Abstract: P338

Statin treatment reduces matrix degradation capacity of proinflammatory polarized macrophages

Authors:
P J Hohensinner¹, B Thaler¹, B Ebenbauer¹, K Huber², J Wojta¹, ¹Medical University of Vienna, Cardiology - Vienna - Austria, ²Wilhelminen Hospital - Vienna - Austria,

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Background and Aims: Macrophages are versatile immune cells involved in tissue degradation and remodeling. Proinflammatory macrophages have the highest capacity of matrix degradation and proteolysis. Within atherosclerotic lesions, proinflammatory macrophages are associated with unstable plaques. Statins have been demonstrated to increase plaque stability. Changes of macrophage tissue degradation behavior under statin treatment is currently unknown.

Methods: Polarized macrophages were tested in vitro for matrix degradation capacity with or without statin treatment.

Results: Proinflammatory macrophages show high matrix degradation capacity which is lost after statin treatment. Statin concentrations were within a physiological range and did not influence overall macrophage polarization. Proinflammatory macrophages showed however a loss of filopodia where activators of MMPs are located. Loss of matrix degradation in proinflammatory macrophages was not associated with changes in MMP14 but with loss of uPAR localization at filopodia. Supplementation of mevalonate restored localization of uPAR to cellular protrusions.

Conclusion: Statins reduce the matrix degradation capacity of proinflammatory macrophages by reducing uPAR localization to cellular filopodia.