Abstract: P355

A monoclonal human IgG1 phosphorylcholine antibody reduces vein graft remodelling, angiogenesis and intraplaque haemorrhage

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Introduction: Natural IgM antibodies against oxidized phospholipids (oxPLs) containing phosphorylcholine (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 PC antibodies are associated with increased risk for cardiovascular events in general and vein graft failure in particular. Antibodies against phosphorylcholine are known to have anti-inflammatory properties including inhibition of endothelial cell activation. Vein grafts are frequently used for bypass surgery, despite the relatively high failure rate of the grafts. Graft failure is due to inflammation triggered vascular remodelling and long-term failure is caused by unstable accelerated atherosclerosis. Intraplaque angiogenesis is a feature of atherosclerotic plaque development and progression. Intraplaque angiogenic neovessels are often immature, irregular and fragile due to compromised structural integrity, resulting in a high susceptibility to leakage of circulating cells - intraplaque haemorrhage - leading to an increased cholesterol deposition, atheroma growth and plaque instability.

Purpose: To investigate the effects of a new fully human IgG1 monoclonal antibody against PC (PCmAb) on vein graft remodelling and especially on intraplaque angiogenesis.

Methods: Hypercholesterolemic male ApoE3Leiden mice underwent vein graft surgery, by means of interpositioning of a donor caval vein in the carotid artery of a receiver mouse. The mice were treated with weekly intraperitoneal injections of 5 mg/kg PCmAb (n=11) or vehicle (n=12) until sacrifice at 28 days. The vein grafts were harvested and immunohistochemistry was used to evaluate lesion size and plaque angiogenesis. The effect of PCmAb on the angiogenesis behaviour of endothelial cells was evaluated in vitro by migration and proliferation assays.

Results: Treatment with PCmAb antibodies resulted in a 32% decrease in vein graft lesion area compared to vehicle treatment. Moreover, the PCmAb group revealed a significant decrease of 34% in the number of neovessels, and their maturity increased with 40% as shown by increased pericyte coverage of the plaque neovessels. Together, these lead to a reduction of intraplaque haemorrhage when compared to the vehicle group. The anti-angiogenic capacity of PC-mAb was further illustrated in vitro by a significant inhibition of endothelial cell proliferation and migration by 20% and 30% respectively, compared to controls.

Conclusions: PCmAb is an effective inhibitor of vein graft remodelling and intraplaque angiogenesis. Moreover, they show an inhibitory effect on EC migration and proliferation in vitro. Therefore, PCmAb holds promise as a new therapeutic approach to prevent vein graft disease.