetic determinants of fatty acid status and metabolism which modify the physiological effects of dietary intake.

WHO

This consortium brings together 5 experts from Germany, Spain and the UK.

HOW

Lipid metabolites as navel biomarkers will be identified in prospective studies on type 2 diabetes. Potential for dietary modification will be tested in controlled trials. Specific FAs and navel lipid metabolites will be tested as biomarkers of dairy fat intake and as markers ofcardiometabolic health. Polyphenols and candidate genes as determinants ofresponse to FA intake will be evaluated in the trials and cohorts.

FUNDING

FAME receives approximately 0.83M€.
Project coordinator: **Prof. Matthias Schulze** (German Institute of Human Nutrition, Germany)

FiberTAG

TAGging dietary Fiber intake and their interest for health by measuring biomarkers related to the gut microbiota

WHAT

The FiberTAG project will establish a set of biomarkers linking dietary fiber (DF) intake and gut-microbiota related health effect. We aim at refining the concept of DF based on navel biological effects that can occur upon gut microbiota-nutrients interaction by using existing cohorts and by developing innovative approaches to evaluate the health interest of navel insoluble DF.

WHO

The FiberTAG consortium gathers 4 academie principal investigators from Belgium, France, Germany and Canada, respectively. They gather complementary research expertises such as 1) host physiology with emphasis on management of cardio-metabolic disorders, 2) intervention studies based on diet and prebiotic DF, 3) microbial ecology, 4) data integration and modelling. Two industrial partners will develop and provide selected insoluble fiber for the intervention studies.

HOW

Specific metabolites selected as biomarkers of microbiota-driven fermentation and gut-related functions will be analyzed in 5 existing cohorts of healthy or overweight populations in which the fecal microbiota composition and DF intake have been (or will be) analyzed. New intervention studies will be performed in healthy and cardiometabolic risk volunteers to evaluate the interest for health of two insoluble fibers (chitin-glucan and a wheat bron fraction).

FUNDING

FiberTAG receives approximately 1.36M€.
Project coordinator: **Nathalie Delzenn** (Université catholique de Louvain, Belgium)

HEALTHMARK

Metabolic HEALTH through nutrition, microbiota and tryptophan bioMARKers

WHAT

HEALTHMARK will investigate the complex associations between the gut microbiota, tryptophan availability and bioactive microbial metabolites of tryptophan, and diet and metabolic health. Phenotypes of obesity with low visceral adipose tissue as well as metabolically healthy obese phenotypes will be used to characterize metabolic health. The gut microbiome will be looked at as a potential reservoir of health-related biomarkers, bath in terms of composition and function (microbial metabolites) open to modulation by diet.

WHO

HEALTHMARK is an interdisciplinary and transnational project. The project comprises five partners from EU countries (Germany, lreland, France and ltaly) with complementary expertise and exemplars of scientific excellence in this research area.

HOW

HEALTHMARK will identify, replicate and validate biomarkers in.existing human population studies - the DONALD, the Rhineland, the Obesity, and the MUCOL Study- which have dietary information, information on body composition, and biological samples. Gut microbiota composition will be assessed by 165 ribosomal RNA sequencing. The project will use targeted and untargeted metabolomic approaches to determine levels of relevant precursors, metabolites and bioactives in blood and urine samples.

FUNDING

HEALTHMARK receives approximately 1.31M€.
Project coordinator: **Ute Nöthlings** (University of Bonn, Germany)

OXYGENATE

Oxylipins signature to monitor the cardiometabolic status and its response to dietary intervention

WHAT

There is an urgent need to find reliable early biomarkers ofthe cardiometabolic syndrome (CardMetS) allowing intervention before irreversible damage develops while assessing the efficacy ofnutritional prevention. Targeted lipidomic profiling ofoxylipins could provide relevant candidate biomarkers. The main objective is to uncover and validate the oxylipin signatures reflecting the trajectory from health to CardMetS and its relationships with diet.

WHO

The OXYGENATE project brings together partners from France, Germany, Canada, Denmark and Poland with complementary and multidisciplinary expertise in nutrition, analitycal chemistry/lipidomics, nutritional epidemiology and cardiometabolic health.

