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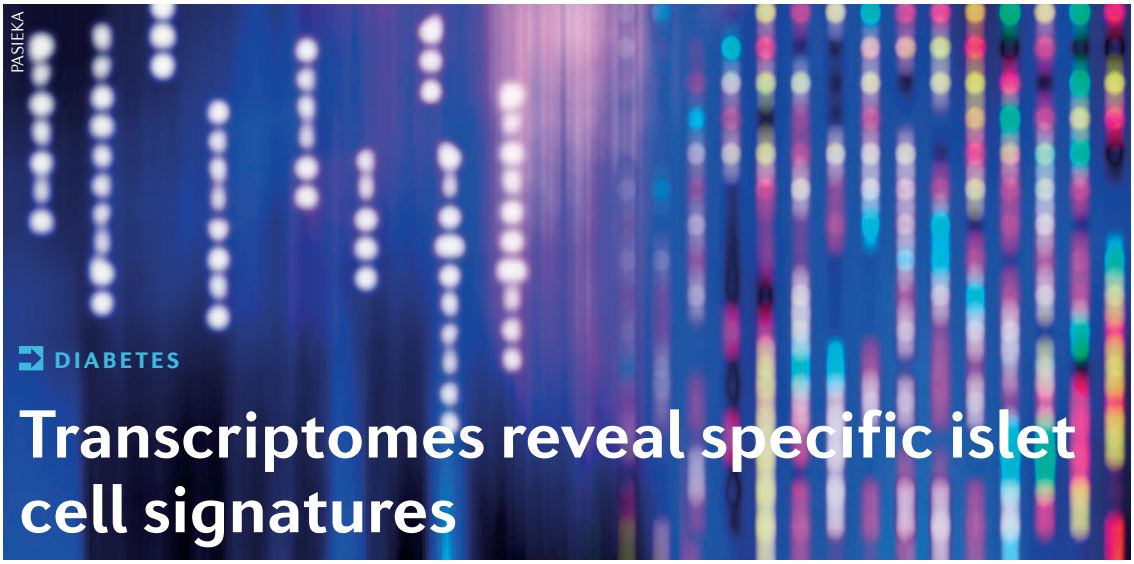

DIABETES

Transcriptomes reveal specific islet cell signatures

> … these analyses provide a useful resource for future studies on the genetic determinants of T2DM

Whole-genome sequencing of individual islet cells has been challenging, owing to the scarcity of certain cell types, such as δ and ε cells, and the fact that only ~1% of the pancreas is made up of islets. Now, advances in high-capacity single-cell RNA sequencing have enabled investigators to profile the transcriptomes of individual islet cell types from both healthy individuals and those with type 2 diabetes mellitus (T2DM) to reveal new possible pathophysiological changes in gene expression.

In one study, Segerstolpe and colleagues used pancreatic tissue from six healthy individuals and four patients with T2DM. Islets were dissociated and sorted into individual cells, on which transcriptome analysis was performed. The team were able to identify cell types solely on the basis of their transcriptomic profile, which resolved them into five clusters representing the α, β, γ, δ and ε cells. Interestingly, the δ and ε cells, which are in very low abundance in the islets, had distinct expression of the GHRL receptor and GHRL, respectively; δ cells also expressed the leptin receptor. These data indicate that, despite their scarcity, δ and ε cells might indeed have important physiological functions.

The team also identified a number of cell-specific transcripts that were correlated with increasing BMI in the healthy individuals. Finally, a comparison of transcriptomes from healthy cells and those from patients with T2DM identified differentially expressed transcripts, some of which might be altered to compensate for the reduced β-cell mass seen in T2DM.

Another study by Xin and colleagues also included donors who were healthy or with T2DM ($n = 6$ and 12, respectively). Again, using an unbiased, expression-profile-based approach the investigators also identified specific α, β, γ and δ (also called PP) cells.

The team found only 20 genes that are specific to certain islet cells and 245 genes that were altered in patients with T2DM, 28% of which had no known function.

"Many of these genes have not previously been associated with disease and are involved in controlling cell cycle, proliferation and function in other cell types," clarifies Jesper Gromada, who led the study. "Our findings could help shed light on the mechanisms for the decline in β-cell mass in T2DM."

Taken together, the results of these analyses provide a useful resource for future studies on the genetic determinants of T2DM.

Tim Geach

ORIGINAL ARTICLES Segerstolpe, Å. *et al.* Single-cell transcriptome profiling of human pancreatic islets in health and type 2 diabetes. *Cell Metab.* http://dx.doi.org/10.1016/j.cmet.2016.08.020 (2016) | Xin, Y. *et al.* RNA sequencing of single human islet cells reveals type 2 diabetes genes. *Cell Metab.* http://dx.doi.org/10.1016/j.cmet.2016.08.018 (2016)