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PANCREAS

ERα signalling drives β-cell formation and replication

In mice, the formation of pancreatic β cells during embryonic development and regeneration after injury in adulthood is controlled by estrogen receptor α (ERα) signalling, according to new research. The findings, published in *Diabetes*, identify ERα as a possible therapeutic target to restore β-cell mass and thereby control glucose homeostasis in patients with type 1 diabetes mellitus.

The researchers performed partial duct ligation (PDL) surgery on adult mice to mimic severe pancreatic injury and loss of β-cell mass. PDL-treated mice had increased 17β-estradiol (E_2) levels, ERα activity, *Esr1* (which encodes ERα) transcript levels and nuclear localization of ERα in β cells, in concert with increased β-cell proliferation. These responses were abrogated when ERα signalling was attenuated either chemically (by use of tamoxifen) or genetically (in $ERα^{-/-}$ mice); conversely, *in situ* delivery of E_2 induced β-cell formation. ERα signalling during embryogenesis of the endocrine pancreas resulted in similar effects to those seen in pancreata of PDL-treated adult mice.

Although ERα signalling has previously been shown not to increase β-cell proliferation in rodent models of diabetes mellitus or in human islets transplanted in diabetic mice, the current study supports the involvement of ERα in β-cell proliferation in embryonic and adult pancreata. Commenting on the findings, lead investigator Harry Heimberg says, "As estrogen can be preferentially delivered to the endocrine pancreas when conjugated to GLP-1 (thus avoiding unwanted adverse effects), correct targeting of the drug to human β cells to increase their proliferation in a controlled way should be feasible."

David Holmes

Original article Yuchi, Y. *et al.* Estrogen receptor α regulates beta cell formation during pancreas development and following injury. *Diabetes* doi:10.2337/db14-1798