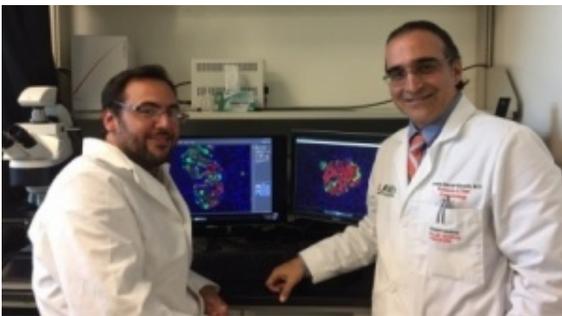


Research Illuminates Potential Pathway to Type 2 Diabetes

Researchers at the Diabetes Research Institute at the University of Miami Miller School of Medicine are taking a closer look at a cell signaling pathway known to be important in regulation of insulin sensitivity. Specifically, they want to learn more about how changes in this mammalian target of rapamycin (mTOR) pathway within beta cells of the pancreas can lead to development of type 2 diabetes.



From left, Manuel Blandino Rosano, Ph.D., with Ernesto Bernal-Mizrachi, M.D.

The pathway controls intracellular and extracellular signaling that regulates cell metabolism, growth, proliferation and survival throughout the body. mTOR is one of the nutrient-sensitive pathways deregulated in many diseases, including diabetes.

“During the pathogenesis of diabetes, the nutrient and dietary

environment are important for developing insulin resistance and beta cell failure, which is the last stage before development of type 2 diabetes,” said Ernesto Bernal-Mizrachi, M.D., an internist specializing in endocrinology, diabetes and metabolism at the Diabetes Research Institute. “We did a study to look at how nutrient-sensitive pathways can impact different tissues, focusing on changes in the pancreas.”

The study by Bernal-Mizrachi, lead author Manuel Blandino Rosano, Ph.D., and colleagues, was published online in *Nature Communications*. It links loss of mTOR complex 1 signaling with beta cell failure and diabetes through reduction in proliferation, size and survival of beta cells in mice.

The results could carry important implications for prevention or treatment of type 2 diabetes in people in the future.

“This finding allows us to focus on some important targets to develop pharmaceutical agents that could be used to treat diabetes,” Bernal-Mizrachi said. A next step could be drug screening to identify potential agents that induce positive changes in the mTOR pathway, for example.

“We are just embarking on this ... but I’m always optimistic,” Bernal-Mizrachi said.

The study findings could also help illuminate why some people treated with mTOR inhibitors such as rapamycin analogs remain at higher risk for developing type 2 diabetes.

“These medications are used as immunosuppressants in transplantation and to treat some malignancies,” Bernal-Mizrachi said. “But there is an increase in the incidence of

diabetes in patients who take these medications, so these studies may provide a potential explanation of the mechanism behind how these medications lead to diabetes.”