Abstract

Islets of obese (Ob/ob) mice lacking Gαz secrete more insulin than cells from lean mice. This could provide insight into how type 2 diabetes develops and how to prevent its progression.

* Gαz is a signaling molecule that prevents insulin secretion

Hypothesis

If Gαz inhibits insulin secretion, then removing Gαz should allow more insulin secretion to occur. More insulin secreted into the bloodstream could prevent high blood sugar levels and thereby prevent type 2 diabetes.

Type 2 Diabetes Mouse Model

The obese (Ob/ob) mice have a mutation in the Leptin gene that causes the mice to overeat, become obese, insulin resistant, and ultimately diabetic. We compare lean and obese mice that express and do not express the Gαz protein to identify the role of Gαz in type 2 diabetes progression.

Gaz promotes Type 2 Diabetes, but not obesity

The presence or absence of Gaz does not affect body weight.

Gaz limits insulin content in isolated islets

Gaz limits insulin content in isolated islets. Islets lacking Gaz secrete more insulin in response to high glucose compared to islets with Gaz.

Conclusions and Future Directions

• The EP3-Gαz pathway impairs normal beta-cell function by limiting insulin content of beta-cells and thereby reducing the amount of insulin that can be secreted.

• Mice lacking Gaz are able to retain insulin content and secrete enough insulin into the bloodstream to prevent high blood sugar levels.

• The EP3-Gαz pathway is up-regulated in the type 2 diabetic state.

• Future work includes investigation into how specifically the EP3-Gαz pathway regulates beta cell health and function.

• We hypothesize that Gaz primarily works by preventing the generation of cAMP.

• The second messenger, cAMP, is known to augment insulin secretion and promote beta cell survival and proliferation.

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