Title: Targeting microglia to treat retinal degenerative diseases?

Author: António Francisco Ambrósio

Affiliations:
1- Institute for Biomedical Imaging and Life Sciences (IBILI), Faculty of Medicine, University of Coimbra, Portugal
2- CNC.IBILI Consortium, University of Coimbra, Portugal
3- Association for Innovation and Biomedical Research on Light and Image (AIBILI), Portugal

Abstract:
Retinal degenerative diseases, such as diabetic retinopathy and glaucoma, are leading causes of vision loss and blindness worldwide. These chronic diseases have no cure, the treatments available are not abundant and are not very effective. Diabetic retinopathy is considered a microvascular disease, and its hallmark is the breakdown of blood-retinal barrier. However, retinal neural cells, and particularly retinal ganglion cells (RGCs), can be also affected. Glaucoma is characterized by the degeneration of RGCs and atrophy of optic nerve (composed by axons of RGCs), and elevated intraocular pressure (IOP) is the major risk factor to develop this disease. In the last decade, increasing evidence has demonstrated that low-grade chronic inflammatory processes have a key role in retinal dysfunction and degeneration. Microglial cells, the immune cells of the central nervous system, have been implicated in the neuroinflammatory processes occurring in the retina, thus contributing to disease progression. Our main goal has been to identify targets in retinal microglia in order to control their reactivity. We have been using in vitro and animal models of retinal degenerative diseases.

We have been identifying distinct molecules in retinal microglia, namely neuropeptide Y receptors, adenosine A2A receptors, sodium vitamin C co-transporter-2 (SVCT-2) and Src kinase, which can be targeted to inhibit microglia reactivity. We also found evidence that by controlling microglia activation, thus inhibiting the release of pro-inflammatory cytokines, we are able to rescue RGCs from degeneration triggered by exposure to increased hydrostatic pressure, which mimics increased IOP.

Altogether, our findings, using in vitro and animal models, indicate that microglial cells can be targeted by different ways to prevent retinal neuronal degeneration, which may open new avenues to translate these findings into new and effective therapies for the treatment of retinal degenerative diseases characterized by an inflammatory component.