

Research represents major breakthrough in macular degeneration

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University of Kentucky researchers, led by Dr. Jayakrishna Ambati, have made a major breakthrough in the "dry" form of age-related macular degeneration known as geographic atrophy (GA). GA is an untreatable condition that causes blindness in millions of individuals due to death of retinal pigmented epithelial cells. The paper, "DICER1 loss and Alu RNA Induce Age-Related Macular Degeneration via the NLRP3 Inflammasome and MyD88," was published in the April 26 online edition of the premier journal *Cell*.

Ambati, professor of physiology, and professor and vice chair of ophthalmology and visual sciences at UK, is a leader in the field of macular degeneration research. Previous research from the Ambati laboratory published in the journal *Nature* showed that in human eyes with geographic atrophy there is a deficiency of the enzyme DICER1, leading to accumulation of toxic Alu [RNA molecules](#) in the retinal pigmented epithelium. The *Cell* paper shows that when these RNAs build up in the eye they trigger activation of an immune complex known as the NLRP3 inflammasome. In turn, this leads to the production of a molecule known as IL-18, which causes death of retinal pigmented [epithelial cells](#) and vision loss by activating a [critical protein](#) known as MyD88.

Importantly, Ambati and colleagues found evidence that activity of the inflammasome, IL-18, and MyD88 were all increased in human eyes with GA. They then showed that blocking any of these components could prevent retinal degeneration in multiple [disease models](#). The

researchers are excited that blocking these pathways could herald a new potential therapy for GA, for which there is no approved treatment.

Provided by University of Kentucky

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