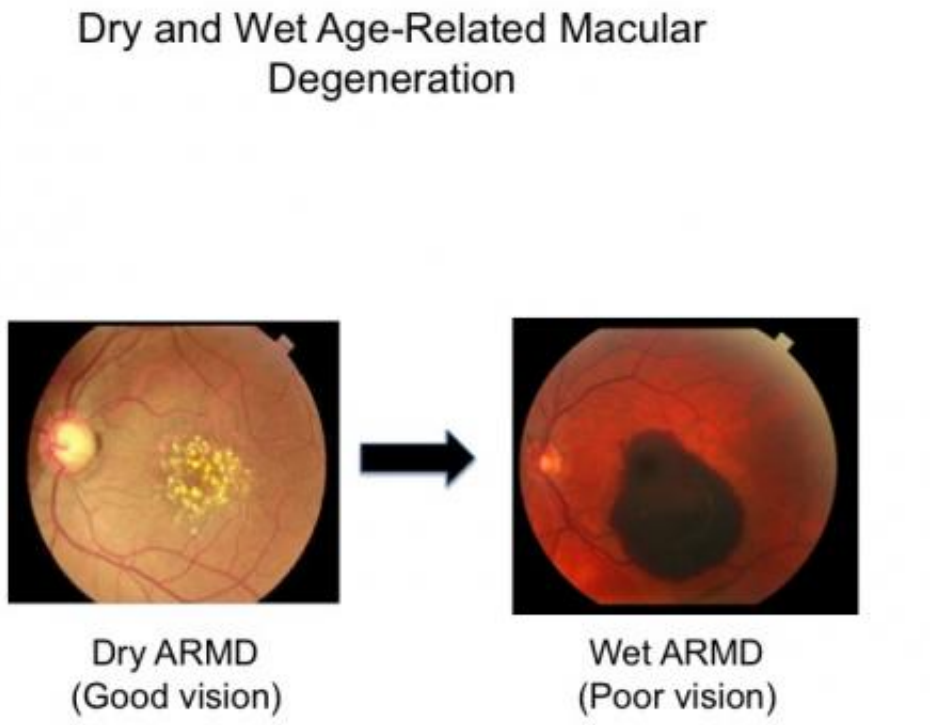
Research points to promising treatment for macular degeneration

September 10 2013



(Medical Xpress)—Researchers at the University of North Carolina School of Medicine today published exciting new findings in the hunt for a better treatment for macular degeneration. In studies using mice, a class of drugs known as MDM2 inhibitors proved highly effective at regressing the abnormal blood vessels responsible for the vision loss

associated with the disease.

"We believe we may have found an optimized treatment for macular degeneration," said senior study author Sai Chavala, MD, director of the Laboratory for Retinal Rehabilitation and assistant professor of Ophthalmology and Cell Biology & Physiology at the UNC School of Medicine. "Our hope is that MDM2 inhibitors would reduce the treatment burden on both patients and physicians."

The research appeared Sept. 9, 2013 in the *Journal of Clinical Investigation*.

As many as 11 million Americans have some form of macular degeneration, which is the most common cause of central vision loss in the western world. Those with the disease find many daily activities such as driving, reading and watching TV increasingly difficult.

Currently, the best available treatment for macular degeneration is an antibody called anti-VEGF that is injected into the eye. Patients must visit their doctor for a new injection every 4-8 weeks, adding up to significant time and cost.

"The idea is we'd like to have a long-lasting treatment so patients wouldn't have to receive as many injections," said Chavala. "That would reduce their overall risk of eye infections, and also potentially lower the economic burden of this condition by reducing treatment costs." Chavala practices at the Kittner Eye Center at UNC Health Care in Chapel Hill and New Bern.

All patients with age-related macular degeneration start out with the "dry" form of the disease, which can cause blurred vision or blind spots. In about 20 percent of patients, the disease progresses to its "wet" form, in which abnormal blood vessels form in the eye and begin to leak fluid

or blood, causing vision loss.

While anti-VEGF works by targeting the growth factors that lead to leaky blood vessels, MDM2 inhibitors target the abnormal blood vessels themselves causing them to regress—potentially leading to a lasting effect.

Chavala and his colleagues investigated the effects of MDM2 inhibitors in cell culture and in a mouse model of macular degeneration. They found that the drug abolishes the problematic blood vessels associated with wet macular degeneration by activating a protein known as p53. "p53 is a master regulator that determines if a cell lives or dies. By activating p53, we can initiate the cell death process in these abnormal blood vessels," said Chavala.

MDM2 inhibitors also have conceivable advantages over another treatment that is currently being investigated in several clinical trials: the use of low-dose radiation for wet macular degeneration. Radiation works by causing DNA damage in cells leading to an increase in p53 and cell death. MDM2 inhibitors activate p53 without causing DNA damage. Also, MDM2 inhibitors can be given by eye injection, which is advantageous over some forms of radiation treatment that require surgery to administer.

Provided by University of North Carolina at Chapel Hill School of Medicine