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Researchers discover how insulin-producing cells increase during pregnancy

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Researchers funded by JDRF have discovered that the hormone, serotonin, may be involved in the increase of insulin-producing beta cells during pregnancy. The findings reveal one of the mechanisms underlying beta cell expansion during pregnancy, and are the latest advances underscoring the potential for regeneration as a key component of a possible cure for type 1 diabetes.

The study, published online today in the journal *Nature Medicine*, was conducted by a team of researchers led by Dr. Michael German, Associate Director and Clinical Director of the Diabetes Center at the University of California San Francisco. The Juvenile Diabetes Research Foundation was a funder of the study.

Studying the gene expression and signaling pathways that regulate the increase of functional beta cells in pregnant mice, the researchers identified that a gene (tryptophan hydroxylase-1 or Tph1) involved in the production of serotonin is dramatically increased in beta cells of the mother during pregnancy. Serotonin is a hormone well known for its various roles in moderating behavior in animals and humans.

According to Dr. German, two pregnancy hormones (prolactin and placental lactogen) triggered the expression of the Tph1 gene in islet cells, leading to an increase in the synthesis and release of serotonin by beta cells. The released serotonin then binds to specific protein molecules (5ht2b receptors) on beta cells, which are both increased in number during pregnancy and stimulated beta-cell proliferation. At

birth, the process is reversed when another form of the serotonin receptor (5ht1d) is turned on in beta cells and inhibits beta-cell proliferation, bringing the number of beta cells back down to normal non-pregnant levels. "These findings uncover a previously unknown, integrated pathway linking beta cell mass with the anticipated increase in insulin requirement during pregnancy," said Dr. German. "We are currently investigating the role of this pathway in beta cell function in pregnant women as well as working to identify targets in the pathway that could be used to come up with new drugs to promote beta cell regeneration in people with type 1 diabetes."

"This novel finding by Dr. German and his team could have tremendous implications in the potential development and use of regenerative drugs and therapies for type 1 diabetes," said Patricia Kilian, Ph.D., Program Director of Regeneration at JDRF. "It addresses a critical research goal within our Regeneration program, and we are excited to see how this will translate to humans to create applicable cure therapeutics for type 1 diabetes."

Regeneration Research

To cure people with type 1 diabetes, researchers will need to stop the autoimmune attack that causes diabetes, and restore the ability to produce insulin by either replacing or regenerating insulin producing cells.

Among the fastest-growing scientific areas JDRF supports is research aimed at regenerating insulin producing cells in people who have diabetes. This involves triggering the body to grow its own beta cells, either by copying existing ones - some are usually still active, even in people who have had diabetes for decades - or inducing the pancreas to create new ones.

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