Proposed Research Activity

Identification and characterization of the common mechanisms leading to retinal ganglion cells degeneration in diabetic retinopathy and glaucoma.

Diabetic retinopathy (DR) is the most common retinal vascular disease and is the leading cause of blindness among young adults in developed countries (1).
The cellular/molecular dysfunctions behind the development of DR are poorly understood and for this reason there is presently no way to prevent the disease that can only be aggressively treated (laser photocoagulation or intravitreal anti-VEGF injectons) once it reaches the final, proliferative stage.
Recent studies have shown that, in case of diabetes, early neuronal abnormalities (degeneration and death of retinal ganglion cells (RGC)) precede the development of DR (2), a finding that reminds the pathogenesis of glaucoma, a neurodegenerative disease characterized by the progressive death of RGC and consequent irreversible visual loss (3). The link between DR and glaucoma is supported by the evidence that diabetic patients are three times more likely to develop glaucoma (4). Whether RGC degeneration in DR and glaucoma follows common or different functional and molecular pathways is unknown.
Aim of this project will be to clarify, taking advantage of specific animal models, whether RGC viability is differently affected by DR and glaucoma and if the simultaneous presence of both diseases gives rise to an increase of cell suffering/death when compared to DR or glaucoma alone.
The evolution of both ocular diseases and in particular the change of thickness of the RGC layer along time will be monitored in vivo by ophthalmic coherence tomography (OCT). At the end of the protocol, the animals will be sacrificed, the retinas will be extracted and organized as flatmounts (to count RGC, evaluate the apoptosis, inflammation, etc) or used for evaluation of gene expression.
The results of this study will allow to clarify whether RGC degeneration in DR and glaucoma share a common pathway and, consequently, whether DR may benefit (primary prevention) from an early neuroprotective treatment as presently done in case of glaucoma.

1. Kempen JH, O'Colmain BJ, Leske MC, et al., Eye Diseases Prevalence Research Group, The prevalence of diabetic retinopathy among adults in the United States, Arch Ophthalmol, 2004;122:552–63.
2. Martin, P.M., Roon, P., Van Ells, T.K., Ganapathy, V., Smith, S.B., 2004. Death of retinal neurons in streptozotocin-induced diabetic mice. Invest. Ophthalmol. Vis. Sci. 45, 3330–3336
3. Quigley HA. Neuronal death in glaucoma. Prog Retin Eye Res. 1999;18:39–57.
4. Wong VH, Bui BV, Vingrys AJ. Clinical and experimental links between diabetes and glaucoma. Clin Exp Optom. 2011 94:4-23.