210 **A ROLE FOR THE IL-1RI CO-RECEPTOR TILRR IN ATHEROSCLEROSIS AND VASCULAR REPAIR**

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**Introduction** The toll-like and IL-1 receptor regulator (TILRR) is a recently described co-receptor that binds the type I IL-1 signalling receptor (IL-1RI), and enhances signal amplification at the level of the receptor complex. IL-1 is a pro-inflammatory cytokine with a central role in responses linked to progression of atherosclerosis. The current project assesses the impact of TILRR on vascular pathology and remodelling. Immunocytochemistry demonstrated a cell specific increase in TILRR expression in the atherosclerotic plaque and a transient up-regulation in response to vessel injury. The data are consistent with a role for TILRR in IL-1-mediated signals during atherosclerosis and vascular repair.

**Methods and Results** Atherosclerotic plaques from human and mice ($ApoE^{-/-}$, $LDLR^{-/-}$) were stained with an anti-TILRR antibody and the monocyte marker Mac-3, using two-colour fluorescence. The data show a high level of TILRR expression in areas containing vascular lesions, with low levels in undamaged tissue. Specifically, the experiments demonstrate a correlation of TILRR expression (DyLight 594) within the plaque, with staining for Mac-3 (DyLight 488), in agreement with data from FACS analysis showing high levels of TILRR in the macrophage/monocyte population in atherosclerotic mice. The role of TILRR in development of atherosclerosis was assessed by selective blocking of TILRR function in ApoE $^{-/-}$ mice on a high fat diet. Results showed a significant reduction in plaque development following injection of an antibody targeting TILRR/IL-1RI interaction. These observations are consistent with initial results from screening human samples by qPCR, which demonstrate increased TILRR expression in patients with vascular disease compared to levels in healthy controls. A set of experiments, which used carotid ligation to assess the role of TILRR in vascular remodelling revealed a transient increase in TILRR expression at early times after ligation (2 wks) with only weak staining at later stages (4 wks). Ongoing studies use TILRR KO to further analyse the role of TILRR in vascular repair and disease.

**Conclusion** The data demonstrate an increase in TILRR expression in macrophage/monocyte cell types and are consistent with a role for TILRR in the inflammatory response underlying development of atherosclerosis. Further, the transient increase in expression following carotid ligation suggests a role for TILRR in early stages of vascular repair.

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