Gut microbiota, subclinical carotid atherosclerosis and major cardiovascular risk factors in general population: which association?

Baragetti A.[1,2*#], Severgnini M.*[3], Olmastroni E.[4], Caredda G.[5], Conca Dioguardi C.[5], Angius A.[6], Rotta L.[7], Grigore L.[2,8], Pellegatta F.[2,8], Norata G.D.[1], Catapano A.L.[1,8§], Peano C.[5,9§]

#presenting athor

[1] Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy
[2] SISA Center for the Study of Atherosclerosis, Bassini Hospital, Cinisello Balsamo, Milan, Italy
[3] Institute of Biomedical Technologies, National Research Council, Segrate, Milan, Italy
[4] Epidemiology and Preventive Pharmacology Service (SEFAP), Department of Pharmacological and Biomolecular Sciences, University of Milan, Milan, Italy
[5] Genomic Unit, Humanitas Clinical and Research Center, Rozzano, Milan, Italy
[6] Institute of Genetic and Biomedical Research, National Research Council, Cagliari, 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

Keywords: Atherosclerosis, gut microbiota, next generation sequencing, diagnostic markers, microbial metabolites

Increasing evidence indicates that alterations in Gut Microbiota (GM) composition and functions associate with advanced cardiovascular diseases (CVDs), although relation of causality is difficult to assess due to interference of multiple cardiovascular risk factors (CVRFs). We profiled GM in low CVD risk subjects selected from a population-based study (PLIC Study) to investigate the association between intestinal bacterial community and markers of Subclinical Carotid Atherosclerosis (SCA), marker of initial stages of CVD manifestation. GM composition was assessed through 16S rRNA amplicon sequencing from 345 faecal samples; in addition, a complete Gut Metagenome shotgun sequencing was performed on 23 subjects with advanced stenotic atherosclerotic lesions (arterial stenosis >30% in diameter) compared to 23 age and gender matched low CVD risk subjects without SCA.

Key differences in bacterial taxa were as follow: Bacteroides relative abundance reduced in SCA (14.6% compared to 16.3% in non-SCA) while Escherichia increased (2.8% compared to 1.4% in non-SCA), Coriobacteriaceae and Streptococcus (1.18% compared to 0.35% in non-SCA). To get further insights in these differences, Gut Metagenome sequencing was performed and subjects with advanced SCA displayed a significant increase of the genera Dorea, Klebsiella and Citrobacter compared to those subjects without SCA. In particular, functional metabolic pathways analysis clustered bacterial species responsible for metabolic dysbiosis in SCA and advanced stenotic atherosclerotic lesions, highlighting enhanced amino acids metabolism and carbohydrates degradation.

In conclusion, we provide new and specific signature of GM dysbiosis in relation to SCA and its progression in the general population, whereas the metagenomic analysis at functional level led to the identification of bacterial species that could be considered new as potential biomarkers for clinical diagnosis/prognosis of carotid atherosclerosis progression.