Annual Report
Title: The role of gliosis in advanced retinal degeneration
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Development of photoreceptor replacement therapies for inherited retinal degeneration assumes that the retinal neurons that carry signals to the brain remain intact well after the loss of all photoreceptors. The central aim of this project was to characterize the changes that occur in the inner retina (ganglion cells) at late stages of retinal degeneration and in particular determine the role that support cells called glial cells, play in maintaining ganglion cell integrity.

Our work revealed that overall, ganglion cells remain remarkably intact at late stages of retinal degeneration, even when there are signs of change in other neurons in the retina. However, there are shifts in the way neurons communicate with ganglion cells. For example, the level of excitatory input to ON types of ganglion cells is reduced and the level of inhibitory input is reduced in OFF types of ganglion cells. This information may have important implications in how scientists design electronic retinal implants.

Our second series of experiments was aimed at determining whether support cells contribute to the inner retinal changes observed. Our results, using a novel mouse model of retinal degeneration show that glial cells undergo significant changes, that on the one hand influence the health of cone photoreceptors, and on the other hand are associated with early formation of new neurons. These results suggest that at very late stages of degeneration there are reparative mechanisms initiated within the retina that could, if targed pharmacologically, be important in replacing some photoreceptors.

In summary, this project unearthed some very important fundamental information that will be used by those developing electronic implants. We published several papers (documented below) and have several more in the preparation.

Publications:

Kalloniatis M[C], Loh C[C], Acosta M[C], Tomisich G[C], Zhu Y[C], Livison-Smith L[C], Fletcher EL, Chua J[C], Sun D[C], Arunthavasothy N[C] (2013) Retinal Amino acid neurochemistry in health and disease. Clin Exp Optom 96:310-332

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O'Brien EE[S], Greferath U[P], **Fletcher EL**[SA] (2014) The effect of photoreceptor degeneration on ganglion cell morphology. J Comp Neurol 522:1155-1170

Zhu Y[C] Mistra S[C], Nivson-Smith L[C], Acosta ML[C], Fletcher EL, Kalloniatis M[C] (2013) Mapping cation entry in photoreceptors and inner retinal neurons during early degeneration in the P23H-3 rat retina. Vis Neurosci 30:65-75

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Chua J[C], Nivison-Smith L[C], Fletcher EL, Trenholm S[C], Awatramani G[C], Kalloniatis M[C] (2013) Early remodelling of Muller cells in the rd/rd mouse model of retinal dystrophy. J Comp Neurol 521:2439-2453 Contribution=10%