Frank Giblin

Professor
Eye Research Institute

Aging's effect on human lens

Frank Giblin, Director of Oakland University's Eye Research Institute (ERI), has studied the mechanism of cataract formation for 35 years. Cataracts blind 20 million people worldwide and account for 1.5 million surgeries each year in the United States.

Giblin began at OU as a postdoctoral fellow with Venkat Reddy, a co-founder (with V. Everett Kinsey) of the ERI. Collaborative studies conducted with Reddy for many years established the vital role of an antioxidant called glutathione in keeping the lens transparent. Giblin's current five-year, $2 million grant from the National Eye Institute extends until 2012.

Giblin investigates the role of oxygen (O_2) and ultraviolet light in causing nuclear cataract, a major type of human maturity-onset cataract that forms in the center of the lens. It is essential that a healthy, transparent lens maintain an extremely low level of O_2 in its center to prevent oxidation of molecules called sulfhydryl groups into disulfides, resulting in crosslinking of lens proteins into large aggregates, causing light scatter and cataract. Giblin was able to demonstrate that treating guinea pigs with elevated levels of O_2 (hyperbaric O_2, HBO) for a few hours per week raised the level of O_2 in the lens center and caused increased light scatter. With his OU research colleagues Francis Simpanya and Victor Leverenz, as well as a NASA collaborator, Rafat Ansari, he showed in vivo that the increased scatter was linked with high molecular weight protein aggregate formation in the lens center. His work with OU collaborator Uma Venkateswaran in the Department of Physics, using Raman spectroscopy, demonstrated increased formation of disulfide in the lens center after HBO treatment.

A current hypothesis in the nuclear cataract field is that age-related liquefaction of the vitreous humor (the gel between the lens and the retina) may allow higher levels of O_2 to travel from the retina into the lens center, causing nuclear cataract. In recent collaborative studies with retinal surgeons at Beaumont Hospital, including Michael Trese, Giblin was able to show that enzyme-induced liquefaction of vitreous humor enabled O_2 to migrate much faster from the retina to the lens center.

Giblin also believes that a certain type of ultraviolet radiation present in sunlight, UVA light, can contribute to age-related nuclear cataract in humans. He has shown that long-term exposure to low levels of UVA light produces changes in the center of the lens that are very similar to early stages of nuclear cataract, including high molecular weight protein aggregate formation and loss of transparency. He continues to test his hypothesis that a substantial decrease in the level of glutathione in the human lens nucleus, occurring after the age of 50, may allow UVA light to become more toxic toward lens proteins, causing aggregate formation and insolubilization.

In Giblin's lectures to ERI student researchers, he stresses the importance of taking good care of one's eyes throughout life to help maintain clear vision for a lifetime. For eye tissues in general, including the cornea, lens and retina, this includes wearing eye protection when appropriate, minimizing exposure to the sun, not smoking, exercising on a regular basis and eating a healthy diet including fruits, vegetables, nuts and fish to provide essential vitamins, carotenoids and omega-3 fatty acids for all the eye tissues.

Representative Recent Publications

1. Yevseyenkov VV, Das S, Lin D, Willard L, Davidson H, Sitaramayya A, Giblin FJ, Dang L, Takemoto DJ. 2009. Loss of protein kinase Cγ in knockout mice and increased retinal sensitivity to hyperbaric oxygen. *Arch Ophthalmol* 127:500-506.

2. Giblin FJ, Quiram PA, Leverenz VR, Baker RM, Dang L, Trese MT. 2009. Enzyme-induced posterior vitreous detachment in the rat produces increased lens nuclear pO_2 levels. *Exp Eye Res* 88:286-292.

3. Simpanya MF, Wistow G, David LL, Giblin FJ, Mitton KP. 2008. Expressed sequence tag analysis of guinea pig (Cavia porcellus) eye tissues for NEIBank. *Mol Vis* 14:2413-2427.

4. Simpanya MF, Ansari RR, Leverenz V, Giblin FJ. 2008. Measurement of lens protein aggregation in vivo using dynamic light scattering in a guinea pig/UVA model for nuclear cataract. *Photochem Photobiol* 84:1589-1595.

5. Nachman-Clewner M, Giblin FJ, Dorey KC, Blanks RHI, Dang L, Dougherty CJ, Blanks JC. 2008. Selective degeneration of central retinal photoreceptors after hyperbaric oxygen in normal and metallothionein-knockout mice. *Invest Ophthalmol Vis Sci* 49:3207-3215.

6. Quiram PA, Leverenz VR, Baker RM, Dang L, Giblin FJ, Trese MT. 2007. Microplasmin-induced posterior vitreous detachment affects vitreous oxygen levels. *Retina* 27:1090-1096.

7. Gosselin M-E, Kapustij CJ, Venkateswaran UD, Leverenz VR, Giblin FJ. 2007. Raman spectroscopic evidence for nuclear disulfide in isolated lenses of hyperbaric oxygen-treated guinea pigs. *Exp Eye Res* 84:493-499.

8. Simpanya MF, Ansari RR, Suh KI, Leverenz VR, Giblin FJ. 2005. Aggregation of lens crystallins in an in vivo hyperbaric oxygen/guinea pig model for nuclear cataract: dynamic light scattering and HPLC analysis. *Invest Ophthalmol Vis Sci* 46:4641-4651.