HOW

Using an optimized targeted lipidomic approach and leveraging 2 independent prospective cohorts (i.e. the Polish PURE and the French NutriNet-Santé cohorts) and 2 whole-diet interventions (Shopus and iMAPS) the consortium will identify and validate oxylipin signatures (i) differentiating individuals at different stages of CardMetS and with different dietary patterns and (ii) evolving consistently with dietary interventions affecting the cardiome-tabolic end points.

FUNDING

OXYGENATE receives approximately 0.72M€.
Project coordinator: **Cecile Gladine** (INRA, France)

SALAMANDER

SALivAry bioMarkers of meditarraneAN Diet associated with long-tERm protection against type 2 diabetes mellitus

WHAT

Saliva offers the advantages ofsimple and non-invasive sampling and is a rich source of biomarkers thanks to the high diversity ofits microbiome, proteome and metabolome. Saliva composition is also dependent on diet. The SALAMANDER project aims at identifying and validating salivary signatures indicative of healthy dietary choices (adhe-rence toa Mediterranean diet) with a positive long-term health outcome (protection against T2DM).

WHO

SALAMANDER brings together partners from France, the United Kingdom and Spain.

HOW

Using the UKBiobank resource, subjects will be categorized based on their health status (T2DM) and diet. The saliva microbiome, proteome and metabolome ofselected subjects will be analyzed, and analytica! data integrated to define a multimarker signature of a healthy Mediterranean diet associated with protection against T2DM. The validation phase will also include elderly subjects ofthe EN RICA and 3City-Bordeaux cohorts, to verify whether such signatures are conserved with ageing.

FUNDING

SALAMANDER receives approximately 0.62M€.
Project coordinator: **Martine Morzel** (INRA, France)

JPI a healthy diet for a healthy life

SALIVAGES

Innovative Technological Approaches for validation of Salivay AGEs as novel biomarkers in evaluation of risk factors in diet-related diseases

WHAT

Recent findings convincingly demonstrate that Advanced Glycation End Products (AGEs) are modifiable by diet and reflect changes in healthy state. SALIVAGES will investigate whether that diet-induced AGEs can act as reliable biomarkers of changes in health status and/or risk, focusing on the most highly accessible source of AGEs, the saliva.

WHO

The project is proposed by a highly qualified multidisciplinary research team with complementary experience in different fields of biochemistry, pathology, pharmacology and analytica! chemistry. The scientific network involves five European countries: ltaly, Spain, lreland, Romania and Germany.

HOW

SALIVAGES will provide innovative and original tools for assessing status and efficacy of interventions, namely biosensors, metabolomics and biomimic approaches. lt will also deepen understanding of the early events leading to the changes in health status, by multidisciplinary approaches based on the integration of preclinical biological and molecular studies, analytical and food chemistry, information technologies, and glycomic analyses.

FUNDING

SALIVAGES receives approximately 1.1M€.
Project coordinator: **Massimo Callino** (University of Turin, Italy)

The ERA-HDHL has received funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement n.696295

VALID

Valerolactones and healthy Ageing: Linking Dietary factors, nutrient biomarkers, metabolic status and inflammation with cognition in older adults.

WHAT

Polyphenols, particularly procyanidins (abundant in foods such as tea, cocoa, grapes, nuts and berries), may be beneficia! in maintaining better cognitive function in ageing, but investigating their role in relation to health is hampered by the lack of robust biomarkers of dietary intake. The consortium will validate novel plasma biomarkers of procyanidin-rich foods and link them with inflammation, metabolic health and cognition in an ageing European population.

WHO

VALID brings together partners from the UK, lreland and ltaly with interdisciplinary expertise in nutrition, food bioactives, immunology, geography and clinical gerontology, with the aim of conducting impactful research linking dietary polyphenols with cognitive health in older adults. VALID builds on the Joint Irish Nutrigenomics Organisation UINGO) project and specifically its component Trinity, Ulster, Department of Agriculture (TUDA) cohort study.

HOW

VALID draws on the TUDA cohort, a unique resource on 5200 adults aged 60-102 years recruited from the UK and lreland, providing a range of biomarkers and health measures. Apart from performing new analysis on bio-banked TUDA samples, VALID will access 'TUDA5+', a follow-up study of 1000 participants from the original cohort 5 years after initial investigation, to determine the role of procyanidin-rich foods in preventing cognitive decline over a 5-year follow-up period.

FUNDING

VALID receives approximately 0.6M€.
Project coordinator: **Helene McNulty** (Northern Ireland Centre for Food and Health, UK)

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