New discovery may improve treatment of one of the world's leading causes of blindness

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An inflammatory eye condition that is one of the world's leading causes of blindness could be treated much more effectively and easily thanks to a new discovery here.

In experiments with laboratory rats, scientists at the University of Texas Medical Branch at Galveston have developed a potential new therapy for uveitis — the inflammation of the uvea, a layer of tissue that lies just below the outer surface of the eyeball and includes the iris.

The condition, which can be caused by both autoimmune and infectious diseases, is estimated to cause from 5 to 15 percent of all cases of total blindness in the United States. Although exact figures are unavailable, the researchers say uveitis causes an even higher proportion of blindness in developing countries, because of the greater incidence there of infectious diseases and more limited availability of health care.

"The only thing a clinician can do now for uveitis is to treat the patient with steroids to reduce inflammation," said UTMB biochemistry and molecular biology assistant professor Kota Ramana, senior author of a paper on the discovery published in the October issue of Investigative Ophthalmology & Visual Science (now available online at http://www.iovs.org). "But steroids have serious side effects, and you can't use them for a long period of time."

That's not much of a problem when uveitis is produced by an infection that can be killed off in a few days with antibiotics, UTMB biochemistry

and molecular biology professor and paper co-author Satish Srivastava explained. But if the source of the uveitis is an autoimmune disease like arthritis or lupus, in which the immune system mistakenly generates chronic inflammation in response to substances naturally present in the body, the lack of an alternative to steroids creates great difficulties for patients.

Ramana and the paper's other authors, Srivastava and postdoctoral fellow Umesh Yadav, took a different route to reduce inflammation, building on work Srivastava's group has already successfully applied to fighting colon cancer and sepsis in animal experiments. Working with rats that had been injected with a uveitis-generating bacterial toxin, they demonstrated that the eye-damaging inflammation could be stopped by treatment with a compound that blocks the action of aldose reductase, an enzyme essential to the production of inflammatory signaling molecules.

"We measured inflammatory markers in the untreated rats' eyes — during inflammation there are a lot of inflammatory signaling proteins and inflammatory cells secreted in the aqueous humor, the clear liquid inside the eyes," Ramana said. "The concentrations of those proteins and cells are much lower when we used the aldose reductase inhibitor. When we also studied different sections of the eyes of rats treated with aldose reductase inhibitor, for example the retinal region, we saw the same reduction in the signaling molecules that cause damaging inflammation."

The specific aldose reductase inhibitor used in the experiments was zopolrestat, which is currently in phase 3 clinical trials as a treatment for diabetic complications. But Srivastava said the same effect would likely be produced by other aldose reductase inhibitors, including one now approved for use in Japan.

"We have not reached the clinical trial stage as yet, but we are not far away," Srivastava said. "If the trials work out, we'd like to go for topical

administration in drops, which would mean that only the tissues of the eye would be affected by the drug."

Source: University of Texas Medical Branch at Galveston