Regeneration of the exocrine pancreas is delayed in telomere-dysfunctional mice.

Abstract:
Telomere shortening is a cell-intrinsic mechanism that limits cell proliferation by induction of DNA damage responses resulting either in apoptosis or cellular senescence. Shortening of telomeres has been shown to occur during human aging and in chronic diseases that accelerate cell turnover, such as chronic hepatitis. Telomere shortening can limit organ homeostasis and regeneration in response to injury. Whether the same holds true for pancreas regeneration in response to injury is not known. In the present study, pancreatic regeneration after acute cerulein-induced pancreatitis was studied in late generation telomerase knockout mice with short telomeres compared to telomerase wild-type mice with long telomeres. Late generation telomerase knockout mice exhibited impaired exocrine pancreatic regeneration after acute pancreatitis as seen by persistence of metaplastic acinar cells and markedly reduced proliferation. The expression levels of p53 and p21 were not significantly increased in regenerating pancreas of late generation telomerase knockout mice compared to wild-type mice. Our results indicate that pancreatic regeneration is limited in the context of telomere dysfunction without evidence for p53 checkpoint activation.