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Expression Profile Approach to Glaucoma Gene Detection

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Purpose: To identify candidate glaucoma genes.

Design: Use information on changes in gene expression in response to glaucoma risk conditions to identify candidate glaucoma genes.

Participants: Human primary culture trabecular meshwork cells were obtained from donor eyes or corneal buttons provided by the Midwest Eyebank and Transplantation Centers. Donors were 12, 16, 17, 60 and 74 years of age and not known to have glaucoma.

Methods: Myocilin data were used to create a model by which the same gene can play different roles in familial-, steroidal-, late onset or isolate forms of glaucoma. Affymetrix U133A gene chips were used to assay gene expression levels from primary culture human trabecular meshwork cells derived from young and old donors, or from young cells grown with or without dexamethasone.

Outcome measures: Statistically significant ($p < 0.005$) change in expression of a gene in excess of three fold under both glaucoma risk conditions, aging and dexamethasone exposure. Genes with expression levels considered absent in both samples being compared were removed from the data set.

Results: More than 1,500 probes (<7% of the probes on the chip) showed statistically significant levels of change in response to either of the two risk conditions. Comparison of the two data sets identified 379 probes with significantly altered expression under both conditions. A total of sixteen shared response genes were found to have changed in excess of three fold, in the same direction, in response to both risk factors: seven genes that increased under both conditions and nine genes that decreased under both conditions.

Discussion: The talk will present the model and deal with the striking enrichment accomplished through comparison of data sets derived from different glaucoma risk conditions. Notably, although the myocilin gene showed some of the most substantial responses to dexamethasone, it was not among the shared response genes, in part because of substantial variation in expression levels from one donor to the next. The sixteen genes with shared responses in excess of three fold will be discussed as candidate glaucoma genes.

Supported by NIH EY09580 (J.E.R.), NIH EY07003 (Core), Research to Prevent Blindness, and the Van Arnam Glaucoma Research Fund. No financial or proprietary conflicts.