

Study suggests genetic testing for young people diagnosed with type 1 diabetes

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A Joslin Diabetes Center study among people treated for type 1 diabetes for many years has discovered that a minority may have monogenic diabetes, a non-autoimmune inherited condition that in some cases does not require insulin treatment.

"Our finding has [clinical implications](#)," says George L. King, MD, Joslin

Senior Vice President and Chief Scientific Officer, and senior author on a paper describing the work published in the *Journal of Clinical Investigation*. "We are recommending that everyone under 18 who is diagnosed with type 1 [diabetes](#) be screened for monogenic diabetes, which is not being done at this time."

This result is part of an ongoing research initiative among Joslin Medalists, who have lived with type 1 diabetes or insulin-dependent diabetes for at least 50 years. The Joslin team also reported other significant discoveries about the activity of insulin-producing [pancreatic beta cells](#) over time in this population.

As the name suggests, monogenic diabetes is produced by a mutation in at least one gene that affects insulin secretion, explains Marc Gregory Yu, MD, first author on the paper. The condition makes up something between 1 and 5% of diabetes cases, many in a form known as mature onset diabetes of the young (MODY).

Yu worked with co-senior author Marcus Pezzolesi, Ph.D., and other Joslin colleagues to test for 29 genes implicated in monogenic diabetes, plus other genes known to help drive autoimmune type 1 diabetes.

Among 1,019 Medalists tested, about 8% had a monogenic diabetes mutation that might drive disease. Within that group, slightly less than half did not exhibit the genetic variations that needed to trigger type 1 diabetes—which suggested that they might respond well to oral drugs rather than only to insulin. In the remainder of the group, who displayed both types of genetic alterations, "we don't really know which genetic condition is causing their diabetes," King says.

Joslin investigators expect to launch a clinical trial within months to see if oral diabetes drugs can help Medalists with mutated monogenic diabetes genes manage their disease more effectively. "This will be the

first clinical study looking at the administration of oral drugs in an older population with monogenic diabetes," Yu says. If the trial results are positive, they may suggest changes in care for tens of thousands of people among the million-plus individuals in the United States who have been diagnosed with type 1 diabetes.

In addition to their [genetic analysis](#), the Joslin team made discoveries about the presence and behavior of beta [cells](#) both in living Medalists and in pancreases donated by many Medalists after death.

For decades, scientists believed that all beta cells eventually are destroyed in type 1 diabetes. However, earlier studies of Medalists and other sets of longtime survivors had proven that small numbers of the cells still appear in all individuals with type 1 diabetes. In the current study, Susan Bonner-Weir, Ph.D., a senior investigator in Joslin's Section on Islet Transplantation and Cell Biology, and co-workers confirmed this finding of beta cells in all of the 68 donated pancreases that were examined.

Additionally, the Joslin team reported discoveries from experiments among living Medalists in which these volunteers were given infusions that could stimulate their insulin production. Bonner-Weir showed that the results of these infusion tests matched up well with later analyses of beta cells in postmortem analysis of donated pancreases.

Moreover, examining how Medalists responded to insulin-stimulation testing over time produced one unexpected result. Typically, the low levels of insulin production in this population drop with age. However, a few Medalists actually increased their signs of insulin production when they repeated one stimulation test several years later. "These beta cell functions can come and go, which clearly shows that [clinical trials](#) studying ways to regenerate [beta cells](#) need to have a control group of participants," King says.

Provided by Joslin Diabetes Center

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