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Apoptosis and neuroprotection an exciting and rapidly expanding field of research in ophthalmology

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The International Workshop "Apoptosis and Neuroprotection in Ophthalmology: From Basic Research to New Therapeutic Strategies for Eye Disease" was held on 15 February 2002 at the University of Rome "Tor Vergata." Some of the major experts in this field from Canada, Europe, Israel, and the United States presented their work and discussed the new prospects for treatment of neurodegenerative eye disease. This special issue of the *European Journal of Ophthalmology,* which contains the peer-reviewed proceedings of the workshop, is dedicated to clinical ophthalmologists. Our aim is to provide a clear and complete overview of an important and rapidly expanding area of research that is creating exciting new prospectives for the therapy of a variety of ophthalmological disorders. Apoptotic death of retinal cells or those that make up the visual pathways is the final pathological event in numerous neurophthalmologic diseases. The opening paper by Giuseppe Carella of the University of Milan provides a review of the eye diseases in which programmed cell death has been shown to play a role. Sergio Capaccioli of the University of Florence then offers a detailed examination of apoptosis as "an active death process." The cell contributes to its own elimination by activating a program of self-destruction in which specific gene products trigger a cascade of ultimately fatal molecular events. Clinical interest in the phenomenon of apoptosis stems from the fascinating possibilities it offers for therapeutic intervention, i.e., pharmacologic or gene-related therapies aimed at preventing or interrupting the cell-death program. In the field of ophthalmology, the objective of neuroprotection is to strengthen the resistance of retinal cells and neurons against the pathogenic agents — no easy task, particularly when the causative agents are multiple and/or poorly understood.

For instance, hereditary photoreceptor cell dystrophies, which are discussed by Donald Fox of the University of Houston, can be caused by wide variety of genetic mutations, many of which have yet to be identified. Classic gene-replacement therapy for these disorders would be excessively complex and costly. The individual mutation responsible for each patient's disease would first have to be identified, and the method to be used for its correction would have to be developed. However, in many of these degenerative diseases, including various forms of retinitis pigmentosa, apoptosis has been shown to represent the common pathway to photoreceptor cell death, regardless of the specific mutation that causes the disease. This observation has paved the way for development of antiapoptotic therapeutic strategies that might be effective for various forms of retinal-cell dystrophy. By decreasing the rate of photoreceptor-cell death, which is a lengthy and progressive process, the patient's visual acuity might be preserved for longer periods of time.

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Neville Osborne of Oxford University examines the possibilities for antiapoptotic therapies for glaucoma. In this case, delaying the process of apoptotic destruction of ganglion cells would give the ophthalmologist more time to optimize conventional therapies aimed at reducing intraocular pressure. In addition, neuroprotective strategies alone might be effective for those forms of glaucoma in which ganglion cell death continues in spite of relatively low intraocular pressures (low-pressure glaucoma). Several of the workshop participants repeatedly stressed the fact that glaucoma must be considered a degenerative disease of the central nervous system. Therefore, the ophthalmologist's interventions should be aimed not only toward the attenuation of ocular hypertension and other risk factors but also toward ensuring neuroprotection. Osborne's presentation provides an overview of the factors that trigger retinal cell apoptosis in glaucoma. Recent studies have identified two possible mechanisms that might lead to this event: 1) Inhibition or blockade of axonal flow secondary to ocular hypertension, which could deprive the retinal cells of neurotrophic factors produced in the lateral geniculate nucleus, and 2) Ischemic events involving the glutamate excitotoxicity cascade. Osborne also provides data from recent studies, most of which have been conducted in his laboratory, on the efficacy of certain molecules in neuroprotective therapy of glaucoma.

Michal Schwartz of Israel's Weizmann Institute of Science in Rehovot provides results from innovative studies conducted by her group on the neuroprotective potential of the immune system. The effects exerted by the immune system following stimulation with a specific vaccine have been harnessed to prevent neurologic damage in experimental models of ocular pathology caused by trauma, ocular hypertension and chemical agents.

A section of this volume has been dedicated to studies regarding the lateral geniculate nucleus, an important station in the visual pathway between the retina and the visual cortex. Yeni Yucel of the University of Toronto presents morphological findings that document the involvement of this structure in experimental glaucoma. The volume closes with a paper by our group on the role of apoptosis in experimental models of amblyopia, with discussion of the molecular mechanisms that trigger programmed cell death in the lateral geniculate nucleus and potential methods for their pharmacological inhibition.

These papers present the most recent and significant advances in our understanding of the genetic and molecular mechanisms underlying the phenomenon of programmed cell death in neuro-ophthalmologic disease and the exciting possibilities they reveal for treatment. Each presentation has been designed around the theme of the workshop, "Neuroprotection in Ophthalmology: From Basic Research to New Therapeutic Strategies for Eye Disease," which underlines the need for active and productive exchange between basic and clinical research aimed at producing new and more effective strategies to combat these severe diseases of the visual system.

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