# Intestinal permeability modulation through a polyphenol-rich dietary pattern in the older subjects: MaPLE project outcomes and perspectives

**European Joint Programming Initiative "A Healthy Diet for a Healthy Life" (JPI HDHL) - http://www.healthydietforhealthylife.eu/**

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## Background

There is growing interest on research strategies focused on healthy aging. The balance between inflammatory and anti-inflammatory networks can be compromised in the older subjects. In addition, it has been reported that during aging an altered intestinal permeability (IP) can be present and this may cause the translocation of bacterial factors from the lumen to the blood stream activating immune function and inflammation. Thus, a reduced IP may be a new target to improve health status in the older subjects. In this regard, dietary approaches providing food bioactives with specific protective properties such as polyphenols (PPs) could be considered as potential new strategies for the management and/or prevention of IP related conditions (Fig. 1).

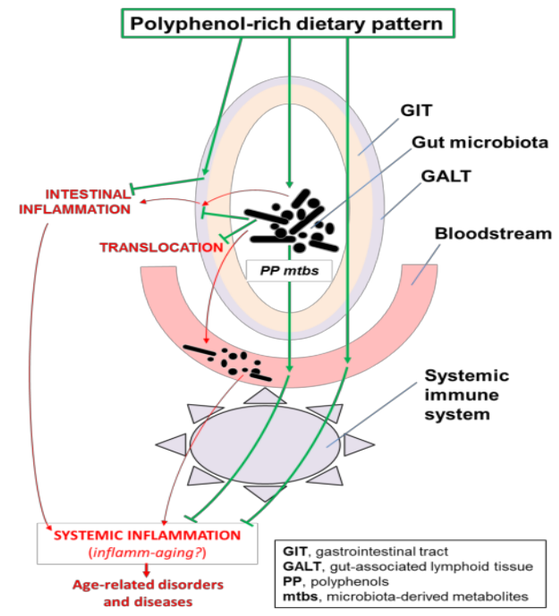



*Fig.1 – MaPLE rationale*

## Aim of the Study

MaPLE project aims to test the hypothesis that a polyphenol-rich dietary pattern, in older subjects with established IP, can lead to beneficial changes at intestinal and systemic level in terms of improved IP and related metabolic and functional parameters, thus promoting a healthy phenotype.

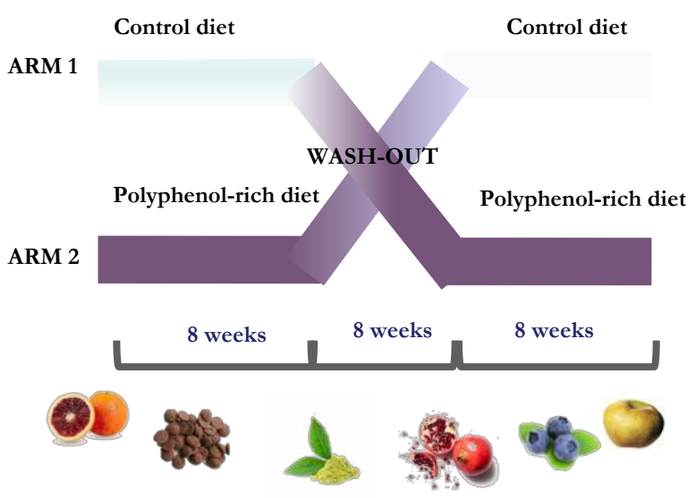
**INCLUSION CRITERIA**

Age ≥ 60 years, good cognitive status (MMSE score ≥24), Mini Nutritional Assessment (MNA) score ≥24, autonomous eating and self sufficiency evaluated by Barthel Index and Tinetti balance assessment, adequate oral Health and presence of intestinal permeability condition.

**EXCLUSION CRITERIA**

Celiac disease, recent antibiotic treatments, severe liver disease and severe renal insufficiency (dialysis), severe Chronic Obstructive Pulmonary Disease or severe heart failure class III or IV NYHA - New York Heart Association, and malignant tumor that required treatment in the previous 2 years.

*Fig. 2- Study design*




## Results

Compliance with dietary instructions was high and subjects well accepted the PR foods. As regard to IP, mean values of serum zonulin levels at recruitment were higher compared to that observed in apparently healthy volunteers. Correlation analysis have been performed on data stratified on the basis of zonulin median values (higher or lower) as reported in Fig 4. Energy and nutrient intake did not differ in the two periods of intervention (PR-diet *vs* C-diet) except for a small increase of carbohydrates and a decrease of fat intake following the PR-diet while polyphenol intake increased as expected (Fig. 5).

