

Mouse studies advance treatment for common eye diseases

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Human eye. Image: Wikipedia.

Working with mice, a multicenter team of researchers has found a new way to reduce the abnormal blood vessel growth and leakage in the eye that accompany some eye diseases. The finding could lead to the development of new drugs for wet macular degeneration and diabetic macular edema.

The team reports their findings in the Sept. 2 issue of *The Journal of Clinical Investigation*.

The current standard of clinical care for [wet macular degeneration](#) and [diabetic macular edema](#) is repeated injections into the eye of antibodies against a protein called VEGF. Each injection costs thousands of dollars. This study revealed a way to indirectly mitigate the bad effects of VEGF

by activating a biochemical chain of events, or pathway, that suppresses the protein.

This indirect way of reducing VEGF's effects is not as dangerous as directly blocking the protein. Antibodies that block VEGF must be injected into the eye to minimize side effects to the rest of the body, such as stroke. But a drug with the indirect action identified in this study could potentially be injected under the skin with relative safety, the researchers say. Patients could thus give themselves the drug, potentially reducing the need for frequent clinic visits and injections in the eye. The study also indicates that people with particularly severe disease may have a much better outcome if the current eye injections are combined with type of skin injections reported on in this study, the researchers say.

"We've known for several years that activating the Tie2 pathway that indirectly suppresses the effects of VEGF had great potential, and the new approach we tested in this study provides a great way to take advantage of that," says Peter Campochiaro, M.D., the George S. and Dolores D. Eccles Professor of Ophthalmology at the Johns Hopkins University School of Medicine and a faculty member at the Wilmer Eye Institute at Johns Hopkins. "This new agent not only makes blood vessels in the eye less responsive to VEGF, but it also reduces leakage caused by other proteins that are active in eye diseases."

Working with mice genetically engineered to have vascular eye diseases, the team treated some with injections into the eye of an antibody that blocks an enzyme called VE-PTP. VE-PTP normally suppresses the pathway that reduces [blood vessel growth](#) and leakage, so the net effect was to activate the pathway.

The second method involved the use of a small molecule, AKB-9778, developed by Aerpio Therapeutics, which also blocks VE-PTP. Because of its size, AKB-9778 can easily enter the eye from the bloodstream, and

the indirect action appears not to carry the same risks to the body as directly blocking VEGF, Campochiaro says. "If further studies show that the small molecule is safe and effective for people, patients could give themselves an injection under the skin every day," he says. "Our studies in animals so far suggest it doesn't have major side effects." If confirmed in clinical studies, this could reduce the need for patients to come in frequently to get injections in the [eye](#). He says AKB-9778 may have the additional benefits of stabilizing [blood vessels](#) in other parts of the body and lowering blood pressure.

An estimated 2 million people in the United States suffer from [age-related macular degeneration](#), with the incidence expected to rise to 3.5 million by 2030 and to 5.5 million by 2050. Roughly 20 percent of patients with age-related [macular degeneration](#) suffer from [abnormal blood vessel](#) growth and vascular leakage, says Campochiaro, and so may be helped by this new therapy, if it proves to work in clinical trials. An equally large number of patients have diabetic macular edema and could also potentially benefit from the treatment. The incidence of these diseases is increasing very quickly, because our population is aging and the number of patients with diabetes is increasing so rapidly, he says.

The finding could also have implications for other diseases, Campochiaro notes, because VE-PTP is a phosphatase, a type of enzyme that had never before been blocked with therapeutic effect. Targeting other members of this common family of enzymes might also prove beneficial, he says.

Provided by Johns Hopkins University School of Medicine

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