Role of p110delta PI3K in the carotid restenosis

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Restenosis is a narrowing of arterial lumen which occurs upon an endothelial arterial damage and represents a limiting long term success of intervention in the arteriopathy disease.
Accumulating evidence indicates that recruitment of inflammatory cells compartment in the site of artery injury is a critical step in the pathogenesis of restenosis. The molecular mechanism of restenosis is still unclear. Several signalling pathways are involved into pathogenesis of intima hyperplasia, including phosphoinositide 3- kinase (PI3K) driven-cascade. PI3K is a lipid kinase family which controls many biological cellular functions such as proliferation, growth, differentiation, migration. Class IA PI3K is divided into three isoforms (p110alpha, p110beta, p110delta). While p110alpha and p110beta are ubiquitously expressed, p110delta is restricted in white blood cells. To investigate the role of p110delta PI3K in the pathogenesis of restenosis we used a mice in which p110delta PI3K has been ($p110\delta^{D910A/D910A}$) catalytically inactivated.
$p110\delta^{D910A/D910A}$ mice show defects in proliferation and differentiation of B and T lymphocyte (Okkenhaug et al., 2002; Ali et al., 2004) and in migration of macrophages (Papakonstantis et al., 2008). $p110\delta^{D910A/D910A}$ mice were subjected to arterial injury and monitored for 30 days. In this work, we report that p110δ inactivation abolishes the inflammatory cell recruitment in an *in vivo* model of artery injury resulting in strong inhibition of restenosis. This approach might have a great pharmacology interest because it suggests the possibility of using an isoform-specific inhibitor of PI3K to prevent the restenosis.

References:

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