**Exploring Vision-protecting Agents from Australian Propolis**

**Yipeng Lin1**, Rujee Duke1, Colin Duke1, Fanfan Zhou1.

Molecular Drug Development Group, Sydney Pharmacy School, The University of Sydney1, Sydney 2006, Australia

**Background and aims.** Oxidative stress is a major pathogenic factor in retinal degenerative diseases such as dry ge-related macular degeneration (AMD) and diabetic retinopathy (DR), primarily through its detrimental effects on Müller glial cells and the retinal pigment epithelium (RPE). These vision-threatening conditions currently lack effective treatments. Although numerous antioxidant compounds have been evaluated using single-stimulus oxidative stress models, most have failed to demonstrate clinical efficacy. This gap is largely attributed to the oversimplified nature of these models, which fail to capture the complex, multifactorial oxidative stress environment in the retina. This study aims to establish dual oxidative stress models—incorporating both light-induced and chemical stimuli—and utilize them to evaluate the antioxidative potential of compounds derived from Australian propolis.

**Methods.** Human Müller and RPE cell lines were used to establish the dual oxidative stress models. A total of 71 compounds isolated from Australian propolis and their derivatives, were screened for retinal protective effects using cell viability assays. Lead compounds identified from the initial screening were further evaluated through reactive oxygen species (ROS) assay and cell death analysis. Western blotting was conducted to investigate key signalling pathways involved in the cellular response to oxidative stress and compound treatment.

**Results.** Two compounds, UK6 and C11, exhibited the most potent protective effects against dual oxidative stress in both Müller and RPE cells. Mechanistic investigations revealed that UK6 primarily attenuates necrotic cell death in Müller cells, whereas C11 enhances Nrf2-mediated antioxidant signalling in RPE cells. Both compounds significantly reduced ROS accumulation and improved cell viability under oxidative stress conditions.

**Conclusion.** UK6 and C11 represent promising candidates for the development of novel antioxidative therapies targeting retinal degenerative diseases. Their demonstrated efficacy in dual-stimulus oxidative stress models underscores their potential for retinal protection under complex pathological conditions, such as dry AMD and diabetic retinopathy.

**References:**

1. Li, Y., et al., *Ginkgo biloba extracts protect human retinal Muller glial cells from t-BHP induced oxidative damage by activating the AMPK-Nrf2-NQO-1 axis.* J Pharm Pharmacol, 2023. **75**(3): p. 385-396.

2. Li, Y., et al., *Procyanidin B2 and rutin in Ginkgo biloba extracts protect human retinal pigment epithelial (RPE) cells from oxidative stress by modulating Nrf2 and Erk1/2 signalling.* Exp Eye Res, 2021. **207**: p. 108586.