



# CNS STABILITY & DEGENERATION

Group Leader: Dr Jan Provis

Our work is focused on aspects of neural and glial cell biology in the mammalian central nervous system (CNS) that affect its long-term stability. The CNS has a very high metabolic rate, required to maintain function; deficiencies in metabolism result in loss of neural function and ultimately lead to degeneration. Our studies investigate diseases of CNS degeneration, in the light-sensitive retina (eg, retinitis pigmentosa), cerebral cortex (including Alzheimer's disease), and mechanisms regulating morphogenesis and maintenance of cone photoreceptors in primates.

In *retinitis pigmentosa* an individual experiences a gradual loss of vision in the peripheral visual field, initially leaving central vision relatively unaffected, as shown. Eventually, however, central vision is also lost. Understanding the mechanisms of visual loss of this kind, and developing strategies to prevent its progression, is one of the major goals for the research done in CSD.

## HIGHLIGHTS

- The Group joined other vision scientists from the ANU and the Universities of Sydney, Queensland and Western Australia, in a successful application for an ARC Centre of Excellence in Vision Sciences, which will frame and shape the Group's next five years.
- The results of detailed analysis of expression patterns of fibroblast growth factors (FGFs) in the developing primate retina, which have taken several years to finalize, have been published this year. For the first time, we identify molecular factors involved in the narrowing and elongation of cone photoreceptors at the primate fovea. Foveal cones are longer and thinner than elsewhere in the retina, facilitating their close-packing and providing the structural basis for high-resolution vision.
- Two major papers on the neuropathology of Alzheimer's disease. The work suggests that an important element of brain aging is the breakdown of cerebral capillaries, each breakdown producing a small bleed, detectable only post-mortem using techniques developed by Dr Cullen. The frequency of these micro-haemorrhages increases with age, and increases again with dementia. Further, each micro-haemorrhage is the site of a plaque, the degenerative formations associated by others with Alzheimer-like dementias. The work suggests that age-related dementias, such as Alzheimer's disease, are the result of age-related fragility of the cerebral microvasculature.
- Work testing the oxygen-toxicity hypothesis of retinal degeneration proceeded on several fronts. A particular innovation was work analyzing gene expression in the retina challenged with hyperoxia. This showed an unexpected biphasic response – initial enhancement of retinal function, followed at two weeks by the expected degenerative changes. Gene expression, enzyme function and retinal function assays are being used to explore the early, enhancing effects, which may offer acute therapeutic potential.