vasculature than healthy placental sections. Thrombi could be observed in both large conduit and small resistance vessels, with many small vessels completely occluded. In FGR, total fibrin deposition in placental tissue was significantly increased ($p<0.001$), as was fibrin expression specifically located within fetal vessels ($p<0.05$). In contrast, tissue factor levels remained unaltered. Blood samples from fetal growth restricted babies demonstrated increased closure time in platelet function assays (122±12.6 s) compared to healthy controls (90.10±5.46 s), and platelet counts were significantly reduced ($p<0.05$). The red blood cell count, white blood cell count and mean platelet volume were not significantly different.

Conclusions These data indicate that in FGR there is increased platelet activation and thrombosis in fetoplacental vessels, which may contribute to increased vascular resistance through the occlusion of small resistance arteries. Anti-thrombotic therapies, which cross the placenta may therefore be beneficial in FGR to prevent placental thrombosis and improve pregnancy outcome.

190 HAEM AND CARBON MONOXIDE (CO) MODULATION OF LARGE-CONDUCTANCE CA2+-ACTIVATED K+ (BK) CHANNEL ACTIVITY

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Haemolysis is a distinctive feature of certain diseases such as haemorrhagic stroke and sickle cell anaemia. The haem released from red blood cells during haemolysis can build up to toxic levels producing further complications such as cell and tissue damage. Intracellular haem concentration is mainly regulated by haem oxygenase (HO) enzymes which degrade haem to carbon monoxide (CO) and other molecules. Nevertheless, the high haem concentrations during haemolytic diseases can saturate the HO system potentially increasing concentrations of both CO and free haem.

Arterial smooth muscle cells (SMCs) express a variety of ion channels including large-conductance Ca^{2+}-activated K^+ (BK) channels. Activation of BK channels produce spontaneous transient outward currents (STOCs) which hyperpolarize SMCs resulting in cell relaxation and vasodilation. Therefore, BK channels have a negative feedback role to limit SMC contraction. Intracellular haem has been reported to inhibit single BK channel activity whereas CO has been shown to produce stimulatory effects. However, little is known about the effects of haem and CO on STOCs or whole-cell BK currents. The aim of this study is to investigate the effects of haem and CO on STOCs.

SMCs were isolated from the mesenteric artery of male Wistar rats. Single BK channel currents and STOCs were recorded using excised (inside-out) and perforated whole-cell patch techniques respectively. CO was applied using CO-releasing molecule 3 (CORM-3) which was prepared before each use. Data are presented as mean± SEM and statistical analyses were performed using paired and unpaired Students T-test as appropriate. Consistent with previous reports, application of haem (100 nM) to the cytoplasmic side of inside-out patches reduced BK channel activity to $4.7 \times 10^{-3} \pm 3.4 \times 10^{-3}$ times that of control ($n=4$, $p<0.05$) whereas CORM-3 (30 μM) increased channel activity by 5.7±0.4 fold ($n=8$, $p<0.05$) at low $[Ca^{2+}]_i$ (300 nM). Surprisingly, during perforated whole-cell recordings, extracellular haem (5 μM) increased STOC amplitude by 16% (1.16±0.04, $p<0.05$, $n=3$). This effect was further enhanced in the presence of the HO-inhibitor, zinc protoporphyrin-IX (ZnPP-IX) (1.4±0.1, p 0.01, $n=4$). Extracellular application of CORM-3 (30 μM) increased STOC frequency (1.81±0.26, $p<0.01$, $n=8$) without significantly affecting STOC amplitude.

In summary, the stimulatory effects of haem on STOCs contradict excised patch data. This suggests that the effects of haem might be influenced by intracellular components which are absent in excised patches. Results from ZnPP-IX studies further imply that the effects of haem on STOCs might be mediated independent of its degradation product, CO. Therefore, information gained from further studies could improve our understanding of the vascular changes that occur during haemolytic diseases.

191 ROLE OF MIR-214 IN ANGIOTENSIN II INDUCED HYPERTENSIVE HEART DISEASE

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Background Cardiac dysfunction is one of the hallmarks of hypertension. It is characterised by cardiac fibrosis, diastolic dysfunction and development of heart failure. The mechanisms of hypertensive heart disease are not fully understood. Recent studies suggest a role of miR-214 in regulation of fibrosis. Thus, the aim of this work is to investigate the role miR-214 has in the cardiac sequelae of hypertension.

Methods Hypertension was induced in three month old miR-214 knock out (KO) and wild type (WT) littermates using 490 ng/kg/min angiotensin II (Ang II) for 14 or 28 days ($n=4$–6). Blood pressure was monitored by tail cuff plethysmography. Cardiac fibrosis was assessed by picrosirius red and Massons trichrome staining. Mir214 expression was assessed by Taqman and *in situ* hybridisation (ISH). Cardiac function was assessed by echocardiography. Effects of Ang II on fibrosis genes was studied in primary cardiac fibroblasts.

Results 14 day Ang II infusion caused 4-fold induction of miR-214 in the left ventricle of C57bl/6 mice ($p<0.001$) which was confirmed by ISH. Loss of miR-214 was associated with increased cardiac fibrosis in picosirius red (2.8% ±0.52 vs. 4.8%±0.7; $p<0.005$) caused by Ang II, without effect on blood pressure. This was associated in a significant up-regulation of *COL1A1* mRNA compared with their WT littermates ($p<0.01$). Echocardiography revealed enhanced development of ventricular wall thickening and diastolic dysfunction in mir214 KO when compared to WT mice (E/A ratio: 1.79±0.39 vs 0.59±0.04; $p<0.05$). In contrast to *in vivo* observations, *in vitro* fibroblast studies show that KO fibroblasts showed significantly reduced induction of *COL1A1* ($p<0.05$) and *COL3A1* ($p<0.05$) compared with WT fibroblasts upon Ang II and IL-17 suggesting that involvement of miR-214 in cardiac dysfunction is not directly modulated by the effects in fibroblasts but through other mechanisms that need to be further addressed.