GUT MICROBIOTA FUNCTIONAL DYSBIOSIS AND IMPACT OF INDIVIDUAL DIET IN SUBCLINICAL CAROTID ATHEROSCLEROSIS

Ischemic Cardiovascular Diseases (CVD) still contribute to excessive mortality worldwide despite the growing knowledge on the role of classical cardiovascular risk factors (CVRFs) and considerable advances in treatment. In the search for novel modifiable risk factors to improve CV prevention, Gut microbe (GM) represents one of the most appealing. GM composition controls a plethora of immuno-inflammatory and metabolic pathways interacting with the host through metabolic exchange and co-metabolism of substrates. Changes in GM have been related to metabolic alterations, responsible for diseases related to elevated CVD risk (e.g. type 2 diabetes (T2D) and Metabolic Syndrome (MetS)). To address whether these relations can explain the already described association between GM and clinically established CVD is a difficult task, as CVRFs are per se relevant confounders. Although specific bacterial taxa and strains are associated with advanced coronary atherosclerosis, little is known on whether and which alterations in GM compositions and diversity occur yet at preclinical stages. Gut Microbiota dysbiosis associates with Atherosclerotic Cardiovascular Diseases, but whether this also holds true in subjects without clinically manifest ACVD represents an intriguing challenge of personalized prevention.

To identify taxonomic and functional signatures which may occur before the clinical manifestation of CVD such as carotid atherosclerosis, we studied GM composition in subjects at initial stages of the atherosclerotic process (i.e. Subclinical Carotid Atherosclerosis, SCA) without Type 2 Diabetes or metabolic syndrome. We connected exposure to diet (self-reported by food diaries), markers of Subclinical Carotid Atherosclerosis (SCA) with individual taxonomic and metagenomic functional GM profiles (from fecal bacterial DNA) of 345 subjects without previous clinically manifest ACVD, by 16S-based rRNA gene amplicon sequencing and a complete GM shotgun sequencing on 23 subjects with advanced SCA vs 23 age- and gender-matched subjects without SCA.

Subjects without SCA reported to consume higher amounts of cereals, leafy vegetables, milky products, yoghurts, fish, bakery and sugary products versus those with SCA (who viceversa reported to consume more meats). Subjects with advanced SCA associated with increased abundance of bacterial genera and species, such as Escherichia coli, Dorea longicatena, Streptococcus parasanguinis, Streptococcus anginosus and Coprococcus comes, predicted to over-represent metabolic pathways related to the biosynthesis of phosphatidylethanolamine (PE) and palmitate, arginine, glutamine, biotin, phylloquinone, ubiquinone and menaquinone syntheses. Vice versa in absence of SCA other genera and species, mainly Faecalibacterium prausnitzii, were predicted to over-represent pathways related to sulfur oxidation and starch degradation.

The observation that the biosynthesis of PE was the most up-represented in subjects with advanced SCA prompted us to focus on the L-carnitine degradation pathway, metabolically linked to L-carnitine/ γBB/trimethylamine (TMA) metabolic cascade, which resulted significantly over-represented in subjects with advanced SCA and was almost entirely (~94%) due to E. coli contribution. The caiC, caiD and caiE genes were significantly upregulated as well, whereas caiB showed a similar trend towards upregulation.

Individual GM profiles in presence of SCA were clustered with exposure to multiple dietary sources. These findings might contribute to the hypothesis of future strategies of personalized dietary intervention for primary CVD prevention setting. Despite further research is warranted on larger number, this explorative finding is suggesting for a specific...
metagenetic contribution of E. coli in supplying local inflammation at the site of atherosclerosis.

References:


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Contacts: clelia.peano@irgb.cnr.it; marco.severgnini@itb.cnr.it

Website(s):

Authors: Marco Severgnini1*, Andrea Baragetti2*, Elena Olmastroni3, Giada Caredda2, Carola Conca Dioguardi9, Elisa Mattavelli2,6, Andrea Angius5, Luca Rotta6, Javier Cibella4, Clarissa Consolandi1, Veronica Zampoleri2,6, Liliana Grigore6,8, Fabio Pellegatta6,8, Flavio Giavarini2, Donatella Caruso2, Giuseppe Danilo Norata2,6, Alberico L. Catapano2,8§ and Clelia Peano4,9§

1 Institute of Biomedical Technologies, National Research Council, Segrate, Milan, Italy; 2 Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy; 3 Epidemiology and Preventive Pharmacology Service (SEFAP), Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy; 4 Genomic Unit, IRCCS, Humanitas Clinical and Research Center, Rozzano, Milan, Italy; 5 Institute of Genetic and Biomedical Research, National Research Council, Cagliari, Italy; 6 S.I.S.A. Center for the Study of Atherosclerosis, Bassini Hospital, Cinisello Balsamo, Milan, Italy; 7 Department of Experimental Oncology, IEO, European Institute of Oncology, IRCCS,
Milan, Italy; 8 Multimedica IRCCS, Milano Italy; 9 Institute of Genetic and Biomedical Research, UoS Milan, National Research Council, Rozzano, Milan, Italy

* These two authors equally contributed
§ These two authors are Corresponding authors