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MECHANISMS OF DISEASE

Getting back to β -cell basics

β -cells are found in the pancreas and excrete insulin, which allows the body to process glucose. Diabetes, which results from a deficiency in insulin and a consequent inability to process glucose, is caused by either a lack of β -cells or inefficiently functioning β -cells. But what if β -cells could be replenished to suppress diabetes? Reporting in *Cell*,

Xiaobo Xu and colleagues have found endogenous β -cell progenitors in adults, which could provide a possible source of healthy β -cells.

During embryonic development, β -cells are produced by a transient

population of progenitor cells. Although researchers have searched for these progenitors in adults, until now it appeared that the only source of new β -cells in adults was old replicating β -cells.

To speed up β -cell turnover, which makes it easier to find new β -cells, Xu and colleagues performed partial duct ligation (PDL) on the pancreases of adult mice. PDL restricts the drainage of digestive fluids from the pancreas, thereby killing exocrine cells but increasing the proliferation of the islets of Langerhans, where β -cells are localized. One week after PDL, the number of β -cells in the pancreas had doubled. Notably, this doubling coincided with the increased expression of neurogenin-3 (*Ng3*), a well-established marker of the embryonic islet cell progenitors. Furthermore, inhibition of *Ng3* expression, using short hairpin interfering RNA, slowed the increase of β -cells following PDL.

The authors next wanted to determine whether NGN3-positive cells could give rise to new β -cells. NGN3-positive cells were purified from the pancreases of adult mice

that had undergone PDL, and were injected into NGN3-deficient pancreases. As assessed in various experimental settings, these NGN3-positive cells could differentiate into insulin-secreting β -cells and other pancreatic hormone-producing cells.

For Xu and colleagues, these adult β -cell progenitors “represent an obvious target for therapeutic regeneration of β -cells in diabetes.” They propose two strategies: progenitor β -cells could be cultured and differentiated *in vitro* and then transplanted; or progenitor β -cells could be activated and differentiated *in situ*. However, it still remains to be seen whether replicating β -cells or their progenitors offer more promise for the generation of new β -cells.

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ORIGINAL RESEARCH PAPER Xu, X. *et al.* β cells can be generated from endogenous progenitors in injured adult mouse pancreas. *Cell* **132**, 197–207 (2008)

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