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#### TUMOR-SUPPRESSING PROTEIN REGULATES BETA CELL GROWTH

JDRF researchers at Stanford University have found that a protein known to suppress tumors also plays a role in restraining insulin-producing beta cells from multiplying – raising the possibility that a therapy aimed at reducing levels of that protein could regenerate beta cells in people with diabetes.

The protein, *menin*, was already known to play a role in preventing cancer in the pancreas and other organs by tamping down the growth of new cells. The Stanford finding suggests that *menin* is naturally reduced by hormones during pregnancy so beta cells can expand to produce more insulin in response to increased body mass.

The discovery, made in mice by Seung Kim, Satyajit Karnik, and colleagues, is published in the journal *Science*.

The finding helps solve a puzzle that has baffled doctors—why 2 to 5 percent of women develop diabetes temporarily while pregnant, a condition called gestational diabetes. The research suggests that gestational diabetes occurs when the body does not adequately reduce *menin* production during pregnancy.

To test *menin*'s role in gestational diabetes, the researchers created mice that overproduce the hormone. When these mice became pregnant, the islets couldn't grow sufficiently and the animals developed diabetes.

The researchers also showed that a hormone called prolactin, which is abundant in pregnant women, naturally represses *menin* levels and stimulates beta cell growth. When they gave prolactin to nonpregnant mice, *menin* levels dropped and beta cell mass increased.

Understanding how *menin* is regulated could help researchers design therapies that spur the growth of insulin-producing beta cells, increasing insulin production and enabling people with type 1 diabetes to improve control of blood sugar levels.

To follow up on this finding, JDRF is funding Dr. Kim and Mathew Meyerson, of Harvard Medical School, with an Academic Research and Development grant. The aims of the follow-up project are to validate this role for *menin* in humans and identify peptides that inhibit *menin*'s actions. This will allow researchers to test if inhibiting *menin* might be a safe, effective means of expanding beta cell mass in people.

#### HUMAN SKIN CELLS REPROGRAMMED TO EMBRYONIC STATE

Two separate teams of scientists have reported that they turned human skin cells into cells that look and act like embryonic stem cells. These reprogrammed cells are called “human induced pluripotent stem cells.”

The scientific journals *Cell* and *Science* reported last week that researchers added four genes to skin cells, which reprogrammed the cells' chromosomes and made them turn into what appear to be embryonic stem cells – cells theoretically capable of turning into any of the cell types of the body. Previously, the only way to get these kinds of cells was by using human embryos.

The science builds on similar findings with mouse cells reported in June of this year.

JDRF noted that while the work is still in its early stages, it represents an exciting development in the search to better understand and develop new therapies for type 1 diabetes and other diseases. It will be critical to compare induced pluripotent stem cells with embryonic stem cells regarding their potential to differentiate into cells that secrete insulin in response to glucose.

The science still has significant hurdles – the retroviruses used to insert the genes have the potential to cause tumors. Researchers will be working on using a cocktail of chemicals and small molecules to create the same effect on the cells, and on how to differentiate these stem cells into insulin-producing cells.

Calling the research “another important step forward in stem cell research,” JDRF noted that the work complements a number of ongoing efforts supported by JDRF and others to use stem cells and precursors of insulin-producing beta cells as both a research tool, and as a potential therapy for type 1 diabetes. It does not, however, lessen the importance of pursuing existing or proposed research involving embryonic or adult stem cells. While JDRF

looks forward to exploring the potential of this new approach as we work to find a cure for type 1 diabetes, it is too early to de-emphasize any aspect of our research based on these exciting, but early results.

This advance is important because of its potential to possibly accelerate progress in the field of Replacement – one of the five “cure therapeutic” research areas JDRF has identified as offering the most promise in leading to a cure for type 1 diabetes. Although much more research remains to be done, the studies open the possibility that researchers might ultimately be able to use a patient’s skin cells to generate new cells – such as beta cells or heart cells – that could potentially be transplanted into them.

The new research was published in *Cell* by scientists at Kyoto University in Japan and the Gladstone Institute for Cardiovascular Disease in San Francisco, and in *Science* by researchers at the University of Wisconsin.