Dr J.M. Collinson
University of Aberdeen

In collaboration with Dr John D West (Univ. Edinburgh) and Prof Deborah Henderson (Univ. Newcastle).

Student: tba

The roles of the planar cell polarity genes in a classical anatomical system: the cornea

The cornea. The apparent simplicity of the vertebrate belies a surprisingly dynamic cellular organization. Direct observation of transgenic corneal epithelial cells has revealed centripetal migration from the edge of the corneal epithelium to the centre, throughout adult life. Female mice carrying an X-linked LacZ transgene on a housekeeping promoter (*XLacZ*) demonstrate striping patterns of □-gal expression in the adult corneal epithelium often with a swirling formation at the centre.

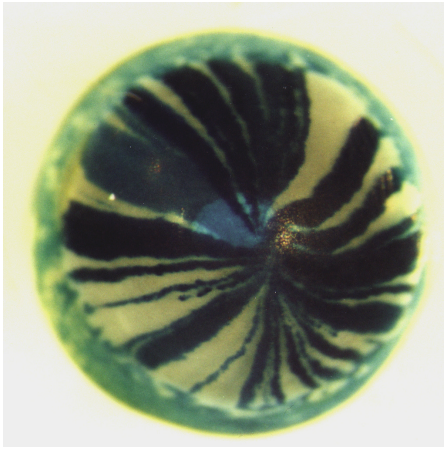

Figure 1. Patterns of radial cell migration in the adult mouse corneal epithelium. Revealed by X-Gal staining of LacZ mosaic mice.

Nothing is known about the guidance cues that drive this cell migration, but the patterns are disrupted in corneal diseases such as aniridic keratitis, which can lead to blindness, and also after corneal wounding. The planar cell polarity (PCP) pathway is a variant of non-canonical Wnt-signaling that is known to give directionality to epithelial cells in embryonic development. For example, PCP genes are required for closure of the neural tube and development of the inner ear. Less is known about roles of PCP pathway genes in the adult, but for the first time we have identified expression of multiple PCP core component genes in the adult corneal epithelium, and it seems likely that they control the cell migration.

This project will determine: **a)** what are the roles of planar cell polarity (PCP) genes in controlling dynamic cellular orientation in the cornea and **b)** whether manipulation of PCP components could be used to accelerate ocular surface regeneration. We will do this pharmacologically, and also genetically by creating mutations of PCP genes in experimental corneas.

We aim to understand fundamental processes of cell migration that generate classical anatomical structures and answer unresolved questions about the roles of PCP genes once embryogenesis has finished. Furthermore, we will be doing this in a clinically relevant model where there is a realistic expectation, through this work, to understand and ameliorate disease processes.