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Diabetes researchers fear worsening access to human islets

For three weeks out of every month, Rohit Kulkarni's work on human islets is stalled. That's because these miniorgans have a short lifespan after they have been isolated from their native pancreas. Moreover, their supply is limited, so researchers have to be particularly careful with their personal stock. "We get shipments of islets every two to three weeks," says Kulkarni, a cell biologist at the Joslin Diabetes Center in Boston, "which only leaves one week a month to really do any work with them."

For Kulkarni and other diabetes researchers, the situation may be about to get worse.

Beginning this fall, the US National Institutes of Health (NIH) will award the first grants as part of the agency's new Human Islet Research Network (HIRN), a program launched in November 2013 to support studies into the cell type that is dysfunctional in people with type 1 diabetes. Although the HIRN doesn't require researchers to work with human islets, chances are that many scientists who weren't working with the hard-to-get cells before will soon take advantage of this funding opportunity.

It's this added competition that researchers like Kulkarni are afraid will add pressure to an already inundated system. "Time may be running out for those of us working in this field if the system of distributing islets isn't improved," says Kulkarni. Along with Andrew Stewart, director of the Diabetes, Obesity and Metabolism Institute at the Icahn School of Medicine at Mount Sinai in New York, Kulkarni plans to submit a whitepaper to the NIH this month outlining the need for more resources.

Destroyed or dysfunctional pancreatic beta cells are the primary cause diabetes; thus, researchers seek to study the insulin-producing beta cells that are housed within islets. "We are using islets to test novel drugs that will improve their function for the production and secretion of insulin," says Franck Mauvais-Jarvis, a diabetes researcher at Tulane University in New Orleans. The advantage of having islets, he adds, is that "you have an intact miniorgan you can test *in vitro*."

Getting islets for research has always been tough. The complications begin with obtaining pancreata from which to isolate islets. According to the latest figures, only about 1,900 pancreata were recovered in 2012 from deceased donors across the US; roughly 1,000 of these were transplanted into people with diabetes, with nearly 600 pancreata sent for research use (the remaining are discarded due to poor quality). In contrast, organ procurement organizations around the country removed more than 16,000 kidneys and 7,000 livers from donors.

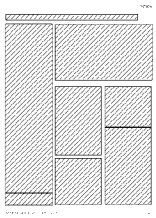
Even if researchers were to make a concerted effort to recover more pancreata, the sheer expense of obtaining the organs would deter them from doing so. Currently, procuring a pancreas for transplant can cost anywhere from $10,000 to over $40,000, although many facilities offer a reduced price if they know the organ will be used for research. "We are able to receive a pancreas for between $3,000 to $6,000," says Camillo Ricordi, director and chief academic officer of the University of Miami Diabetes Research Institute in Florida. Still, the expensive five-hour process required to isolate islets from the pancreata can drive the price up to roughly $20,000, and even the best isolations yield only half of the nearly 1 million islets usually found in a single organ.

Sharing the cost

The NIH began special programs to facilitate the distribution of human islets in 2001, leading to the formation of the Integrated Islet Distribution Program (IIDP) in 2009 with support through the National Institute of Diabetes and Digestive and Kidney Diseases. The program consists of a coordinating center and six islet isolation and distribution centers spread across the US. It offers human islets to researchers at a discounted price: investigators pay for 25% of the total cost, whereas the other 75% is reimbursed by the NIH.

The IIDP has been operating at full capacity for nearly a decade, with the demand for islets soaring above what they can supply. To provide islets for the roughly 100 active users under its wing, the IIDP employs a complex algorithm that takes many factors into account when calculating which researchers are eligible for the latest stock of islets. These include the project type and the time researchers have been waiting. And although the IIDP's system ensures equal opportunity for everyone, the evenhandedness makes it more difficult for investigators to procure timely shipments.

"We used to receive offers from the IIDP about islets roughly three times a week back



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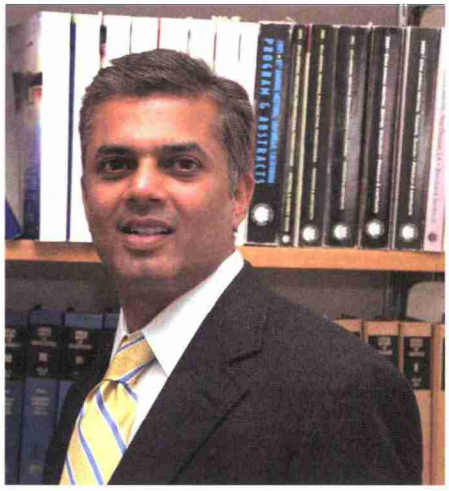
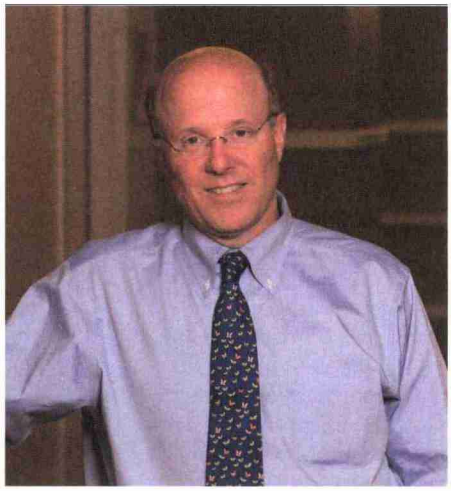
in 2008," Mauvais-Jarvis says, "but that's now been reduced to maybe every two weeks."

Kulkarni and Stewart intend to submit a whitepaper to the NIH this month that highlights the difficult process of acquiring islets for research, as well as proposed solutions. They plan to recommend that the current IIDP budget, roughly $2 million, be doubled to get more human islets distributed to the growing number of islet researchers. In addition, they plan to call for funding to develop better quality control standards throughout the process, from organ removal to islet preparation.

The logistical problems surrounding islet research aren't news to the NIH, however. The continued funding for IIDP is in recognition of these problems. Still, Michael Appel, the scientific officer responsible for overseeing the IIDP, sees room for improvement. "We at the NIH have to figure out a way to increase the budget for IIDP and continue to offer this service to researchers," Appel says. "We have to continue fostering this kind of research."

Shraddha Chakradhar





Rohit Kulkarni; Andrew Stewart

Islet appeal: Rohit Kulkarni (left) and Andrew Stewart (right) are petitioning the NIH for more islet funding.