Notes from Dr. Anand Swaroop's presentation at the CRB1 research symposium March 23, 2013

Anand Swaroop PhD, Chief of the Neurobiology-neurodegeneration and Repair Lab at the National Eye Institute talked about knowledge-based therapeutic strategies for retinal and macular degeneration.

His lab explores photoreceptor degeneration in the context of aging, development, diseases associated with many genes, and treatments. He distinguished 3 types of diseases with genetic components:

- Mendelian disorders with a primarily retinal phenotype
- Syndromic disorders with a highly penetrant retinal phenotype (such as Bardet-Biedl syndrome, which is one of several conditions that impair cilia and also affect the brain and kidneys)
- Multifactorial disorders that reflect input from more than one gene plus the environment (age-related macular degeneration, diabetic retinopathy, and glaucoma)

Dr. Swaroop compared paradigms for treating disease. "Gene-based therapies are sexy and exciting and they get the headlines, but they are expensive and time-consuming to use for whole populations. There are just so many genes and mutations," he said. RetNet currently lists 232 genetic loci, with 192 genes involved in retinal dystrophies.

Stem cell therapies are alternatives to gene therapies. Stem cell-generated implants can replace photoreceptors or be used to grow 3D reconstructions of ocular structures in a dish, to use for small molecule screening to alter or rescue disease phenotypes, based on knowledge of interacting cell signaling networks and disease pathways.

Dr. Swaroop summarized the biology of photoreceptors. In humans, rods outnumber cones 20:1 (106 million rods to 5-6 million cones). Photoreceptors are highly metabolically active, with the outer segments regenerated every 10 days. Stringent control of differentiation and homeostasis is required for functional maintenance, and dysfunction or death of photoreceptors leads to vision loss. Rods degenerate and die first; cones are like queen bees and rods are like the soldiers. Rods and cones descend along lineages from shared retinal neuroepithelial progenitor cells.