Results: Expression analysis during CF differentiation showed the cardiac developmental genes TBX20 and GATA4 were upregulated in the CPC stage, indicating progression down a cardiac specific lineage. HSPG2 expression increased throughout the differentiation, leading to hiPSC-CFs with an expression level similar to that of primary CFs. Activation of hiPSC-CFs for 72 hours with 10ng/ml TGFβ induced the expression of αSMA^{+} stress fibres, indicating that a myofibroblast fibrotic phenotype could be modelled. Screening of the CRISPR/Cas9-targeted hiPSCs identified heterozygous clones with reduced perlecan mRNA (~50% by qPCR), and protein expression by immunofluorescence.

Discussion: Our results show that we can successfully model cardiac fibrosis through the differentiation and activation of hiPSC-CFs. Our CRISPR/Cas9 system successfully targeted the HSPG2 gene, creating clonal hiPSC lines with reduced expression. Our future work will use these perlecan targeted hiPSC lines within our model system to investigate the regulatory role of perlecan during cardiac fibrosis.

Hyaluronan derived from the limbus is a key regulator of corneal lymphangiogenesis

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Introduction: Corneal lymphangiogenesis and angiogenesis leads to the loss of corneal transparency. We have recently shown that in the cornea hyaluronan (HA) is present primarily in the limbal region. We investigated whether HA could play a role in regulating corneal lymphangiogenesis.

Materials and Methods: Wild-type (wt) and hyaluronan synthase (HAS) knockout mice—specifically combined *Has1*$^{-/-}$ and *Has3*$^{-/-}$ null mice (*HAS1*$^{-/-}$;*HAS3*$^{-/-}$) and conditional *Has2* knockout mice (*HAS2*$^{\Delta/\Delta CorEpi}$), were used. The mice were subjected to injury, alkali burn or suture placement, to investigate the role of HA on corneal lymphangiogenesis. Corneal buttons were also obtained from different developmental time-points to study the role of HA in lymphatic vessel development. The corneas were analysed by whole mount immunohistochemistry and entire corneas were imaged under an LSM 800 confocal microscope using the both the z-stack and tiling mode. Primary lymphatic vessel endothelial cells from human dermis (hDLECs) and lymph node (hLLECs) were used for tube formation assay and cell proliferation assay in vitro.

Results: After injury both wild-type and *HAS1*$^{-/-}$;*HAS3*$^{-/-}$ mice presented both an increase in HA expression and lymphangiogenesis. Interestingly, lymphatic vessels extended exclusively into HA rich areas. In stark contrast, *HAS2*$^{\Delta/\Delta CorEpi}$ mice did not upregulate HA synthesis after injury and, in turn, did not present lymphangiogenesis. Our developmental studies revealed first HA is expressed in the corneal limbus and thereafter lymphatic vessels invade this region. Our in vitro studies corroborated our in vivo data, with both HA increasing the proliferation and tube formation ability of hDLECs and hLLECs.

Discussion: HA regulates corneal lymphangiogenesis, both during development and after injury. These findings raise the possibility that therapeutic blockade of HA-mediated lymphangiogenesis could be used to reduce corneal scarring and also prevent rejection after corneal transplantation.

A novel model of nephrotic syndrome results from a point mutation in Lama5 and is modified by genetic background

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Introduction: The laminin α5 chain is essential for embryonic development and, in association with laminin β2 and laminin γ1, is a major component of the glomerular basement membrane (GBM). Variants in *LAMA5* were recently identified in children with nephrotic syndrome. We have identified a novel missense variant (E884G) of *Lama5* in the uncharacterized L4a domain of LAMA5 where homozygous mice develop massive proteinuria.

Materials and Methods: Mice were originally identified as from a phenotype-driven screen of ENU mutagenized mice and subsequently backcrossed. Mice underwent biochemical analysis of plasma and urine. Histological and