the expression of its own receptors, which indicates that OSM might be an important contributor to de novo formation of blood vessels.

doi:10.1016/j.vph.2006.08.242

B12.03

Adherent platelets recruit and induce differentiation of murine embryonic EPCs

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The homing and differentiation mechanisms of endothelial progenitor cells (EPCs) at sites of vascular lesions are unclear. To investigate whether platelets play a role in the recruitment and differentiation of EPCs, we made use of a robust mouse embryonic EPC (eEPC) line that reliably differentiates to a mature endothelial phenotype. We found that platelets stimulate chemotaxis and migration of these murine eEPCs. Further, the substantial adhesion of murine eEPCs on immobilized platelets that occurs under dynamic flow conditions is inhibited by neutralizing anti-PSGL-1 and anti-VLA-4 (α1-integrin) monoclonal anti-bodies but not by anti-CD11b (aM-integrin; MAC-1). Coincubation of murine eEPCs with platelets for 5 days induced differentiation of EPCs to mature endothelial cells as verified by positive von Willebrand factor immunofluorescence and detection of Weibel Palade bodies through electron microscopy. We conclude that platelets may play a critical part in the capture and subsequent differentiation of murine eEPCs at sites of vascular lesions, revealing a possible new role of platelets in neoendothelization after vascular injury.

doi:10.1016/j.vph.2006.08.243

B12.04

Anti-inflammatory peptide approaches for preventing vascular inflammation

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Inflammatory signalling remains a significant problem in the development of atherosclerotic lesions and restenosis, where balloon angioplasty and/or stent delivery can trigger local damage and leukocyte recruitment. It is believed to be the underlying cause for other processes involved in restenosis. It is proposed that by inhibiting local inflammatory processes neointima formation will be reduced. Melanocyte stimulating hormone (MSH) peptides are potent inhibitors of inflammation acting via the melanocortin-1 receptor (MC-1R). Therefore, the aim of this work was to localize the MC-1R on porcine vascular smooth muscle (VSM) and endothelial cells and to investigate whether MSH peptides would inhibit inflammatory signalling by detection of NF-kB. The presence of MC-1R was detected using immunolabelling in both cell types. Immunofluorescence microscopy was also used to investigate the inhibitory potential of a-MSH as determined by the relative position of NF-kB. a-MSH was found to maximally inhibit TNF-a stimulated activity by 55±5% (VSM cells) and 52±8% (endothelial cells) at 10–9 M ($n=3$, $p<0.05$). NF-kB is also known to control the expression of many genes including E-selectin, P-Selectin and ICAM-1. Endothelial cells were therefore stimulated with TNF-a and adhesion molecule expression detected using immunofluorescence microscopy. Flow cytometry was used in order to study the effects of a-MSH on E-Selectin expression. a-MSH was found to inhibit TNF-a stimulated expression in a dose responsive manner from 10–8 M to 10–12 M. Complete inhibition was observed at 10–8 M. This work suggests that the MSH peptides have potential in decreasing inflammation and adhesion molecule upregulation in cytokine stimulated endothelial and VSM cells. This may be of therapeutic value in the prevention of vascular inflammation and in particular in restenosis via the use of drug eluting stents. Work is currently underway to investigate the effect of a-MSH on P-Selectin and ICAM-1 expression, to study the effect of a-MSH in vivo on leukocyte infiltration and NF-kB translocation and to explore the effect of a-MSH on apoptosis.

doi:10.1016/j.vph.2006.08.244

B12.05

Development of pronounced transplant arteriopathy in dark agouti renal allografts transplanted into transgenic Fischer 344 recipient rats: A model to study the role of host-derived progenitor cells in renal TA

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Transplant arteriopathy (TA), a hallmark of chronic allograft nephropathy (CAN), is characterized by uncontrolled smooth muscle cell proliferation resulting in occlusive arterial