Molecular and Cellular Responses in the Eye to Glaucoma

Ocular Gene Expression in Experimental Glaucoma

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ANIMAL MODELS FOR GLAUCOMA RESEARCH

Glaucoma is a group of optic neuropathies characterized by the death of retinal ganglion cells (RGCs) and their axons. To better understand the mechanism of RGC damage, various experimental models have been used, including both in vitro and in vivo models. In vitro culturing of cells from postmortem tissues allows the study of how cells isolated from other cell types respond to various stimuli. Many cell types can be extracted from eye tissues and cultured, including RGCs (1), trabecular meshwork cells (2), ciliary muscle cells (3), and lamina cribrosa cells (4). Although the simplicity of this system makes it very attractive, conditions may differ greatly from those of the in vivo ocular environment. The organ culture system involves the culturing of pieces of whole tissue, such as retina (5), ciliary body, or trabecular meshwork (6), and allows the study of cell responses in association with neighboring cells or extracellular matrix. Although the cellular responses in organ culture are more like those encountered in human glaucoma than are those of the more simple cell-culturing system, the experimental responses elicited, including tissue reorganization and cellular differentiation, may differ from human glaucomatous cell responses. Although postmortem human eyes are used to study the histopathology of glaucoma, their availability is limited and the eyes obtained are heterogeneous and have no controls, making difficult the investigation of gene expression changes related to glaucoma development and progression.
In contrast to the above-mentioned systems, animal models of glaucoma allow for more physiologic conditions; so, cells in the retina and optic nerve more closely mimic the ocular conditions in human glaucoma. Furthermore, in contrast to in vitro systems, the response in animal models to certain stimuli, for example, to a new drug, is actually the combined responses of many cell types, which is similar to the response of the human ocular system in glaucoma. To generate glaucoma models, the monkey, rat, and mouse are generally used, and as each animal model has advantages and disadvantages, the choice of animal species is important. The rat model is the most commonly used because the eye is moderate in size and handling of the animal is comparatively easy. The monkey ocular system is closer to the human ocular system than is that of the rat, but the cost is high, availability is somewhat limited, and handling can be difficult. The mouse has a smaller eye than the rat, and measurement of intraocular pressure (IOP) is more difficult than in other models, but the mouse has the advantage of transgenic and mutant strains, which are scarcely available in other species.

Rat Glaucoma Model

Axons of the rat optic nerve are unmyelinated and are supported by astrocytes at the scleral level, similar to primate eyes, but the lamina cribrosa of the rat eye is relatively

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**Fig. 1.** Rat glaucoma model induced by episcleral vein ligation. (Top) Schema of episcleral vein ligation. (Bottom) Photographs of episcleral vein before (left) and after (right) ligation.