DIABETES

NEW TREATMENT
APPROACH FOR T1DM

Glycaemia and HbA_{1c} levels can be normalized with a monoclonal anti-glucagon receptor antibody in rodent models of diabetes mellitus, according to new research. Importantly, these results were achieved without administering insulin.

Since insulin therapy was first used to treat patients with type 1 diabetes mellitus (T1DM), it has been clear that the monotherapy is unable to normalize glucose homeostasis. Indeed, patients with T1DM experience post-prandial surges in glucose levels that are up to four times higher than those seen in people without diabetes mellitus. “[Therefore], subcutaneous injection of insulin would not match the high local levels of intra-islet insulin, thereby permitting unfettered hyperglucagonaemia and hyperglycaemia,” hypothesizes Roger Unger, senior author of the article. The team used three types of experiments to test this hypothesis.

In the first experiment, in which a normal hamster cell line was used, increasing the concentration of glucose resulted in increased production of glucagon. These results were then confirmed in perfused pancreata from rats with chemically induced T1DM. The third set of experiments involved mice with autoimmune diabetes mellitus. Mimicking conditions in human patients, mice were injected with insulin to normalize glucose levels. Levels of glucagon were three times higher when the mice had abnormally high levels of glucose than after the insulin injection (when levels of glucose were normal). These findings suggest that high levels of glucose stimulate the production of glucagon in the absence of insulin. The mice were then treated with an antibody against the glucagon receptor, which resulted in normalization of blood levels of glucose, as well as HbA_{1c} levels.

“These results open up a brand new therapeutic chapter in the field of diabetes mellitus,” says Unger. He suggests that insulin doses could be reduced if glucagon levels were also suppressed, which could reduce the incidence of some treatment-associated complications in patients with T1DM. “The final phase of this effort requires translation from preclinical studies to humans,” comments Unger. The authors hope that these clinical trials will commence soon.

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Original article Wang, M.-Y. *et al.* Glucagon receptor antibody completely suppresses type 1 diabetes phenotype without insulin by disrupting a novel diabetogenic pathway. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.1424934112