**PS-1.3 SDF-1/CXCR4/CXCR7 is pivotal for vascular smooth muscle cell proliferation and chronic allograft vasculopathy (W)**

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**Introduction**: Chronic rejection remains a major obstacle in transplant medicine. Efficient therapeutic strategies are lacking. Recent studies suggest a crucial role of the chemokine SDF-1 on neointima formation after injury.
Here, we investigate the potential therapeutic effect of inhibiting the SDF-1/CXCR4/CXCR7 axis with an anti-SDF-1 Spiegelmer (NOX-A12) on the development of chronic allograft vasculopathy (CAV).

**Methods:** Two established experimental models of CAV were used. Heterotopic heart transplants (HTx) from H-2bm12 to B6 mice and fully MHC mismatched aortic transplants (AoTx) from Balb/c to B6 were performed. Mice were treated with NOX-A12. Control animals received a non-functional Spiegelmer (PoC). Samples were retrieved at different time points between 4-8 weeks after transplantation and analysed by histology, RT-PCR and proliferation assay.

**Results:** Blockade of SDF-1 caused a significant decrease in neointima formation as measured by intima/media ratio (1.0 $\pm$0.1 vs. 1.8$\pm$0.1, $p<0.001$ AoTx; 0.35$\pm$0.05 vs. 1.13$\pm$0.27, $p<0.05$ HTx). In vitro treatment of primary vascular smooth muscle cells isolated from the thoracic aorta with NOX-A12 showed a significant reduction in proliferation as measured by BrdU incorporation (0.42 $\pm$ 0.04 vs. 0.24 $\pm$ 0.03, $p<0.05$). Cytokine levels as TGF-β, TNF- α and IL-6 were significantly reduced under SDF-1 inhibition (3.42$\pm$0.37 vs. 1.67$\pm$0.33, $p<0.05$; 2.18$\pm$0.37 vs. 1.0$\pm$0.39, $p<0.05$; 2.18$\pm$0.26 vs. 1.6$\pm$0.1, $p<0.05$).

**Conclusion:** SDF-1/CXCR4/CXCR7 plays a critical role for the development of chronic allograft vasculopathy (CAV). Therefore, pharmacological inhibition of SDF-1 with NOX-A12 may represent a therapeutic option to ameliorate chronic rejection changes.