

Adult stem cells from human cord umbilical cord blood successfully engineered to make insulin

May 25 2007

In a fundamental discovery that someday may help cure type 1 diabetes by allowing people to grow their own insulin-producing cells for a damaged or defective pancreas, medical researchers here have reported that they have engineered adult stem cells derived from human umbilical cord blood to produce insulin.

The researchers announced their laboratory finding, which caps nearly four years of research, in the June 2007 issue of the medical journal *Cell Proliferation*, posted online this week. Their paper calls it "the first demonstration that human umbilical cord blood-derived stem cells can be engineered" to synthesize insulin.

"This discovery tells us that we have the potential to produce insulin from adult stem cells to help people with diabetes," said Dr. Randall J. Urban, senior author of the paper, professor and chair of internal medicine at the University of Texas Medical Branch at Galveston and director of UTMB's Nelda C. and Lutchter H. J. Stark Diabetes Center. Stressing that the reported discovery is extremely basic research, Urban cautioned: "It doesn't prove that we're going to be able to do this in people — it's just the first step up the rung of the ladder."

The lead author of the paper, UTMB professor of internal medicine/endocrinology Larry Denner, said that by working with adult stem cells rather than embryonic stem cells, doctors practicing so-called

regenerative medicine eventually might be able to extract stem cells from an individual's blood, then grow them in the laboratory to large numbers and tweak them so that they are directed to create a needed organ. In this way, he said, physicians might avoid the usual pitfall involved in transplanting cells or organs from other people — organ rejection, which requires organ recipients to take immune-suppressing drugs for the rest of their lives.

Huge numbers of stem cells are thought to be required to create new organs. Researchers might remove thousands of donor cells from an individual and grow them in the laboratory into billions of cells, Denner explained. Then, for a person with type 1 diabetes, researchers might engineer these cells to become islets of Langerhans, the cellular masses that produce the hormone insulin, which allows the body to utilize sugar, synthesize proteins and store neutral fats, or lipids. "But we're a long way from that," Denner warned.

Denner said this research, which reflects a fruitful collaboration with co-authors Drs. Colin McGuckin and Nico Forraz at the University of Newcastle Upon Tyne in the United Kingdom, used human umbilical cord blood because it is an especially rich source of fresh adult stem cells and is easily available from donors undergoing Caesarian section deliveries in UTMB hospitals. "However," he added, "embryonic stem cell research was absolutely necessary to teach us how to do this."

Embryonic stem cells have been engineered to produce cardiac, neural, blood, lung and liver progenitor cells that perform many of the functions needed to help replace cells and tissues injured by many diseases, the paper notes. Among the insights into cell and tissue engineering gained from work with embryonic stem cells, it adds, are those "relevant to the engineering of functional equivalents of pancreatic, islet-like, glucose-responsive, insulin-producing cells to treat diabetes."

The researchers said they tested adult stem cells in the laboratory to ensure that they were predisposed to divide. Then they used a previously successful method in which complex signals produced by the embryonic mouse pancreas were used to direct adult stem cells to begin developing, or "differentiating," into islet-like cells.

As they grew these adult stem cells in the laboratory, the researchers conducted other tests in which the cells to be engineered showed evidence of a characteristic, or marker, known as SSEA-4 that was previously thought to exist only in embryonic cells. They also found that, just as embryonic cells have been shown to do, these adult stem cells produced both C-peptide, a part of the insulin precursor protein, and insulin itself. Confirming the presence of the C-peptide was especially crucial, the researchers suggested, because although insulin is often found in the growth media with which the cells are nurtured and is often taken up by such cells, the presence of the C-peptide proves that at least some of the insulin was produced, or synthesized, by the engineered cells.

Source: University of Texas Medical Branch at Galveston

Citation: Adult stem cells from human cord umbilical cord blood successfully engineered to make insulin (2007, May 25) retrieved 4 May 2024 from <https://medicalxpress.com/news/2007-05-adult-stem-cells-human-cord.html>

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