PKCε regulates vessel formation by peri-vascular adipose tissue (PVAT) cells

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Vessel formation is crucial in tumour growth and tissue regeneration. Protein kinase C (PKC) ε has a well-known role on hematopoietic and mesenchymal progenitor cell differentiation and proliferation (Gobbi et al. 2013). Although PKCε has a demonstrated role in vascular restenosis, data on PKCε and vascular progenitor differentiation are still lacking. The aim of this work was to study the role of PKCε in vessel formation by adult adipose tissue cell progenitors. We, first, isolated the vessel progenitors from the adipose tissue localized between aortic arch and pulmonary artery of adult mice by collagenase/elastase digestion followed by magnetic immunoselection of Sca1+ cells (Passmann et al. 2008). We, then, tested their capability to form vessels in collagen gels and to differentiate to endothelial and smooth muscle lineage after treatment with PKCε specific activator and inhibitor peptides. The functional experiments showed that the pharmacological activation of endogenous PKCε abrogated tubule formation with a concomitant decrease of smooth alpha-actin (SMA) and platelet endothelial cell adhesion molecule (PECAM) together with the up-regulation of p-PAK1 expression. *In vivo* transient over-expression of PKCε significantly reduced SMA and PECAM expression levels in vessel wall cells. Together our data suggests that PKCε may affect vessel wall remodelling balancing the "phenotypic switching" (Salmon et al. 2013) between the proliferative and the differentiated state of smooth muscle and endothelial progenitor mesenchymal cells.

References

- [1] Gobbi et al. Protein kinase C ϵ in hematopoiesis: conductor or selector? *Semin Thromb Hemost.* 2013 Feb;39(1):59-65.
- [2] Passman et al.(2008). A sonic hedgehog signaling domain in the arterial adventitia supports resident Sca1+ smooth muscle progenitor cells. Proc Natl Acad Sci USA. 105: 9349–9354
- [3] Salmon et al. (2013). KLF4 regulates abdominal aortic aneurysm morphology and deletion attenuates aneurysm formation. *Circulation*; 128: S163-74.

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