progenitor cells in Matrigel were applied to the adventitia of the injured femoral artery, REP+ cells were observed in the intimal 24 hours post-operation, which significantly enhanced neointimal lesions at 2 weeks. This increased neointimal lesion was rescued by pre-treatment of Sca-1+ cells with leptin antagonist CYT-566. In addition, when wild-type Sca-1+ progenitor cells were delivered to the adventitia of the injured artery in leptin receptor deficient mice, a significant increased neointimal formation was observed at 2 weeks, indicating crucial roles of leptin receptor and Sca-1+ progenitor cells in vascular remodelling.

Conclusions- Levels of leptin in both the vessel wall and the circulation are upregulated after vessel injury, leading to the migration of Sca-1+ progenitor cells that enhances neointimal formation.

168 CARDIOPROTECTIVE ROLE OF FINGOLIMOD IN ISCHEMIA-REPERFUSION INJURY BY ACTIVATION OF AKT/ERK PATHWAYS IN RAT MODEL

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Background and purpose Ischaemic Heart Diseases (IHD) are the most common cause of morbidity and mortality. Incidence and prevalence are continuously growing. There is an escalating risk for revascularisation or resuscitation in patients with IHD. Recently, it has been reported that a sphingosine 1-phosphate receptor agonist play an anti-apoptotic and anti-inflammatory role in the ischemia-reperfusion injury.

Objectives The aim of our study is to investigate the cardioprotective effects of sphingosine 1-phosphate receptor agonist fingolimod (FTY720) on global ischemia-reperfusion injury related to the cardiac surgery.

Methods In our experimental study, global ischemia-reperfusion was achieved by cardiopulmonary bypass by cardioplegic arrest on ventilated male Sprague-Dawley rats (300–350 g). The global ischaemic period lasted 10 min in the cardioplegic arrest while reperfusion times were maintained for 60 min and 24 hours. ECG monitoring was done using AD instrument and using Millar catheter, heart rate, systolic and diastolic pressures were recorded and mean arterial pressure was calculated. The statistical significance was considered at P 0.05.

Results The myocardial protection was observed in the group treated with Fingolimod as compared to control groups. Reduced frequency of apoptotic cells and inflammatory mediators were found in the treated group. The level of adenylates was preserved in the treated group as compared to controls (94%, 61% respectively)(p0.001). Reactive Oxygen Species (ROS) were attenuated in the fingolimod-treated group. Fingolimod treatment improved systolic and diastolic ventricular pressures and contractility strength (p0.005).

Conclusions The intravenous administration of fingolimod in global ischemia-reperfusion was cardioprotective. Fingolimod cardioprotection appears to be mediated through preservation of high energy phosphates, reduction in oxidative stress, inhibition of apoptosis and inflammation leading to improved cardiac functions.

169 DEVELOPING CAPTURE ASSAYS TO MEASURE CIRCULATING CRP/OXIDISED LOW DENSITY LIPOPROTEIN COMPLEXES IN PATIENTS UNDERGOING CARDIOPULMONARY BYPASS AND EXAMINING USE OF CRP/OXIDISED LOW DENSITY LIPOPROTEIN COMPLEXES AS A BIOMARKER OF ATHEROSCLEROSIS

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Background Atherosclerosis is a disease of global importance. It is a systemic chronic inflammatory disease with a complex aetiology. LDL is primarily oxidised in the subendothelial space, as plasma antioxidants protect circulating LDL from oxidation. However, small amounts of oxidised LDL (oxLDL) have been detected in plasma. Modified LDL is thought to circulate as part of an immune complex; these immune complexes may also include CRP, complement and IgM antibodies. This project aims to develop a capture ELISA to measure oxLDL/CRP complexes in circulation, to help better characterise circulating immune complexes and explore potential use of oxLDL/CRP complexes a biomarker of atherosclerosis.

Methods A CRP/oxLDL capture ELISA was developed using LO1, a novel mAb specific to oxLDL. Plasma samples were obtained from patients undergoing cardiopulmonary bypass at four different timepoints. Levels of oxLDL, CRP and oxLDL/CRP complexes were determined in patient plasma using capture assays developed during this study.

Results OxLDL levels show an uptrend from baseline to 60mins, followed by significant reduction at 300mins compared to baseline (0.506 ± 0.078 vs 0.456 ± 0.035; $p=0.0138$). CRP concentration initially declines from baseline up to 120mins (1.918 ± 0.915 vs 1.136 ± 0.599; $p=0.0009$), after which levels rise between 120 min and 300 min (1.136 ± 0.599 vs 1.782 ± 0.65; $p=0.0026$). There is no significant difference in levels of CRP/oxLDL complexes across all timepoints.

Conclusion It is possible to measure CRP/oxLDL complexes in plasma. Pro-inflammatory events such as cardiopulmonary bypass are associated with changes in levels of oxLDL and CRP, while oxLDL/CRP levels remain unchanged.

170 FETUIN-A INDUCES NOX1-ROS-DEPENDENT VASCULAR DYSFUNCTION PARTIALLY THROUGH TOLL LIKE RECEPTOR 4 ACTIVATION

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Fetuin-A (FetA) is a plasma glycoprotein important for the regulation of calcium and phosphate homeostasis. It is also an agonist to toll-like receptor 4 (TLR4) and is related to insulin resistance and inflammation. FetA has also been associated with endothelial dysfunction, which is regulated by oxidative stress. Mechanisms whereby FetA influences vascular function are unknown. We hypothesised that FetA through TLR4 and ROS production induces vascular dysfunction. Mesenteric