A host of retinal degenerations, including many types of retinitis pigmentosa, follow a pattern of rod loss followed by cone loss. The rod loss may take many years, causing problems with night vision and peripheral visual field constriction. Only after significant rod loss occurs does cone loss ensue, with its devastating loss of central vision. The pathophysiology for some of these degenerations has been elucidated. In many of these diseases, the underlying genetic pathology is limited to the rods. So, why at the end of the process do we have cone death?

The answer lies in a family of proteins secreted by rods but necessary for cone viability. These proteins are known as rod-derived cone viability factors (RdCVF). When the rod population reaches a critical low, not enough RdCVF is produced to maintain the cones. Cone death with central visual loss then occurs. RdCVF is encoded by a gene that makes another protein product, a thioredoxin enzyme that protects photoreceptor cells against damage from oxidative stress.

To maintain cones we need a supply of RdCVF. When rods are not available to supply it, several proposed therapeutic alternatives are being investigated. RdCVF could be delivered to the retina by injection or nanoparticle technology. It also could be attached to a viral vector and incorporated into viable retinal cells, for example, the retinal pigmented epithelial cells, which would then express and deliver the protein to the cones. Perhaps most exciting is the finding that retinal bipolar cells have the ability to produce RdCVF naturally. Recapturing that potential in disease states by up-regulating the promoter of RdCVF in bipolar cells could preserve cone function by having these cells produce sufficient RdCVF for the cones. Maintaining RdCVF would therefore preserve cone vision in any type of primary rod degeneration regardless of the underlying genetic mechanism of the rod loss.

There is some early evidence that this family of proteins may have generalized protective significance for nerves. This family of proteins may be able to help prevent other neurodegenerative diseases such as Alzheimer’s.

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