

RESEARCH AREA 2

## DIET AND FOOD PRODUCTION

JOINT ACTION:

### Intestinal Microbiomics



The main objective of the **Joint Action Intestinal Microbiomics (IM)** was to increase knowledge on the effects of diet on human intestinal microbiota and on the impact of diet-related variations in the intestinal microbiota on health and/or on chronic diseases, in order to support health promotion and prevention of non-communicable chronic diseases.

The call was initiated to support multidisciplinary transnational research consortia using innovative and scientific approaches to increase knowledge on: 1) the short-term and long-term functional effects of diet, dietary patterns and dietary constituents on human intestinal microbiota; 2) the functional impact of diet-related variations in the intestinal microbiota on human health and/or the development of non-communicable chronic diseases. The outcomes of the projects should contribute to dietary interventions or guidance for modulation of the intestinal microbiome.

Six research consortia were funded with a budget of approximately 6,6 M€. The projects started early 2016 and were completed between February 2019 and May 2020.

## AryIMUNE

### **Aryl hydrocarbon receptor and immunity: Activation by diet, microbiota and probiotics**

---

#### WHAT

The transcription factor AhR is crucial for maintaining intestinal homeostasis. The aim of ArylMUNE is to assess the effects of AhR activation by microbionics-derived components on intestinal immunity and physiology.

#### WHO

ArylMUNE was a consortium of research groups from 3 countries (CA, FR, NL) and was coordinated by Harry Sokol (Avenir Team Inserm, FR). ArylMUNE received approximately 0,8 M€.

#### HOW

The effects of dietary interventions and identified strains of lactic acid bacteria were assessed. AhR agonist presence and activity were evaluated in intestinal content, microbiota, host response and gastrointestinal symptoms. Novel identified microbial candidates were tested in vitro and in mouse models to confirm their effects on AhR activation.

#### MAIN OUTCOMES

The consortium identified alterations in

the gut microbiota function in humans suffering from Celiac disease characterized by an impaired production of aryl hydrocarbon receptor agonists. These alterations could be corrected in a mouse model by using a pharmacologic approach or intestinal bacteria naturally producing AhR agonists which alleviated the severity of the gluten immunopathology. Recommendations developed by ArylMUNE favoring vegetables naturally enriched in AhR agonists alone or in combination with bacteria naturally producing AhR might be interesting in terms of prevention and/or treatment of several diseases including Celiac disease.

#### HIGHLIGHT

The ArylMUNE project included an industrial partner which provided bacterial strains for the research.

## DINAMIC

### **Diet-induced Arrangement of the gut Microbiome for improvement of Cardiometabolic health**

---

#### WHAT

The DINAMIC consortium investigates the interaction between diet and gut microbiota and the potential of modulating these interactions for the prevention of

metabolic dysfunction and cardiovascular complications in humans.

## WHO

The consortium consisted of partners from 7 countries (FR, DE, UK, IE, IT, DK, NL) and was coordinated by two partners: Thomas Clavel (RWTH Aachen University, DE) and Dirk Haller (Technical University of Munich, DE). DINAMIC received approximately 2 M€.

## HOW

The consortium identified specific features associated with disease states, by using prospective human cohorts and microbiota profiling. Clinical trials (dietary interventions and fecal microbiota transplantation) were performed to test causal roles and targeted manipulations of the microbiome under controlled conditions. Meta-omics technologies were employed, aiming at the harmonization of results and the establishment of models towards prediction of detrimental and favourable gut environments with respect to cardiometabolic health.

## MAIN OUTCOMES

DINAMIC demonstrated that the gut microbiome is important for cardiometabolic health. Evidence was provided that a Mediterranean diet is an efficient strategy to reduce inflammation status during controlled energy intake, which might benefit public health by limiting people at

risks of developing cardiometabolic diseases.

## HIGHLIGHT

The largest consortium in this call organized a final symposium in December 2019 in Amsterdam. DINAMIC members from 6 countries presented the combined results of their research, sharing the DINAMIC outcomes with other researchers and other invited stakeholders.

### EarlyMicroHealth

#### Impact of early life diet on microbiome development & later health

---

## WHAT

Microbial colonization of the immature gut of a new-born is essential for the development of its physiological homeostasis. The aim of the EarlyMicroHealth project is to develop early-life interventions to promote the establishment of a healthy microbiota.

## WHO

EarlyMicroHealth consisted of a consortium of research groups of 4 countries (IE, IT, ES, NL) and a collaboration with researchers from China. The coordinator was Miguel Gueimonde (Agencia Estatal Consejo Superior de Investigaciones Científicas, ES). EarlyMicroHealth received approximately 1,3 M€.



## HOW

The consortium worked with a longitudinal cohort study, evaluating factors (e.g. gestational age, antibiotics exposure) that negatively impact early-life microbiota development and the impact of diet and nutrition during the first years of life. Next, the impact of interventions (e.g. omega three fatty acids or probiotics) in minimizing the impact of these factors was assessed.

## MAIN OUTCOMES

The EarlyMicroHealth consortium analyzed the infant microbiome in combination and integration with clinical and nutritional data. The obtained results of the consortium will assist in the development of better strategies for limiting the deleterious impact of early life medical treatments or diets on the microbiota development and later health. Within this project standard procedures, questionnaires and food composition databases were developed offering the opportunity to develop new generations of infant foods and to delineate the future of infant nutrition; a nutrition targeted not just to nourish the infants but also to promote a healthy microbiome development with reduced levels of antibiotic resistance genes.