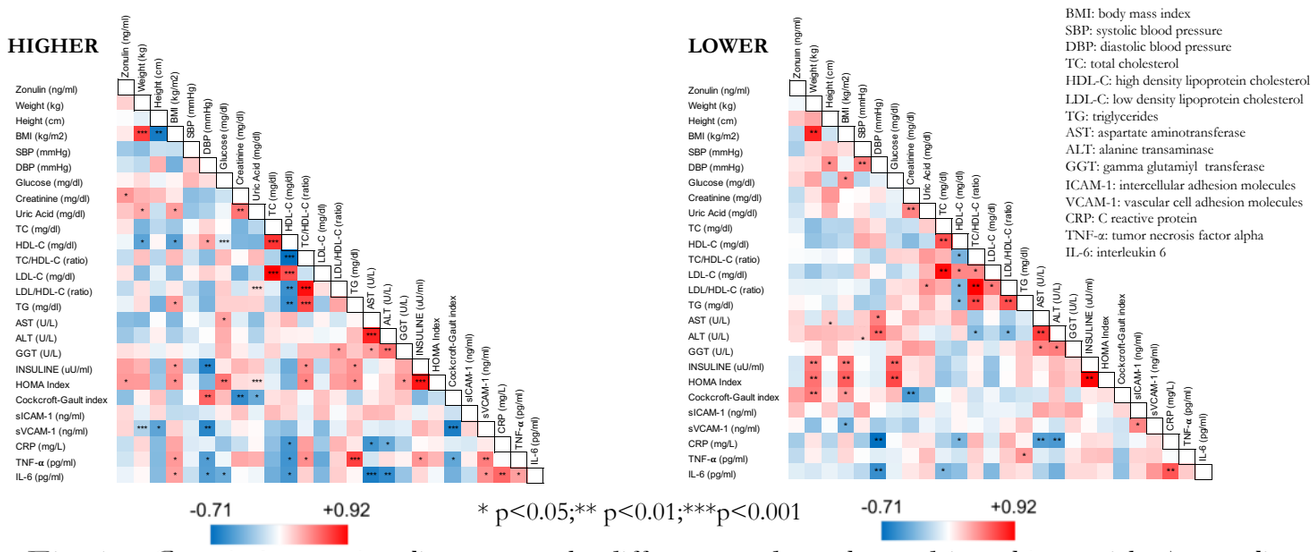



*Fig. 4 – Correlations at baseline among the different markers observed in subjects with a) zonulin levels > median and b) zonulin levels ≤ median*

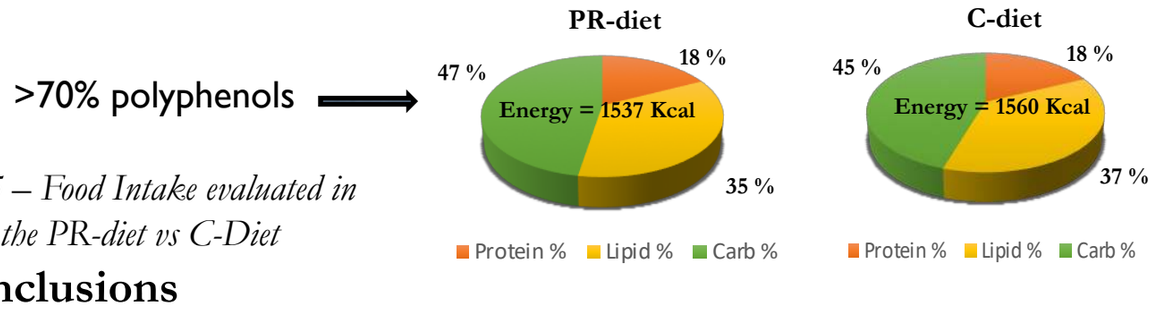



*Fig. 5 – Food Intake evaluated in the PR-diet vs C-Diet*

## Conclusions

MaPLE project will provide new perspective for the implementation of a polyphenol-rich dietary pattern able to promote a protective metabolic phenotype in subjects with IP. In addition data obtained will be pivotal for the future definition of a panel of biomarkers for the evaluation of IP.

## Study design

A randomized, controlled trial (RCT) with a cross-over design (8-week polyphenol-rich diet, PR-diet *versus* 8-week control diet, C-diet; Fig. 2) was performed in a group of 51 older subjects (≥ 60 y), living in a well-controlled setting (Fig. 3). PR-diet added a mean of 724 mg/day total PPs.

## Setting

Civitas Vitae (OIC Foundation, Padua, Italy) hosts older subjects living in nursing homes or in independent residences. A dedicated area for meal preparation enable a control of diet delivered and food intake increasing compliance.

*Fig. 3- MaPLE RCT setting*

## Biomarkers and assessments

**Anthropometrical, physical and clinical evaluation**
-Weight, height, BMI, blood pressure, biochemical parameters

**Food intake** (evaluation of daily menu and weighted food diaries)

**Blood samples**
-Serum zonulin (by ELISA), total bacterial load (qPCR), Taxonomic profiling (16S rRNA gene profiling - MiSeq-Illumina sequencing)
-Inflammatory markers (CRP, IL-6, TNF-α by ELISA)
-Oxidative stress markers (FPG-sensitive sites, $H_2O_2$-induced DNA damage (comet assay)
-Endothelial function markers (sVACM-1 and sICAM-1 by ELISA)
-Metabolic profile: amino acids, biogenic amines, sugars, carnitine-acylcarnitine, metabolites of the TCA cycle, alcohols, and aldehydes

**Urine samples**
-Metabolomic profile: biogenic amines, sugars, carnitine/acylcarnitine, metabolites of the TCA cycle, alcohols, and aldehydes
-Polyphenol-derived metabolites (LC-MS)

**Faecal samples**
-Microbiota composition (16S rRNA gene profiling through -MiSeq-Illumina sequencing)
-Short chain fatty acids (LC-MS)
-Polyphenol-derived metabolites (LC-MS)
-Diet-induced changes in microbiota metabolism (NMR and LC-MS analysis of faecal water)

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