Diabetes

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Cell therapy for type 1 diabetes in a nonhuman primate

Type 1 diabetes (T1D) is a lifelong disease caused by the autoimmune destruction of pancreatic β cells, which causes insulin deficiency. The mainstay of T1D treatment is lifelong insulin replacement, either through multiple daily injections or continuous infusion using a pump. However, some patients have trouble managing the amount of insulin needed every day to prevent hyperglycemia, putting them at risk for hypoglycemia. Islet transplantation is a promising experimental treatment for difficult-to-control T1D, but it comes with the burden of lifelong immunosuppression. A new study in *Cell Stem Cell* reports for the first time the successful treatment of an immunocompetent, diabetic cynomolgus monkey with allogeneic primary rhesus macaque islets without immunosuppression.

The investigators had previously used a CRISPR approach to engineer human hypoimmune primary pancreatic islets, and they showed that the cells survived and alleviated diabetes after transplantation in allogeneic humanized mice in the absence of immunosuppression. Here, Hu and colleagues used a similar approach to engineer hypoimmune ($B2M^{-/-}$, $CIITA^{-/-}$, $CD47^{+}$) primary rhesus macaque islets and test their therapeutic efficacy in a diabetic cynomolgus monkey.

After inducing diabetes mellitus in the recipient monkey via streptozotocin injection, the researchers stabilized the monkey's glucose levels with insulin injections. After 78 days, they transplanted the hypoimmune islets – without giving the animal any drugs to suppress the immune system – and started to gradually reduce the insulin injections before completely stopping them after 12 days. A week after transplantation, the monkey's c-peptide levels – a measure of insulin production – had returned to normal and remained stable throughout the follow-up period of 6 months. The monkey showed tightly controlled blood glucose levels for 6 months, was completely insulin-independent and exhibited no physical or behavioral abnormalities. Importantly, blood analysis indicated that the allogeneic islet cells did not induce immune recognition or any type of immune response in the recipient monkey throughout the study.

Altogether, these findings support further investigation of allogeneic, hypoimmune-edited primary islets as potential future therapy for the treatment of T1D.

Alexandra Le Bras

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