## HIGHLIGHT

The consortium delivered a large number of papers so far (42) and disseminated its

results in already 22 oral presentations targeted at scientists, the general public, and policy makers.

## EarlyVir

**Influence of diet on early life gut virome - a key player in shaping the gut microbiota**

---

## WHAT

Since bacteriophages (viruses attacking bacteria) may play a role in shaping gut microbiota in early life, the aim of EarlyVir was to investigate how the gut virome is influenced by diet, and to study its role in the origins of chronic childhood disorders.

## WHO

EarlyVir was a consortium consisting of research groups from 3 countries (DK, CA, FR) and was coordinated by Hans Bisgaard (Copenhagen Prospective Studies on Asthma in Childhood, DK). EarlyVir received approximately 0,9 M€.

## HOW

The EarlyVir consortium developed the largest single human virome study to date, based on the COPSAC birth cohort. The consortium made their data and methods transparent for the community.

## MAIN OUTCOMES

Over 8000 diverse viruses were identified





n the healthy infant gut flora, and the vast majority of them were unknown to science before this project. The newly developed database allows a unique characterization of the viruses, providing a standard for all further virome analysis. The consortium was granted follow-up funding allowing it to follow the children in the cohort, trying to identify which of these viruses end up protecting them from developing chronic diseases as adults. In the long run the project outcomes might lead to new potential prevention strategies and help fight diseases.

## HIGHLIGHT

EarlyVir was very innovative, as it focused on gut viruses instead of bacteria, resulting in the largest single human virome study to date and the submission of 6 patents.

## GI-MDH

**From infancy to childhood: the intersection of gastrointestinal microbial communities, diet and health**

---

## WHAT

The GI-MDH consortium aimed to study the influence of the timing and nature of solid food introduction in infancy on gastro-intestinal microbial communities and consequent health outcomes, in particular fat accretion and allergic response.

## WHO

The consortium consisted of research groups from 3 countries (CA, DE, NL), coordinated by Eileen K. Hutton (McMaster University, CA). GI-MDH received approximately 0,8 M€.

## HOW

The GI-MDH consortium prospectively collected data from 4 cohorts with multiple biological sampling points, to enable longitudinal characterization of microbial communities, and metagenomic and metabolomic studies on a subset of infants.

## MAIN OUTCOMES

The consortium demonstrated that in the first year of life the development of the microbiome is characterized by an increasing diversity, the birth mode was a major driver of microbiota community structure only in the first month of life, while thereafter diet became the strongest driving force of microbiota composition. The results can be used in the future for standardization of dietary guidelines for infants and toddlers. Furthermore, specific microbial communities associated with chronic disease were identified in infants and children which can be used in the future for prevention and therapy.

## HIGHLIGHT

The GI-MDH consortium organized three large workshops on microbiome-related topics with 40-100 participants. A training activity for health care professionals and training for general practitioners, infectious disease specialists, municipal health service employees, pediatricians and midwives were organized as well.

## MaPLE

### **Gut and blood microbiomics for studying the effect of a polyphenol-rich dietary pattern on intestinal permeability in the elderly.**

---

#### WHAT

The MaPLE project aimed to test the hypothesis that an increased intake of polyphenol-rich foods (e.g. fruits, vegetables, nuts and seeds) reduces intestinal permeability and lowers inflammogenic bacterial factors in the bloodstream, promoting a protective metabolic phenotype in the elderly.

#### WHO

The consortium consisted of research groups from 3 countries (IT, ES, UK). Patrizia Riso (University of Milan, IT) was the project coordinator. MaPLE received approximately 0,6 M€.

#### HOW

A dietary protocol of specific polyphenol-rich foods/beverages was developed, and MaPLE also contributed to the development of the Food-Biomarker ontology. The consortium developed a database including nutritional characteristics of recipes considered in the menus provided to older people in the nursing home, as well as the newly obtained polyphenol data. Next to the polyphenol-rich dietary intervention in older

participants living in a controlled setting, underlying mechanisms were investigated using cultured intestinal cells and animal models.

#### MAIN OUTCOMES

The polyphenol-enriched diet caused reductions in intestinal permeability. Moreover, after the polyphenol-rich intervention microbial-diversity increased, suggesting an improvement in the gut microbial ecosystem. The scientific evidence obtained in MaPLE could result in new dietary recommendations for older citizens but also for industry exploitation (e.g. food, pharmaceutical, medical products) to improve and develop foods, nutraceuticals or devices which contribute to the promotion of a protective metabolic phenotype in the older subjects.

#### HIGHLIGHT

MaPLE was involved in collaborations with a large number of other projects: the JPI HDHL funded consortia FoodBall, D-CogPlast and VALID, a consortium funded under the 7th framework program of the EC and multiple COST actions. Furthermore, 11 lab exchanges took place within the consortium, helping to build and strengthen the microbiomics field.



More detailed information on the funded projects can be found at [www.healthydietforhealthylife.eu](http://www.healthydietforhealthylife.eu) or by using the hyperlinks behind the project's acronym.

JPI HDHL call secretariat Intestinal Microbiomics: ZonMw (NL),  
[jpihdhlprojects@zonmw.nl](mailto:jpihdhlprojects@zonmw.nl)