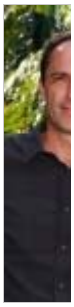
University of Miami
Miller School of Medicine

News

Young Blood Vessels Give New Life to Aging Islets, Researchers Find

11.21.2014



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A team of international researchers, led by investigators at the Miller School of Medicine's Department of Medicine and Diabetes Research Institute (DRI), has found that young capillary vessels can rejuvenate aged pancreatic islets.

The study finding is significant because it suggests that targeting inflammation and fibrosis in the small blood vessels of the islet may offer new treatment options for diabetes. The research has been published in the *Proceedings of the National Academy of Sciences*.

Islets, which contain the beta cells responsible for secreting the blood-glucose-regulating hormones insulin and glucagon, typically decrease in function with age. The researchers hypothesized that the decrease in function might not be due solely to a decrease in glucose-sensing or hormone-secreting capacity, but also to a decrease in blood supply caused by inflammation and scarring of the vessels. Replacing the islet vasculature in grafts transplanted into young mice restored the islets to full function, even at an advanced age.

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"In the study we challenged the view that the age-dependent impairment in glucose homeostasis is solely due to intrinsic dysfunction of islets," said Joana Almaca, Ph.D., a postdoctoral associate in the Department of Medicine and lead author of the article.

To determine how revascularization might affect islet function, the researchers

transplanted pancreatic islets from 18-month-old mice into the eyes of 2-month-old diabetic mice. [This is the equivalent to ages 65 and 18 in humans.] The transplanted islets, which had been revascularized with healthy blood vessels, exhibited strong beta cell proliferation and regained control of blood glucose levels within three months of transplantation.

“This is an unexpected but highly important finding that we predict will have a significant impact on diabetes research in the future,” said Alejandro Caicedo, Ph.D., associate professor in the Department of Medicine’s Division of Endocrinology, Diabetes and Metabolism, who was one of the research team leaders. “The results indicate that beta cell function does not decline with age, and instead suggest that islet function is threatened by an age-dependent impairment in islet vascular function.”

The researchers say that increased demand for insulin over time places stress on the vascular system of islets, leading to vascular inflammation, fibrosis and loss of function.

“While expanding beta cell mass may still be desirable for future diabetes therapy, improving the local environment of the otherwise healthy aged beta cell could prevent age-associated deterioration in glucose homeostasis, and thereby promote healthy aging,” said Per-Olof Berggren, Ph.D., adjunct professor of surgery and the Mary Lou Held Visiting Scientist at the Diabetes Research Institute. “This is conceptually novel and highly exciting.”

“This is another example of how the major DRI investment in shared resources, such as multiphoton, confocal and in-vivo microscopy, have allowed collaborative research and team science efforts across UM and throughout the DRI Federation centers worldwide,” said DRI Director Camillo Ricordi, M.D., Stacy Joy Goodman Professor of Surgery, Distinguished Professor of Medicine, professor of biomedical engineering, microbiology and immunology, and Director of the Cell Transplant Program. “It demonstrates the kind of results that can be obtained when investigators work across traditional academic boundaries to answer questions that are fundamental to both type 1 and type 2 diabetes, such as inflammation and age-related beta cell dysfunction.”

The Miller School research team also included Midhat Abdulreda, Ph.D., assistant professor of surgery; and Rafael Arrojo e Drigo, Ph.D., postdoctoral fellow, and Judith Molina, Ph.D., postdoctoral associate, both in the Department of Medicine’s Division of Endocrinology, Diabetes and Metabolism.

The work conducted at the University of Miami was supported by NIH/NIDDK grants and

by the Diabetes Research Institute Foundation.