



Abstract BS4 Figure 1

**BS5** **DIABETIC CARDIOMYOPATHY IS ASSOCIATED WITH LOSS OF ENDOTHELIAL GLYCOCALYX IN CORONARY MICROVESSELS AND ANGIOPOIETIN 1 RESTORES ENDOTHELIAL GLYCOCALYX AND CORRECTS CARDIAC FUNCTION**

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**Introduction** Endothelial glycocalyx (eGlx) contributes to the microvascular permeability barrier and its dysfunction correlates with albuminuria in diabetic nephropathy. Albuminuria is a potent risk factor for cardiovascular disease. We therefore hypothesised that coronary microvascular eGlx damage also occurs in diabetic cardiomyopathy (DCM).

**Methods** Diabetes was induced in FVB mice with streptozotocin (STZ). DCM was assessed with echocardiography by E/A ratio. A group of diabetic FVB mice received Angiotensin 1 (Ang1) after DCM development.

**Results** FVB mice developed DCM at 7 weeks post STZ injection. Labelling with MAL-I, a specific lectin that binds to eGlx, was reduced in diabetic heart capillaries (DCM vs. ctrl: 1.64±0.27 vs. 2.70±0.27). Electron microscopy of diabetic heart capillaries showed decreased eGlx depth (DCM vs. ctrl: 14.54±0.79 vs. 27.88±5.82nm), increased perivascular space (DCM vs. ctrl: 2.08±0.22 vs. 0.54±0.11fold) and thickened endothelial cells (DCM vs. ctrl: 0.30±0.04 vs. 0.22±0.01µm).

Partial depletion of eGlx in rat hearts with the combination of heparanase and chondroitinase led to decreased cardiac output (enzymes vs. ctrl: 63.47±10.14% vs. 91.68±9.82%).

Ang1 improved diastolic function of FVB mice with DCM (DCM vs. DCM+Ang1: 1.05±0.08 vs. 1.35±0.09 fold relative to pre-treatment). In Ang1-treated diabetic mice, eGlx thickness in heart capillaries (DCM vs. DCM+Ang1: 13.87±0.87 vs. 24.55±2.02nm) and eGlx coverage (DCM vs. DCM+Ang1: 48.08±3.07% vs. 82.44±5.43%) were improved, and

the increased perivascular space due to oedema in DCM normalised (DCM vs. DCM+Ang1: 2.08±0.13 vs. 0.23±0.03fold). **Conclusion** We have shown DCM development is associated with eGlx damage and that injury to eGlx impairs cardiac function. Recovered heart function with Ang1 treatment parallels reversal of eGlx loss. As such, correction of eGlx damage may have therapeutic potential for DCM and other diabetic vascular complications.

**Conflict of interest** None

**BS6** **ENDOTHELIAL-SPECIFIC ERG DELETION LEADS TO DRAMATIC REDUCTION IN CARDIOPULMONARY FUNCTION**

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Heart and lung function work in partnership to maintain cardiovascular and tissue homeostasis. Endothelial (EC)-specific transcription factor ERG is a master regulatory of EC lineage and homeostasis expressed in all vascular beds. We have shown that loss of ERG expression leads to endothelial dysfunction and tissue fibrosis in mouse. Furthermore, we have established ERG loss as a hallmark of patients with chronic disease, such as atherosclerosis and end-stage liver disease. In this study we aimed to determine the functional impact of chronic EC dysfunction on the cardiopulmonary system.

**Methods** 6-week-old VEC-iCre Erg-fl/fl mice were treated with tamoxifen i.p. to induce EC-specific deletion (ErgiEC-KO); mice were profiled longitudinally for 30 days compared to littermate control mice (Ergfl/fl). We assessed cardiac function by electrocardiography (ECG), recorded in conscious mice twice a week using the ECGenie platform, and echocardiography (Echo) at day 14 and 30. Tissue structure and endothelial profiling was assessed by immunohistochemistry in both heart and lung tissue. In a second set of experiments we treated mice ErgiEC-KO with tamoxifen for 14 days prior to trans-