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Letter to the Editor

Reply to "PCSK9: Entering a new era of cardiovascular risk prediction"

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Dear Editor,

We would thank Dr. Schindler and Leucker for their valuable comments [1] on our recent publication in International Journal of Cardiology [2]. We have particularly appreciated their focus on the main innovative aspect of our research study: the potential pro-atherosclerotic activity of proprotein convertase subtilisin/kexin type 9 (PCSK9), which are independent of low density lipoprotein (LDL) levels.

Despite having gained notoriety thanks to its liver-mediated LDL-lowering effect which made it one of the most effective novel therapeutic target for cardiovascular prevention, PCSK9 is produced and holds major roles also in organs other than liver [3]. Brain-derived PCSK9 is deeply involved in neurogenesis and apoptosis. In the kidney, this protein was found to modulate the tubular expression of epithelial sodium channel (ENaC), while PCSK9 production within enterocytes increases post-prandial synthesis of ApoB and very low density lipoprotein (VLDL) [3]. Also, PCSK9 is thought to play a role in response to infection by modulating lipopolysaccharide clearance and hepatocyte susceptibility to viral infections (e.g. HCV) [3]. Of importance, in the arterial wall, PCSK9 was shown to be expressed by endothelial cells, smooth muscle cells and macrophages, where it is supposed to enhance local inflammation, oxidative stress, and LDL accumulation [3]. Accordingly, evidence of an anti-inflammatory effects of anti-PSCK9 antibodies in atherosclerotic plaques have already been reported [3].

In light of those evidences, PCSK9 is emerging as a pleiotropic protein with potential function in a wide range of pathophysiological processes ranging from ischemic stroke to acute coronary syndromes and sever trauma injury [3–5]. Future investigations are needed for validating PCSK9 as a useful and easy-to-assess CV risk marker.

Declarations of interest

None to be declared.

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