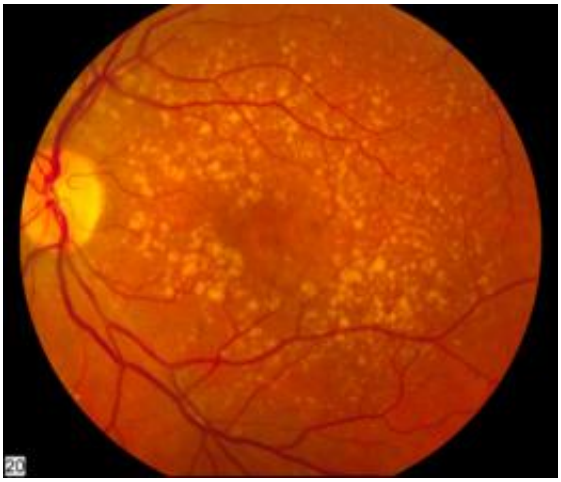
Physics puts new lens on major eye disease

July 3 2012, By Carol Clark



Blood vessels in the human retina. (NIH)

It's not easy for a theoretical physicist and an ophthalmologist to see eye-to-eye. But a collaboration between the two at Emory University proved worth the effort, sparking a new insight into the leading cause of blindness in adults.

The discovery, which ultimately involved seven scientists and four different institutions, was recently published by Public Library of Science (PLoS) Computational Biology.

"We looked at a problem from different angles, and came up with a whole new way of seeing choroidal neovascularization – a major eye disease," says Hans Grossniklaus, a clinical ophthalmologist who is the

F. Phinizy Calhoun Jr. Professor of Ophthalmology and Professor of Pathology at Emory's School of Medicine.

Their results include the first biophysical computer model of how choroidal neovascularization, or CNV, develops. "We can use this model to test new drugs at specific sites and stages during the progression of CNV, which could lead to more effective treatments," says Fereydoon Family, Samuel Candler Dobbs Professor of Physics at Emory.

CNV is the most serious form of age-related macular degeneration. In the early stages of CNV, blood vessels begin to sprout abnormally beneath the center of the retina. These abnormal vessels can leak fluid or blood and scar the layer of tissue on the inside back wall of the eyeball. If untreated, CNV can cause a blind spot in the central field of vision, which is crucial for reading, driving and recognizing faces.

Age-related macular degeneration affects about 1.75 million people in the U.S., mainly aged 50 and over. Due to the rapidly aging population, that number is expected to increase to 3 million annually by 2020, according to the National Institutes of Health.

CNV vision loss changes the above scene into the one below.

In addition to lowering the quality of life for those afflicted, CNV costs a significant amount of Medicare dollars, says Grossniklaus, a leading expert on the pathology of the disease. Injections of anti-angiogenic drugs into the eye can block the development of new blood vessels but cannot cure CNV, so patients often must continue to receive injections to prevent vision loss.

Photos by National Eye Institute/NIH.

Grossniklaus turned to Fereydoon Family in an effort to find better methods of treatment. Family's lab is well-known for using simulation and computational models to decode systems like fractals – seemingly random forms in nature that actually repeat in predictable patterns. Family had previously modeled the branching patterns for the normal growth of blood vessels in the retina.

"I asked him if he could create predictive models for abnormal growth of these vessels," Grossniklaus recalls of their initial conversation, in 2004.

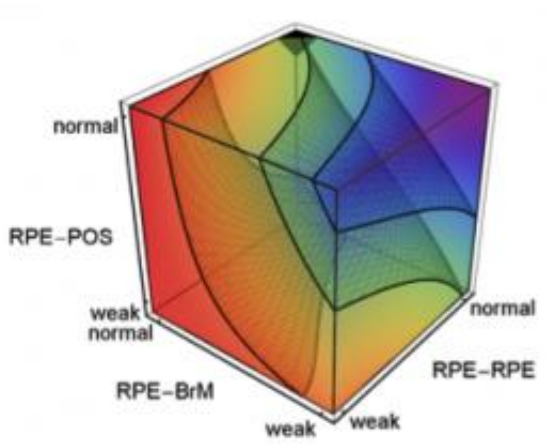
Over the years, Family and Grossniklaus published several papers on various aspects of macular degeneration while trying to develop a realistic computer simulation model on what makes the choroidal blood vessels grow and cause CNV. For the most recent PLoS paper, they joined forces with Yi Jing, from the Los Alamos National Laboratory and Georgia State University; and Abbas Shirinifard, James Glazier and Maciej Swat from Indiana University in Bloomington.

One of the biggest challenges of the collaboration was communicating between specialties, Grossniklaus says. “They were talking physics, and I was talking medicine and biology, and we had to find a common language. That was half the battle.”

Grossniklaus would draw pictures on a white board to show how the blood vessels grew between the center of the retina and the underlying membrane in cases of CNV. The physicists peppered him questions: On what parts of the tissue do the blood vessels grow? How fast do they grow? What are the dimensions? What are the molecules involved?

“It was an iterative process, with a lot of back and forth,” Grossniklaus says. “It was difficult at times, but fun to develop a mutual understanding with people who have a much different perspective.”

Grossniklaus served as “the reality check,” Family says, “as we developed quantitative ways of measuring changes in the eye.”



A serendipitous accident led to the big breakthrough: A package sent from Emory to Indiana was damaged by shaking during shipment. The researchers noticed that regions of the retina with overgrown blood vessels had separated from their underlying membrane, while the parts of the retina with no abnormal blood vessel growth remained attached. That suggested that lack of adhesion might be a key factor in the progression of CNV.

“We began focusing on weakness in adhesion in retinal cells and the underlying retinal pigment epithelium cells. That tactic led to simulations of invading blood vessel growth that agreed with many known clinical cases of CNV,” Family says.

“No one had looked at cell adhesion in relation to CNV before,” Grossniklaus says. “Before, it was thought that the invasive growth of blood vessels caused the tissue to weaken. Now we realize that the weakened tissue is what allows the blood vessels to invade. It’s like the little boy holding his finger in the dike: The blood vessels are ready and wanting to grow. They’re just waiting for the retinal tissue to weaken and

allow them to break through."

Grossniklaus and Family are now teaming up with molecular biologists to conduct more research, focused on retinal pigment epithelium cells. "By better understanding the physical properties of RPE, we may be able to develop drugs designed to strengthen this tissue and keep adhesion strong," Grossniklaus says.

"We also hope to develop models to predict whether someone may be at greater risk for CNV," Family added.

Provided by Emory University