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Scientists find first human iPSC from patients with maturity onset diabetes of the young

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Joslin scientists report the first generation of human induced pluripotent stem cells from patients with an uncommon form of diabetes, maturity onset diabetes of the young (MODY). These cells offer a powerful resource for studying the role of genetic factors in the development of MODY and testing potential treatments. The findings appear in the *Journal of Biological Chemistry*.

Human induced pluripotent stem cells (hiPSCs) are adult cells that have been genetically reprogrammed to exhibit the characteristics of embryonic stem cells, including the ability to differentiate into specialized cell types. The generation of hiPSCs, which was first reported in 2006, was a major scientific breakthrough with the potential to increase understanding of many diseases and aid in drug development.

Maturity onset diabetes of the young (MODY) is a form of diabetes that mainly affects individuals age 25 or younger and accounts for about 1 to 5 percent of all diabetes cases in the United States. Unlike type 1 and type 2 diabetes, which are polygenic and result from alterations in genetic and environmental factors, MODY is a monogenic disease that results from mutations in a single gene. To date, eight types of MODY and eleven MODY genes have been identified. Some types of MODY produce only mild symptoms and are often treated solely with oral diabetic medications.

Joslin Diabetes Center is one of a limited number of research institutes with the capability to generate hiPSCs from patients with diabetes. The cells used to produce the hiPSCs were obtained from patients with five different types of MODY at Joslin Diabetes Center and Haukeland University Hospital, Bergen, Norway. The MODY-hiPSCs are morphologically, molecularly and functionally indistinguishable from human pluripotent stem cells (hPSCs).

As a monogenic disease, MODY provides "a valuable opportunity to directly study in more detail the genetic mechanisms underlying the disease and not be influenced by other factors, such as insulin resistance," says senior author Rohit N. Kulkarni, M.D., Ph.D., a Principal Investigator in the Section on Islet Cell and Regenerative Biology at Joslin and Associate Professor of Medicine at Harvard Medical School.

The scientists will first induce the MODY-hiPSCs to differentiate towards beta cells and in the process learn more about the potential blocks in their ability to differentiate. Using the iPSC-derived beta cells, they plan to study how MODY genes regulate the insulin secretory function. "Generating hiPSCs is an important step forward because we cannot obtain beta cells from living patients. These cells will allow us to do many experiments that otherwise would not be possible," says Dr. Kulkarni.

The scientists also plan to explore ways to correct the genetic defect and use the beta cells derived from the "repaired" hiPSCs to test various treatments. "If we find medications that improve beta cell function, we can go back to the clinic and use them to treat patients," says Dr. Kulkarni. "It will allow us to tailor treatments to a patient's unique characteristics and provide personalized medicine to diabetes patients."

Provided by Joslin Diabetes Center