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SCHOOL OF MEDICINE NEWS

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NIH funding puts researchers on path to restoring vision loss from diabetic eye disease

INDIANAPOLIS -- Researchers at the Eugene and Marilyn Glick Eye Institute and the Indiana Center for Vascular Biology at Indiana University School of Medicine are on the cusp of perfecting stem cell treatments that would halt - and potentially reverse - vision loss caused by diabetic retinopathy.

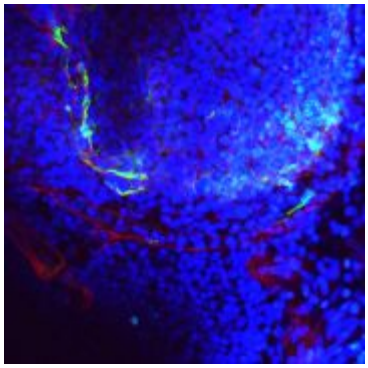
Rajashekhar Gangaraju, Ph.D., assistant professor of ophthalmology and cellular and integrative physiology, Eugene and Marilyn Glick Eye Institute and the Indiana Center for Vascular Biology and Medicine, is the principal investigator in the nearly $2 million study funded by the National Eye Institute, part of the National Institutes of Health.

Long interested in the causes and effects of diabetic retinopathy – his father and grandfather both suffered from diabetes and resulting vision loss – Dr. Gangaraju has focused his research on retinal vascular biology. His research team consists of Keith L. March, M.D., Ph.D., director, Indiana Center for Vascular Biology and Medicine and the Center for Regenerative Medicine, Maria B. Grant, M.D., currently at the University of Florida (and joining the Glick Eye Institute as senior chair in July) and others at the Glick Eye Institute and IU School of Medicine who are conducting complementary research.

Dr. Gangaraju said the five years of funding puts researchers on the path to clinical trials which, if successful, would translate to treatments for the potentially blinding eye disease. The research also could be applied to other vascular diseases, resulting in novel treatments for those conditions.

“Everyone who develops diabetes may suffer from vision loss,” said Dr. Gangaraju. “The vision loss occurs because high blood sugar damages blood vessels, causing leakage and bleeding. The blood vessels are no longer able to carry important nutrients to the retina in the eye; to compensate, more blood vessels are made, but they are fragile and also leak, causing a cyclical environment and worsening damage.”

With the increasing prevalence of diabetes in the United States and throughout the world, vision loss from diabetes continues to rise. Forty percent of individuals with diabetes develop vision threatening retinopathy; that percentage will increase as the population ages and more adults and children are diagnosed with diabetes. Nearly 19 million Americans have diabetes and another 7 million are undiagnosed. Nearly 80 million are categorized as pre-diabetic or at risk of developing the disease.



Adipose stem cells that are genetically tagged with green fluorescent protein and transplanted into diabetic eyes, demonstrate close association to host retinal blood vessels (labeled with red fluorescent protein, blue nuclei), perhaps to stabilize damage

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Preliminary research in Dr. Gangaraju's laboratory shows that stem cells isolated from fat cells and injected into the rodent eye regenerate and repair the damaged cells and improve vision.

"The key to this discovery was based on observations in Dr. March's laboratory that these stem cells, also known as adipose stem cells, in fat tissue are in very close contact with endothelial cells in small blood vessels and capillaries and may serve as a natural source for regenerating damaged blood vessels in the diabetic retina," Dr. Gangaraju said.

"We know the stem cells are migrating towards the blood vessels and are trying to arrest the leakage," Dr. Gangaraju said. "We believe this will be a therapy helpful for early stage diabetics, or those who have begun to suffer the effects of diabetes and have early vision loss due to the leaking blood vessels.

"This work is a precursor to clinical trials involving patients. We believe the basic science mechanisms will translate to a bedside treatment for diabetic patients if we can reach them in the early stage of diabetes," Dr. Gangaraju said.

"The ready availability of adipose stem cells from minimally invasive liposuction will likely facilitate translation of this research into diabetic patients," said Dr. March, co-investigator of the study.

In partnership with the Glick Eye Institute research team, the VC-CAST Signature and Regenerative Medicine Center, an NIH-sponsored Cardiovascular Cell Therapy Research Network (CCTRN), will likely bring these new therapies into the eyes of patients based on the extensive experience with cell-based clinical trials in cardiovascular diseases, Dr. Gangaraju said.

Human phase I clinical trials using adipose stem cells are already being planned in Mexico and Europe for several ocular diseases, Dr. Gangaraju said.

"We anticipate that our research efforts will lead the way to clinical therapies that are quite novel and nationally remarkable," Dr. March said. "The result in animals to date suggests a substantial improvement in visual loss due to diabetes, but it's impossible to know the extent of the improvement until we test these fat-derived cells in patients who urgently need help with their vision."

"In creating the Eugene and Marilyn Glick Eye Institute, Mrs. Glick's dream was that cures for blindness would be realized at the IU School of Medicine. Dr. Gangaraju and his collaborators are helping to make that dream a reality," said Louis B. Cantor, M.D., chairman of the IU Department of Ophthalmology at the Glick Eye Institute.

"In the near future, stem cell therapies using adipocyte derived stem cells as well as peripheral blood and bone marrow derived progenitors will likely be a viable option for patients suffering from macular ischemia, a vision threatening form of diabetic retinopathy that involves lack of blood supply to the area of central vision (macula) and currently has no effective therapy," Dr. Grant said.

Dr. Gangaraju holds an Indiana CTSI Young Investigator Award, supported by the Indiana Clinical and Translational Sciences Institute funded, in part by Grant Number KL2 TR000163, from the National

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The Glick Eye Institute operates four clinics: Downtown at 1160 W. Michigan St. on the IU School of Medicine campus; on Indianapolis' north side at 200 W. 103rd St., Suite 2200 in the Spring Mill Medical Building; in the Witham Health Services' North Pavilion, 2705 N. Lebanon St., Suite 230, in Lebanon; and at1001 Hadley Road, Suite 103 in Mooresville at Franciscan St. Francis Hospital. Faculty physicians also staff the pediatric and adult strabismus clinic at Riley Hospital for Children at IU Health and see patients at Wishard Health Services and Roudebush Veterans Affairs Medical Center, both in Indianapolis.