Abstract: P379

CD22 deficiency alters B cell populations and plasma triglyceride levels but does not affect atherosclerosis in hyperlipidemic mice

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Background: Atherosclerosis is a lipid-driven chronic inflammatory disease that is modulated by various immune cells, including different B cell subsets. While follicular B2 cells are proatherogenic, B1 cells and marginal zone B cells are considered atheroprotective. These protective effects are thought to be mediated by natural IgM antibodies and the negative regulation of proatherogenic T follicular helper cells, respectively. B cell fate decisions are driven primarily by B cell receptor (BCR) signalling. CD22 is a B cell-specific receptor that negatively regulates BCR signalling, thus modulating B cell activity and differentiation. CD22 deficient mice have hyperreactive B cells, as well as reduced levels of marginal zone B cells and an impaired antibody response.

Purpose: In order to further explore the role of B cell receptor signalling and of different B cell subsets in atherosclerosis, we studied the effect of CD22 deficiency on atherosclerosis.

Methods: Bone marrow was isolated from CD22-/- and wildtype control mice and injected into lethally irradiated female LDLR-/- mice (n=15 per group) that were fed an atherogenic diet for 10 weeks. Atherosclerotic lesions were analysed and plasma lipid levels were measured. Additionally, immune cell populations and antibody levels were assessed by flow cytometry and ELISA, respectively.

Results: Unexpectedly, CD22 deficiency led to a marked increase in marginal zone B cells and in splenic and peritoneal B1 cell populations in the context of hyperlipidemia, while the number of recirculating follicular B cells in the blood and bone marrow were reduced. Although this was associated with a significant decrease in T cell-dependent IgG2c antibodies against oxidation-specific epitopes, there was no difference in the levels of IgM antibodies or in T cell numbers. CD22 deficiency had no effect on en face and aortic root lesion size and necrotic area. However, mice that received CD22-deficient bone marrow had significantly lower plasma triglyceride levels (485.5±104.1 vs. 608.3±121.2 mg/dl, p<0.008), suggesting a potential role for CD22 in lipid metabolism.

Conclusion: Our data fail to identify a direct role for CD22 in murine atherosclerosis. However, we found a hitherto unidentified potential link between B cells and lipid metabolism. Further studies should be performed to elucidate the mechanism by which CD22 deficiency affects plasma triglyceride levels.