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Molecular and cellular alterations induced by macrophage-smooth muscle cells cross-talk accountable for atherosclerotic plaque vulnerability

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Statement of the Problem: Patients with diabetes mellitus have an increased risk of myocardial infarction and coronary artery disease-related death, exhibiting more vulnerable plaques. In the last decades, many studies have highlighted gelatinases (MMP-2 and -9) and collagenases (MMP-1, -8, -13) as major players in atherosclerotic plaque vulnerability.

Aim: The aim of this study is to investigate the effect of dialogue between human macrophages (MACs) and smooth muscle cells (SMCs) in high glucose conditions (associated to diabetes), on main MMPs involved in extracellular matrix destruction and atherosclerosis evolution, as relevant for vulnerable plaque progression in diabetic patients.

Methodology & Theoretical Orientation: Cell cross-talk was achieved using trans-well chambers, where SMCs were grown in the bottom chamber and differentiated human MACs in the upper chamber in normal (5mM, NG) or high (25mM, HG) glucose.

Results: We found that cross-talk between MACs and SMCs in HG conditions increased the gene and protein expression of MMP-1 and MMP-9 and also their activity. Higher levels of MCP-1 induced by SMC-MAC dialogue in HG are involved in MMP-1 and -9 up-regulation by a mechanism dependent by CCR2 signaling pathway, involving the phosphorylation of PKC α and activation of transcription factor NF- κ B. Moreover, SMCs exhibit an impaired capacity for collagen fiber assembly as a consequence of their co-culture with MACs.

Conclusions: In conclusion, high levels of MCP-1 released by cell cross-talk in diabetic conditions mediates collagenase and metalloprotease over-expression and activity, features that could be involved in higher vulnerability of atherosclerotic plaque found in diabetic patients.

Biography

Mihaela Vadana pursued her Master of Science Degree in Biochemistry and Molecular Biology from the University of Bucharest, Romania (June 2017). She is pursuing PhD in the Department of Biopathology and Therapy of Inflammation at the Institute of Cellular Biology and Pathology Nicolae Simionescu at the end of 2017. She is the first author of an under revision paper and has presented a poster at National Congress of Cellular and Molecular Biology (2017).

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