Editorial: Impact of the gut microbiota on cardiovascular medicine

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In recent years, accumulating evidence from translational research has highlighted the significant role of the gut microbiota and its metabolites in shaping the cardiovascular and cardiometabolic phenotypes. In particular, combined metagenomic and metabolomic approaches have contributed to our understanding of how intestinal microbial metabolism of dietary nutrients impact metabolic pathways and cardiovascular disease risk (1, 2). A number of metaorganismal circuits have been reported to modulate different aspects of cardiovascular and cardiometabolic conditions, such as arterial hypertension and hypertensive end organ damage (3, 4), lipid metabolism and atherosclerosis (5, 6), glucose metabolism (7), platelet activation and thrombus formation (8–10), and ischemic heart disease (11). Remarkably, recent studies suggest that gut microbial composition also impacts on the efficacy of cardiovascular pharmacotherapy (12, 13). Targeting of distinct gut microbial pathways may help to establish novel strategies in preventing cardiometabolic and cardiovascular diseases.

In the current article collection on the Frontiers in Medicine Research Topic “Impact of the Gut Microbiota on Cardiovascular Medicine” we highlight research and review articles presenting novel insights into the interaction between the gut microbiota and cardiometabolic and cardiovascular (patho-)physiology. Lang et al. provide novel evidence of how manipulation of plasma lipid levels modulates the gut microbiome. In particular, manipulated plasma lipid levels of non-human primates using dietary and pharmacological techniques, and characterized the microbiome using 16S rRNA gene sequencing. Their study showed that high-fat
demonstrate a functional link between the gut-derived metabolite indole-3-propionic acid and mitochondrial function in cardiomyocytes and how this metabolite alters cardiac function. First, the authors screened 25 microbial metabolites in a live-cell metabolic assay using HL-1 cardiomyocytes. They identified indole-3-propionic acid, a microbial tryptophan derivative, as a modulator of mitochondrial function. While acute treatment induced enhancement of maximal mitochondrial respiration, chronic exposure led to mitochondrial dysfunction. In isolated perfused mouse hearts, indole-3-propionic acid was shown to dose-dependently improve cardiac contractility. Since indole-3-propionic acid also reduced maximal respiration in cultured endothelial and hepatocyte derived cellular carcinoma cells, the revealed effect of this microbiota-derived tryptophan derivative is not restricted to cardiac tissue. Cumulatively, their results indicate a direct impact of microbial metabolites on cardiac physiology.

Ding et al. present the study design of a prospective observational case–control study to analyze the variation in the intestinal microflora and metabolites in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) and to observe the outcomes of patients with routine clinical interventions. This study is of particular interest as in the critical care unit, most common clinical interventions such as enteral feeding, proton-pump inhibitors, systemic catecholamines and systemic antibiotics change the intestinal microbiome composition. Since in critically ill patients, changes in the intestinal flora and metabolites co-occur with systemic inflammatory reactions and often bacterial sepsis, the authors hypothesize that intestinal dysbacteriosis after CPB, enhanced by intestinal ischemia-reperfusion injury, is a possible mechanism of inflammation and that bacterial translocation contributes to the development of sepsis.

Finally, Chen et al. summarize current knowledge about antihypertensive drug-microbiota interactions and discuss how these interactions may help to develop gut microbiota-based personalized concepts for disease management, including antihypertensive response biomarkers, microbial-targeted therapies, and probiotics therapy.

These contributions shed further light into the interaction between the gut microbiome and (patho-)physiological pathways in the cardiovascular system and highlight the potential of microbiota-related strategies to improve currently available diagnostic and treatment options in cardiovascular medicine.

Author contributions
AH wrote the first draft of the manuscript. TvM, GP, and CR wrote sections of the manuscript. All authors read and approved the submitted version.

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