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GENETICS

Towards β-cell regeneration

Inducing human β-cells to replicate is very challenging; although harmine analogues can induce β-cell replication, the low rate of replication means that they are unlikely to be useful for the treatment of patients with type 1 diabetes mellitus or type 2 diabetes mellitus. Now, a new paper has mined the genomes of human insulinomas to give new insights into the genetic control of β-cell replication, which could lead to novel treatments for diabetes mellitus.

In order to investigate β-cell replication, Andrew Stewart and colleagues needed a source of β-cells capable of replication. Human neonatal β-cells are difficult to obtain, so the team turned to insulinomas. These benign tumours of the β-cells result in β-cell replication and high production of insulin, which causes hypoglycaemia and psychomotor symptoms. "We viewed them as benign tumours that hold the genetic code to therapeutic β-cell expansion for diabetes mellitus," explains Stewart.

The researchers collected samples of insulinomas and blood cells (as a control) from 22 patients, and also included data from four other insulinomas from a previous report. They performed whole-exome sequencing and RNA sequencing; the results were analysed using advanced bioinformatics. "In a nutshell, we found multiple genomic pathways that insulinomas use to drive human β-cell replication, including the pathways that are used by the harmine family, and showed that they can be manipulated by novel classes of drugs," reports Stewart. "These large data sets are now publically available and constitute a data mine for discovery of novel β-cell regenerative drugs."

Stewart and colleagues have identified several new drug classes by mining this information. However, these drugs are likely to have adverse effects on other cells, so new approaches to target the drugs to the β-cells are required. "We are not far from inducing β-cell expansion in both type 1 diabetes mellitus and type 2 diabetes mellitus," concludes Stewart.

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