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Organotropism of anti-CXCR3/4- and anti-ETAR/-AT1R-mediated leukocyte migration in inflammatory and autoimmune disease

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Introduction: Interactions between G protein-coupled receptors (GPCR) and their endogenous ligands orchestrate a myriad of cellular events, among them cell trafficking and migration. Further, altered expression of GPCR and their ligands has been implicated in different autoimmune and inflammatory diseases. Apart from natural ligands, it has recently been shown that autoantibodies targeting GPCR might play a role in inflammatory and autoimmune diseases such as systemic sclerosis (SSc). Based upon previous findings it is assumed that high concentrations of anti-CXCR3 and anti-CXCR4 antibodies act in a protective manner, while high concentrations of anti-ETAR and anti-AT1R aggravate inflammatory mechanisms. We want to show those effect of antibodies against CXCR3, CXCR4, ETAR and AT1R in a murine model of atherosclerosis.

Methods: We injected IgG preparations containing different levels of autoantibodies directed against CXCR3/4 or ETAR and AT1R from patients with SSc and from healthy controls into a passive murine model of atherosclerosis (C57BL/6, Apoe-/-, high fat diet). Using red oil staining of the atherosclerotic plaques in the aorta, flow cytometry, differential blood count via Vet abc plus, ELISA and immunohistology analyses, it will be examined if those IgG preparations are able to modify leukocyte migration into different tissues like lung and spleen in comparison to peripheral blood.

Results: Preliminary findings of the ELISA indicates migration of leukocytes into the spleen modulated by the anti-GPCR IgG. More preliminary findings, like some results of the red oil staining and the flow cytometry analyses will be shown.

Conclusion: We assume an interplay between anti-AT1R/anti-ETAR & anti-CXCR3/4 and their receptors mediates organotropism of leukocytes in inflammatory & autoimmune diseases. In addition, membrane extracts of CHO cells overexpressing CXCR3/4, ETAR and AT1R will be applied in the same murine model to compare passive and active immunization schemes.