RETINA australia

PHARMACEUTICAL COMPOUNDS

Neuroprotection

Certain drugs are being developed that can protect or slow the damage photoreceptors in conditions like retinitis pigmentosa and age-related macular degeneration (AMD). The photoreceptor cells located the back of the retina are specially designed types of nerve cells; they convert light into electrical energy and pass this signal to other nerves, and eventually to the brain where vision is perceived.

In inherited retinal degenerations the photoreceptors degenerate due to a variety of gene defects within the cell itself, leading to the build-up of waste products which slowly damage the cell and cause it to die. In conditions like AMD the photoreceptors become damaged because the support structures surrounding the photoreceptors become damaged. While gene therapy strategies are dependent on knowing the precise gene that is affected, the advantage with these novel drug therapies is that they are independent of the causative gene for the degeneration.

These neuroprotective therapies can be broadly broken down into two main areas; anti-apoptotic agents and antioxidant compounds.

Anti-Apoptotic Agents

Apoptosis is the term used to describe how cells decide to switch off and die. Apoptosis is a fundamental and essential process in the body. For example, in the womb, our fingers and toes are connected to one another by a sort of webbing. Apoptosis is what causes the webbed cells to die, leaving us with 10

separate digits. However, sometimes apoptosis occurs abnormally, and in retinal degenerations it can lead to the death of the important photoreceptor cells that are required for light and vision. Many compounds are currently being investigated for their “anti-apoptotic” properties.

An example is a recent technology involving the encapsulation of human cells that are genetically modified to secrete ciliary neurotrophic factor (CNTF). CNTF is a human growth factor that preferentially stimulates and protects human cells. This implant is currently in human clinical trials and initial results have been very promising. This is a long-term study and these patients will be monitored for several years to determine the efficacy of this treatment.

Antioxidants

There are many chemicals that can act as antioxidants in the eye. Some can be taken orally (like vitamin supplements), and others which must be delivered directly to the eye (e.g. in the form of eye drops). There is strong basic science support for the value of lutein, zeaxanthin, and omega-3 fatty acids in promoting eye health for patients with AMD, and the scientific and medical community are carefully analysing the results of a large clinical trial called age-related eye disease Study 2 (AREDS2) that was published in 2013-14.

New drugs and combinations of drugs are also being investigated as antioxidants. Recent work from the University of Alicante and others has demonstrated that a compound known as TUDCA is a potent antioxidant. TUDCA is found in high quantities in the bile of black bears and has been synthetically available since 1954. Mice treated with TUDCA demonstrate lower numbers of photoreceptor cell death compared to controls. TUDCA also prevents the reorganisation of the retina seen in the late stage of retinal injury and maintains the network of blood vessels of the retina in a mouse model of RP. Similarly, dietary supplementation with another compound known as Safranal, which is an extract from saffron, and noted for its antioxidant properties slows photoreceptor cell degeneration and suggests that Safranal could potentially be useful to retard retinal degeneration in patients with RP.

Another example is a recent clinical trial led by Newcastle University (Great Britain) that has shown that the potent antioxidant, Idebenone, improved the perception of colour in patients with Leber's hereditary optic neuropathy (LHON). The trial sponsor Santhera Pharmaceuticals received approval in 2015 for the use of its drug Raxone ® for the treatment of people with LHON.