Pierson’s Syndrome is a congenital nephrotic syndrome with ocular manifestations that was described in 2004. The mutation is a null mutation. More recently, a wide array of ophthalmic findings have shown that the β2 domain of laminin, they are thought to interact with laminin polymerization; we have recently shown that the transition between laminin and netrin1 & 3 more similar to the α chain. As netrins have homology with the LN chain: 5-16 laminin isoforms. Laminins bind to cell surface via their LG domains including, Bruch’s, the ILM and the lens capsule. At E13, netrin-4 was deposited in the corneal BM including, Bruch’s, the ILM and the lens capsule. At E13, netrin-4 was deposited in the corneal BM. Aberrant proliferation is seen in the Ntn4 null animal.

Wild Type

Ntn4-/-

PhosH3

Dapi

Ntn4 Null Cornea Develops Normally But is Hyperplastic

Epithelial Proliferation Is Upregulated in the Ntn4 Null Animal

Aberrant Proliferation Is Seen in β2−/− γ3−/− β2−/−γ3−/− animals

β2−/− γ3−/− β2−/−γ3−/− Lambs have a null phenotype with altered corneal development and ocular dysmorphogenesis. The iridial angle is closed in the Lamb2/Lamc3 null along with iridial synechia and abnormal iris size. The iridial angle is closed in the Lamb2/Lamc3 null along with iridial synechia and abnormal iris size.

Whole mounts of cornea from wild type and Ntn4 null animals were studied in whole mount (left) and radial sections. The cornea of the Lamb2 null animals is consistently thicker than that of any of the other null combinations. Whole mounts of cornea from wild type and Ntn4 null animals were studied in whole mount (left) and radial sections. The cornea of the Lamb2 null animals is consistently thicker than that of any of the other null combinations.

Wild Type

Ntn4-/-

Epithelial Layer of the Cornea in Laminin Mutants

β2−/−

γ3−/−

β2−/−γ3−/−

Conclusions:

β2−/− γ3−/− corneas are thicker than wild-type; most of which occurs in the stroma. Lamb2 mutant basal epithelial cells are dysmorphic. In the Lamb2 mutants, endothelial cells are more densely packed than wild type or Lamc3. There is increased proliferation in the Lamb2/Lamc3 null and Ntn4 null animals. The iridial angle is closed in the Lamb2/Lamc3 null along with iridial synechia and abnormal iris size (not shown).

Together with data on the retina, the Lamb2 and Lamb2/Lamc3 mice recapitulate the human Pierson phenotypes. These data suggest that laminins are important during many aspects of ocular development.

In addition these suggest that laminins and netrins may be useful as agents to promote corneal wound healing.

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