Phosphorylcholine antibodies preserve cardiac function and reduce infarct size by attenuation of the inflammatory response following myocardial ischemia-reperfusion injury

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Background: Natural IgM antibodies against oxidized phospholipids containing phosphoryl choline (PC) are present in all individuals. Such PC containing oxPLs are danger associated molecular patterns, to which the innate immune system has developed several receptors, including IgM anti-PC. Low levels of natural IgM anti-PC antibodies are associated with increased risk for cardiovascular events. Antibodies against phosphorylcholine are known to have anti-inflammatory properties. Myocardial infarction is preceded by atherosclerosis and followed by a post-ischemic inflammatory process.

Purpose: to investigate the modulatory effects of a new fully humanized IgG1 monoclonal antibody directed against PC (PC-mAb) in myocardial remodeling and cardiac function following myocardial ischemia-reperfusion (MI-R) injury.

Methods: In hypercholesterolemic ApoE*3-Leiden mice the LAD coronary artery was occluded for 45 minutes followed by permanent reperfusion and treatment with PC-mAb or vehicle. Two days and three weeks post reperfusion left ventricular (LV) function and infarct size (IS) were assessed by cardiac magnetic resonance imaging. LV fibrous content, LV wall thickness and leukocyte infiltration were evaluated (immuno)histologically. The systemic inflammatory response was analyzed using ELISA and FACS.

Results: Contrast-enhanced MRI assessed IS as well as histologically assessed LV fibrous content were reduced following PC-mAb treatment compared to vehicle three weeks post reperfusion. This resulted in significantly reduced end-diastolic and end-systolic volumes by 24% and 42% respectively, leading to a significantly increased ejection fraction by 33% in the PC-mAb group. These observations could be explained by a reduced systemic inflammatory response two days after reperfusion as observed by decreased CCL2 levels and circulating Ly6Chi monocytes. This resulted in reduced leukocyte infiltration in both the ischaemic and non-ischaemic myocardium and preservation of LV wall thickness after three weeks.

Conclusions: PC-mAb treatment attenuates the post-ischemic inflammatory response, leading to a reduction in adverse cardiac remodeling and preservation of cardiac function in hypercholesterolemic ApoE*3-Leiden mice. Therefore, PC-mAb therapy is considered as a therapeutic approach against MI-R injury.