

## Extreme Makeover: Pancreas Edition

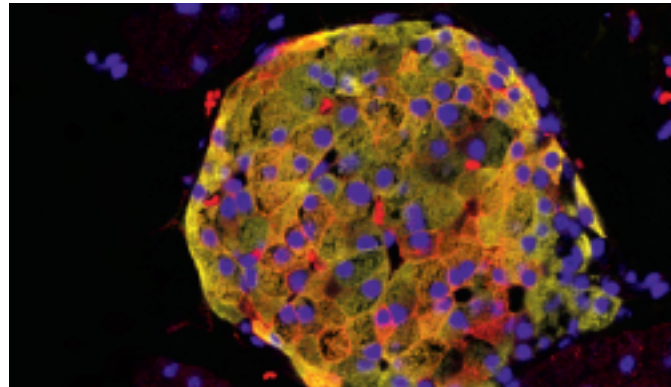
RESEARCHERS CREATE INSULIN-PRODUCING CELLS FROM ADULT PANCREATIC CELLS.

Without using adult stem cells or reverting a cell's programming to its earliest stages, HHMI researchers have flipped an adult cell from one type to another. The team converted one form of adult pancreatic cells into insulin-producing beta cells, the kind of cells destroyed in patients with type 1 diabetes.

The scientists, led by HHMI investigator Douglas A. Melton of Harvard University, repurposed the adult cells by using viruses to introduce three regulatory genes into them. These genes gave the cells their new job descriptions. This novel technique doesn't require wiping out the identity of one cell type before generating a new type. It's like, for example, turning a scientist into a lawyer without sending her all the way back to kindergarten.

"I think this approach could be broadly applicable," says Melton. "It could be applied to the nervous system or to the cardiovascular system."

About 95 percent of the pancreas is made up of exocrine cells, which secrete digestive enzymes—the pancreatic cells that Melton's team started with. Only a tiny percentage of the pancreas consists of insulin-producing beta cells, which are organized into discrete clusters called islets. Melton says the next step in his research is to create groups of beta cells capable of replacing the missing beta cells in patients with either type 1 or type 2 diabetes.



A pancreatic islet, or cluster of hormone-producing cells.

"This is a step forward toward eventually developing a treatment for diabetes," he says. "What we'd like to do is get a collection of those cells together, to make a pancreatic islet."

Functional beta cells not only produce insulin, they also detect how much glucose is in the blood, providing feedback that adjusts the levels of insulin production. The cells produced by Melton's team do this full job, and electron micrographs confirm that they are full-fledged beta cells. The findings were published on August 27, 2008, in an advance online edition of *Nature*. ■ —SARAH C.P. WILLIAMS

### IN BRIEF

#### MALARIA PARASITE'S VITAL PROTEINS IDENTIFIED

After a malaria parasite invades a red blood cell, it sends a crew of proteins inside to remodel, creating a nest for new parasites. The converted blood cell can harden and stick inside blood vessels, a dangerous chain of events.

Alan F. Cowman, an HHMI international research scholar at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, has spent the past five years leading a team of researchers in studying the malaria proteins that oversee this remodeling. The scientists' hard work has finally paid off, with a July 11, 2008, paper in *Cell* identifying 83 of those proteins.

"What this paper has done is identify new proteins that are different from anything we've seen, that are absolutely essential for different functions in the red blood cell," says Cowman.

The researchers began with a list of about 85 malaria proteins and created 55 successful "knockout" parasites—each missing the gene for one of the proteins. They then ran tests on each knockout to see how its missing protein affected function.

Eight of the malaria proteins deposit a sticky layer on red blood cells, and two build knobs on their surfaces. Others

change its structure, and 30 of the proteins were essential for malaria parasites' survival once they're nestled inside the blood cell.

Eventually, understanding the role each protein plays in helping malaria parasites infect their host, and then survive, could lead to new treatments for malaria, targeting the most vital of the parasites' protein crew.

#### ONWARD IN THE SEARCH FOR AUTISM GENES

While scientists agree that the causes of autism are largely genetic, the hunt for autism genes has been slow. Now, by studying large Middle Eastern families, an international team of scientists led by HHMI investigator Christopher A. Walsh has homed in on six new genes involved.

Walsh, of Beth Israel Deaconess Medical Center and Children's Hospital Boston, had been attempting to find genes contributing to autism by comparing autistic and nonautistic siblings. In the United States, small families make this difficult. So he turned toward the Middle East, where families average six children—compared to two or three in the U.S. and Europe. Walsh and his colleagues also narrowed their search by focusing on families in which the parents share a recent ancestor.

After sifting through data from 88 such families in eight countries—Jordan, Saudi Arabia, Kuwait, Oman, Pakistan, Qatar, Turkey, and the United Arab Emirates—the researchers identified five families with individuals missing large segments of their genome. Family members lacking a segment on only one copy of a chromosome did not have autism, but those lacking segments on both copies were affected.

Many of the deletions inactivated genes that help nerve cells strengthen connections—a process necessary for learning and memory, and one that's been implicated in autism before. Moreover, all but one of the deletions reside in the on-off switches that control genes, rather than in the genes themselves. This suggests that autism could be treated by activating the switch in some other way. The results appear in the July 11, 2008, issue of *Science*.

#### A GENE THAT LETS FRUIT FLIES SLEEP

Even though they don't close their eyes when they sleep, fruit flies have sleep cycles similar to humans. They sleep at night, they get groggy if they miss out on rest, and they try to make up for lost sleep.

By probing the extremes of fruit fly slumber, HHMI investigator Amita Sehgal