DIFFERENTIATION: FROM α TO β

Pancreatic α cells have the potential to transdifferentiate into insulin-producing β cells, report researchers from the University of Geneva.

Effective strategies to replace damaged β cells remain a holy grail of diabetes research. "I always thought that the best cell-replacement therapy for type 1 diabetes mellitus should rely on stimulation of endogenous regeneration," states principal investigator Pedro Herrera.

To determine whether adult pancreas retains the intrinsic ability to make new insulin-producing β cells, Herrera's team generated an inducible transgenic mouse model of extreme β-cell loss. Administration of diphtheria toxin to these mice caused massive β-cell death, in the absence of inflammation or autoimmunity, with rapid onset of diabetes, cachexia and death.

Animals kept alive by administration of exogenous insulin exhibited clear signs of spontaneous β-cell regeneration over time (up to 10% of the normal β-cell mass). Surprisingly, lineage tracing analyses identified mature, glucagon-producing pancreatic α cells as the origin of β-cell regeneration.

Spontaneous conversion of α cells to β cells in the adult affected only a small fraction of the total α-cell population. "We are thus devising experiments to understand the signals and factors involved in epigenetic modifications undergone by these cells," Herrera continues. "An obvious goal would be to learn how to modulate and foster the observed α to β transdifferentiation."

The results of this study reveal a potentially high degree of plasticity in adult cell populations. Herrera and his team speculate that modulation of the immune system in patients with type 1 diabetes mellitus might promote spontaneous reconstitution of their pancreatic β cells. "Even a modest regeneration would represent a clear improvement of the quality of life of these patients," Herrera concludes.

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