145 APPLICATION OF GRAPHENE BASED COATING ON CORONARY ARTERY STENTS

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Coronary artery disease is the leading cause of death worldwide. Stent implantation is the mainstay approach to revascularise stenosed coronary arteries. Bare metal stents were the first stents designed, but presented a restenosis risk of approximately 20% of patients due to restenosis. Subsequently, drug eluting stents were introduced, which, however, introduced late in stent thrombosis. We propose the use of a graphene based coating onto bare metal stents in an attempt to significantly reduce stent associated complications and promote vessel healing. Graphene is a single layer of carbon atoms arranged in a honeycomb lattice. The unique properties of graphene make it an ideal material to use as an implantable device coating: It has a high surface to volume ratio; it is impermeable and atomically smooth and has been shown to exhibit bio-compatible properties. Graphene based dispersions were prepared by liquid phase exfoliation in water. Investigations to coat bare metal stents were undertaken. Dip, spin and spray coating methods were explored. Raman spectroscopy was measured to identify and characterise the coated material. Raman spectroscopy demonstrated spray coating to result in the most uniform and thin graphene based coating. In addition, human endothelial cell adherence and proliferation on the graphene based coating was studied. Hoechst 33 342 and phalloidin stains were used to image the cells under fluorescence microscopy. This revealed the adherence of human endothelial cells to be unaffected by the graphene based coating. In conclusion, spray coating created the most uniform and thin graphene based coating onto bare metal stents. Human coronary artery endothelial cell adherence occurred on the graphene coated stents. Future work is aimed at studying bio- and haemo- compatibility of graphene based coating and their performance in a porcine stent model.

146 FREE FETAL HAEMOGLOBIN IMPACTS FETOPLACENTAL VASCULAR STRUCTURE AND FUNCTION: IMPLICATIONS FOR FETAL GROWTH RESTRICTION

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Introduction In fetal growth restriction (FGR), early placentation defects result in placental insufficiency and vasoconstriction, which cumulate in organ failure at the severe end of the spectrum. In other placental pathologies, including preeclampsia, extracellular free fetal haemoglobin (fHbF) is overproduced, where it inactivates the vasodilator nitric oxide (NO). We have previously shown that excess fetoplacental fHbF also occurs in FGR pregnancy, sequestering NO and evoking vasoconstriction. Here, we explore the further effects of fHbF on fetoplacental endothelium, considering altered angiogenesis, altered vasculoprotection, and an immunological response.

Methods We assessed the fHbF evoked synthesis of the pro-angiogenic and pro-inflammatory cell stress mediators DKK-4, NFkB and FABP-1, produced by human chorionic plate arterial endothelial cells (HPAECs) under conditions of unidirectional laminar flow. Secondly, we studied fHbF-evoked NFÃ□Â°B nuclear translocation using fluorescent microscopy; and the downstream NFkB-actuated cytokine profile (IF1α, TNFα) measured in cell medium and lysate by ELISA. Observations were expanded to assessment of fHbF effects on branching and non-branching angiogenesis of HPAECs grown on Matrigel, and expressed as an average of tubule length multiplied by tubule number as a net measure of angiogenesis. As a correlate, endothelial morphology of fHbF and non-exposed static chorionic artery sections was qualitatively analysed by scanning electron microscopy.

Results A cell stress proteome assay demonstrated that fHbF increased synthesis of DKK-4 (>50% increase from control), NFκB (>50% increase) and FABP1 (>100% increase). A pro-angiogenic effect was further corroborated by assessment of villous angiogenesis on Matrigel, where 0.3 mg/ml fHbF was found to promote branching angiogenesis in HPAECs ($n=5$; $p<0.01$). In a separate study of NFκB-mediated endothelial inflammation, 0.3 mg/ml fHbF-evoked NFkB signal transduction demonstrable by nuclear translocation within 2.5 hours, whilst in controls no evidence of NFkB activation was observed ($n=4$ paired lines). In the fHbF group this was paralleled by increased release of NFκB-actuated cytokines into flow-conditioned medium, IFN1± ($n=7$; control vs. fHbF-exposed at 0.2 mg/ml fHbF median fold change 1.42 (range 1.09–2.2) vs. 1 (0); Wilcoxon $p<0.05$), and for TNFα (control vs. fHbF-exposed at 0.2 mg/ml fHbF median fold-change 1.54 (range 1.09–2.22) vs. 1 (0); Wilcoxon $p<0.05$). Morphologically, fHbF evoked widespread blebbing of the luminal endothelium.

Conclusion fHbF causes aberrant pro-angiogenesis, promotes acute inflammation and loss of structural organisation in fetoplacental endothelium. Our findings are relevant to widening understanding the pathophysiology of FGR and exploring the link between FGR and stillbirth, where overproduction of extracellular fetal haemoglobin could represent a novel therapeutic target.

147 PLATELET COX-1 KNOCKOUT MOUSE AS A MODEL OF THE EFFECTS OF ASPIRIN IN THE CARDIOVASCULAR SYSTEM

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