21. THE ROLE OF GUT MICROBIOTA METABOLITES IN ATHEROSCLEROSIS

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Introduction. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide. Changes in gut microbiota metabolites(GMM) is linked to the development of CVD, which includes atherosclerosis, hypertension, and heart failure. Some GMM, such as trimethylamine-N-oxide (TMAO), bile acids (BA), short-chain fatty acids (SCFA), coprostanol and others influence the atherosclerosis.

Aim of study. To research the biochemical pathways of GMM involved in triggering atherosclerosis, thus proving the possibility to use them as predictive markers in cardiovascular disease diagnosis and as treatment targets.

Methods and materials. Research, study and analysis of numerous articles from PubMed, NCBI, HINARI, Google Scholar databases over the last ten years.

Results. TMAO has been correlated with an increased risk of atherosclerotic cardiovascular disease. Following ingestion of animal products rich in phosphatidylcholine, carnitine and choline, gut microbiota(GM) can use them as a carbon source. GM enzyme trimethylamine (TMN) lyases cleave C-N bond of these nutrients releasing TMA waste product, which is further processed into TMAO by the liver enzyme flavin-dependent monooxygenase 3. TMAO activates NF-κB in endothelial cells and leads to increased expression of vascular cell adhesion molecule-1 (VCAM-1), trigger factor for atherosclerosis. TMAO enhances macrophage migration and adhesion due to VCAM-1, thus forming foam cells in plaque that contain cholesterol. Unbalanced GM, could lead to reduced deconjugation of primary bile acids to secondary bile acids, which can increase primary bile acids such as chenodeoxycholic acid, suppress enzyme cholesterol 7-alpha-hydroxylase, then downregulate bile acid production from cholesterol and so its concentration is elevated. SCFAs can lower serum lipid levels by blocking cholesterol synthesis and redirect them to the liver. SCFAs are a microbial-derived metabolites that are mostly formed by Bacteroidetes phylum fermentation of complex carbohydrates. SCFA-producing bacteria can be reduced in certain CVD, dysbiosis of patients with hypertension determined by atherosclerosis. Besides this, species of gut microbiota, such as Eubacterium coprostanoligenes, Bacteroides dorei, Lactobacillus sp. possess the ability to convert absorbable cholesterol to coprostanol, a reduced non-absorbable sterol, which is excreted in feces.

Conclusion. As previously mentioned, there is overwhelming evidence that GMM influences CVD-relevant phenotypes, such as atherosclerosis. Therefore the state of GM must be taken into account during atherosclerosis prevention, diagnosis and treatment.