OBJECTIVE: The prevalence of type 2 diabetes mellitus escalates with aging although beta-cell mass, a primary parameter of beta-cell function, is subject to compensatory regulation. So far it is unclear whether the proliferative capacity of pancreatic islets is restricted by senescence.

MATERIALS AND METHODS: Human pancreatic tissue from n=20 non-diabetic organ donors with a mean age of 50.2+/−3.5 years (range 7-66 years) and mean body mass index of 25.7+/−0.9 kg/m(2) (17.2-33.1 kg/m(2)) was morphometrically analyzed to determine beta-cell volume, beta-cell replication, beta-cell apoptosis, islet neogenesis, and pancreatic duodenal homeobox-1 (PDX-1) expression. RESULTS: Relative beta-cell volume in human pancreata (mean 2.3+/−0.2%) remains constant with aging (r=0.26, P=ns). Beta-cell replication (r=0.71, P=0.0004) decreases age-dependently, while beta-cell apoptosis does not change significantly (r=0.42, P=0.08). Concomitantly, PDX-1 expression is downregulated with age in human pancreatic tissue (r=0.65, P=0.002). The rate of islet neogenesis is not affected by aging (r=0.13, P=ns). CONCLUSIONS: In non-diabetic humans, aging is linked with impaired islet turnover possibly due to reduced PDX-1 expression. As beta-cell replication is considered to be the main mechanism responsible for beta-cell regeneration, these changes restrict the flexibility of the aging
human pancreas to adapt to changing demands for insulin secretion and increase the risk for the development of diabetes mellitus in older subjects.