Project Summary

This is a secondary data analysis project to identifying putative transcription factors and associated *cis*-regulatory motifs/modules that are responsible for regulating gene expressions in trabecular meshwork cells in response to two cytokines, TNF and IL-1, by employing two microarray data sets generated by an NEI grant. These cytokines are thought to mediate the therapeutic efficacy of laser trabeculoplasty, a common treatment for glaucoma. Glaucoma is a common blinding disease affecting over 67 million persons worldwide. The primary risk factor for glaucomatous optic nerve damage is elevated intraocular pressure (IOP). The therapeutic effect of laser trabeculoplasty, a common glaucoma treatment that reduces IOP, appears to be mediated by the cytokines, TNF and IL-1. The main hypothesis is that a number of transcriptional regulation patterns will be common to these two cytokine's modes of action.

Transcription factors and corresponding *cis*-regulatory elements are considered key components in gene regulation, but continue to remain elusive because they are very small, scattered widely over the genome's noncoding regions, and difficult to locate using conventional approaches. By combining biostatistics and bioinformatics tools, we streamlined the identification of putative transcription factor regulatory networks specific for conditions. We will employ a new generation of innovative clustering methods to identify tight clusters of potentially coregulated genes from microarray data, and then identify common known motifs in the DNA sequence data using TRANSFAC database as well as predict putative *cis*-regulatory motifs/modules by using a latest statistical algorithms. TRANSFAC database is the most comprehensive database of known motifs.

Gene expression profiles and subsequent transcription factor analysis have a great potential to identify therapeutic targets for developing new treatments. It will also provide crucial information to design future studies utilizing next generation sequencing method such as ChIP-Seq. The successful completion of this project will significantly enhance our understanding on what specific transcription factors are involved in the changes of gene expressions associated with the glaucoma therapy