Loss of IQGAP1 Lends Advantage to Female Mice Against Predisposition to Type 2 Diabetes

Ashaq Hussain[1], Rawan Moussa[1], Mahasin Osman[2*]

[1]Student, College of Medicine and Life Sciences, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

[2]Associate Professor, Division of Hematology Oncology, Department of Medicine, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

Email: Mahasin.Osman@utoledo.edu

Received: 2024-08-09

Accepted: 2024-09-16

Published: 2025-06-30

Type 2 Diabetes (T2D) is a chronic metabolic disorder characterized by hyperglycemia and elevated insulin resistance accompanied by low levels of insulin production in pancreatic β cells. Although sex differences in T2D manifestation have been recognized in human and animal models the molecular underpinning remains unclear. The scaffold signaling protein IQGAP1 has been implicated in insulin signaling and recycling and its mRNA is down regulated in humans with T2D. Here we report a female-specific protective role of IQGAP1 in mice against predisposition to developing T2D. Our results show significant metabolic differences in male and female mice lacking iqgap1 gene (iqgap1-/-). We find that the loss of iqgap1 lends protection against obesity in male mice only under high fat diet (HFD) conditions. Compared to iqgap1-/- male mice, iqgap1-/- females exhibit significantly reduced body weight under both normal and HFD conditions. Measurements of physiological parameters revealed that iqgap1-/- females have increased insulin sensitivity and better plasma glucose clearance rate than their male counterparts. Analyses of the involved IQGAP1 pathway and organ site of action suggest involvement of ERα-IQGAP1-AMPKα signaling node in the pancreas. Further studies are underway to define how IQGAP1 executes his roles in this process differentially.

Keywords: Diabetes, Pancreatic Beta Cell, Hyperglycemia, Insulin Resistance, Glucose Metabolism

https://dx.doi.org/10.46570/utjms-2025-1402