Title: A hormone produced by bone to treat diabetes

Researchers:

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Research area: Type 2 diabetes

Award: End Diabetes 100 Award, 2021-2024

Summary:

Osteocalcin is a hormone produced by bone and communicating with different organs, including the pancreas, the fat tissue and the muscles. When osteocalcin reaches the pancreas, it promotes the release of insulin, which helps regulate the levels of glucose in the blood. Osteocalcin also travels to other organs such as muscle, where it helps to convert fats and glucose into energy in response to insulin. Hence, osteocalcin could be potentially harnessed as a therapy for type 2 diabetes. Recently, our team has discovered that in mouse osteocalcin a small group of sugars is attached to its structure, a modification called “glycosylation”. We found that glycosylation prevents osteocalcin from being degraded by enzymes in the blood. Glycosylation was not found on human osteocalcin, but we showed that when it was modified so the sugar group could attach, the human hormone was also more stable in blood. The goal of this project is to test if improving the stability of osteocalcin through glycosylation can enhance its therapeutic action.

Methods: In the first part of this project, we will treat diabetic mice with glycosylated osteocalcin and compare the effect on diabetes with plain osteocalcin. Our experiments are designed to test if glycosylated osteocalcin can slow down or reverse type 2 diabetes in mice. In the second part of the project, we will first determine if glycosylated human osteocalcin is more stable than the non-glycosylated form, in non-human primates. Next, we will test the activity of this modified hormone on pancreatic islets from post-mortem human donors.

Outcome: The completion of this project should establish if glycosylated osteocalcin is a promising anti-diabetic agent. It will also determine if this modified protein is more stable in

primate and if it is active on human beta cells. By translating our basic findings to a novel therapeutic approach for diabetes, we believe this project could have a strong impact on the treatment of this disease.