CIMIT MEETING SUMMARY 5/27/03

The meeting was devoted to a single topic: "Neovascularization in the Eye". Patricia D'Amore, PhD, Schepens Eye Research Institute, set the stage with a tutorial on "Biology of Blood Vessel Formation". Vasculogenesis, the formation of new blood vessels in normal development, was contrasted with angiogenesis in which new vessels are formed from existing ones by sprouting of offshoots. Both processes require Vascular Endothelial Growth Factor (VEGF). An understanding of neovascularization requires understanding why blood vessels are stable and what keeps them stable. Experiment with endothelial cells in organ culture suggest that VEGF is needed to maintain blood vessel integrity in adult organs. The problem is complicated by the existence of various isoforms of VEGF which differ in their properties and function. Murine experiments suggest that only one isoform of VEGF results in normal vasculature. Clinical trials aimed at knocking out specific forms of VEGF in the retina are contemplated.

Joan Miller, MD, MEEI gave an overview of Age-related Macular Degeneration (AMD), which is the leading cause of serious visual loss in the developed world. Most retinal disease leads to photoreceptor damage and visual loss. Two thirds of AMD patients exhibit the dry form, characterized by "drusen", yellow deposits which migrate and cause thinning of the retina and eventual patchy visual loss. The wet form of AMD is characterized by the formation of abnormal new blood vessels which penetrate the subretinal space. The change in visual acuity is more rapid and dramatic than in dry AMD; blurred vision and distortion occurs, in part because of bending of the retina by the new vessels.

Paola Salvetti, MD, Schepens Eye Research Institute spoke on "Angiography and treatment using the scanning laser ophthalmoscope". The absorption of the retinal pigment epithelium (RPE) interferes with imaging vasculature by reflectance. Angiography uses a fluorescent dye, either sodium fluorescein (emission at 520 nm) or indocyanine green (emission near 800 nm), along with appropriate excitation light, to make the blood vessels transiently visible. However both light scattering and the emission of fluorescence by deeper blood vessels degrades the images. The confocal scanning laser ophthalmoscope reduces these effects and increases the contrast in the images, allowing better diagnosis of the disease and optimal treatment.

Joan Miller, MD then described the use of Photodynamic Therapy (PDT) for treatment of choroidal neovascularization (CNV). The photosensitizer Verteporfin has been used to treat CNV. Proper dosimetry, including drug dose, fluence, irradiance and timing, is necessary to obtain optimal vessel closure with minimal collateral damage. The treatment was FDA approved after Phase 3 trials involving 1000 patients. The conclusion drawn from the trials is that a modest reduction in the rate of vision loss can be obtained with treatment and retreatment as necessary. Ongoing research to improve the results includes efforts to combine PDT with anti-angiogenesis drugs, targeting the photosensitizer to the VEGF receptors in the vessels and combining PDT with drugs that modulate apoptosis.