Study Illuminates Mechanism That Preserves Pancreatic Beta Cells

Compound boosts GHRH to prevent cell death and preserve beta cell function in type 1 diabetes models.

Ernesto Bernal-Mizrachi, M.D.

Researchers at the University of Miami Miller School of Medicine have shown that the compound MR-409 boosts growth hormone-releasing hormone (GRHR) production in cell and animal models, protecting pancreatic beta cells from destruction. This work could lead to new therapies for people with type 1, and possibly type 2, diabetes. The research was published in the journal *PNAS*.

“In this study, we demonstrate the mechanism of action of this GRHR agonist in insulin-producing cells,” said Ernesto Bernal-Mizrachi, M.D., professor, chief of the Division of Endocrinology, Diabetes and Metabolism and deputy director of beta cell biology. “We also show these compounds will increase survival of beta cells in conditions that are similar to type 1 diabetes.”

Type 1 diabetes is caused by an autoimmune response that selectively destroys insulin-producing beta cells. Without these insulin factories, people with type 1 must rely on injections to survive. However, beta cell destruction happens over a period of months or even years, offering therapeutic
windows to preserve them.

The study originated from a series of conversations between Dr. Bernal-Mizrachi and Andrew Schally, Ph.D., professor of pathology at the Miller School. Dr. Schally won the Nobel Prize in Medicine or Physiology in 1977 for his groundbreaking work on releasing hormones. In recent years, he has been developing compounds that boost hormone peptide production, and Dr. Bernal-Mizrachi suggested this work might be applied to beta cells. Postdoctoral researcher and first author Ruy Louzada, Ph.D., also made significant contributions to this work.

‘A Survival Pathway for Beta Cells’

In the study, the research team exposed animal and human beta cells to a cytokine protein cocktail that roughly mimics the autoimmune response in type 1 diabetes. By boosting GRHR expression, MR-409 protected these critical cells from destruction.

“The compound upregulates an important protein called IRS2,” said Dr. Bernal-Mizrachi. “That increase in IRS2, and other proteins, offers a survival pathway for beta cells.”

GRHR agonists are not a new concept; they have been used for years to support transplanted beta cells. However, nobody had ever fully delineated their protective mechanisms.

On a clinical level, GRHR agonists could help type 1 diabetes patients retain beta cells. However, for that strategy to succeed, the drug would have to be given during the earliest stages of the disease.
These compounds could also help treat type 2 diabetes. Though type 2 diabetes does not initially destroy beta cells, the body’s increasing demands for insulin can tax them over time, leading to cell death. The authors caution that this study was focused exclusively on the mechanisms associated with type 1 diabetes and further work would need to be done to show GRHR agonism would be effective in type 2.

The researchers believe GRHR boosters, similar to MR-409, could be used in a drug cocktail with immune modulators and compounds that support beta cell proliferation. In addition, GRHR agonists have already been approved by the FDA, which could accelerate their clinical adoption.

“These medications are already being used in people in other contexts,” said Dr. Bernal-Mizrachi. “I think that could pave the way for us to perhaps test in humans.”