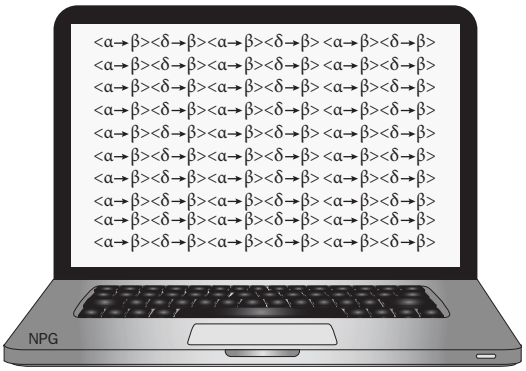
Nature Reviews Endocrinology **10**, 638 (2014); published online 2 September 2014; doi:10.1038/nrendo.2014.158

DIABETES

Reprogrammed pancreatic δ-cells restore insulin production

New research in mice shows that following β-cell ablation two distinct age-dependent mechanisms exist within the pancreatic islets to replenish insulin-producing cells from cells of a non-β-cell origin. The findings have potential implications for the treatment of patients with type 1 diabetes mellitus (T1DM)—an autoimmune disease characterized by the destruction of insulin-producing β cells.

Previous work in adult mice showed that in the absence of autoimmunity glucagon-producing α cells undergo reprogramming to form new insulin-producing cells following β-cell destruction. Building on this knowledge, the researchers investigated the effects of ageing—a known impediment to regeneration—on this regenerative capacity of the pancreatic islets.



RIP–DTR mice, which express a transgene encoding the human diphtheria toxin receptor gene under the control of the rat insulin promoter, were rendered β-cell-deficient by treatment with diphtheria toxin. In treated mice, α-cell conversion to an insulin-producing phenotype occurred from puberty to old age. Surprisingly, although no evidence of α-cell conversion was found in prepubescent mice, these mice spontaneously recovered from diabetes following β-cell loss, indicating the existence of a second pathway leading to the rescue of insulin production.

Further investigation revealed that β-cell destruction in prepubescent mice initiated the reprogramming of somatostatin-producing δ cells to insulin-producing cells via a process of dedifferentiation, proliferation and re-expression of islet developmental (insulin producing) markers.

The findings demonstrate that insulin production in mice can be restored from non-β-cell origins throughout life by the reprogramming of δ or α cells. Lead investigator Pedro Herrera from the University of Geneva, Switzerland, explains: "Demonstrating the involvement of δ-to-β-cell reprogramming in humans will prove extremely difficult owing to the inaccessibility of prepubertal T1DM samples as well as the lack of efficient human islet cell lineage tracing tools. However, our findings suggest that δ cells might be a suitable source of β cells for future regenerative therapies to treat diabetes."

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Original article Chera, S. *et al.* Diabetes recovery by age-dependent conversion of pancreatic δ-cells into insulin producers. *Nature* doi:10.1038/nature13633