

TELOMERASE IS EXPRESSED IN RENAL MEDULLA AND PAPILLA: REGULATION BY OSMOLARITY

Suzanne Czerniak, Teresa Wang, Wendy Ying, Diana L. Carlone, Joseph V. Bonventre, David Breault and Benjamin D. Humphreys
Brigham and Women's Hospital, Children's Hospital and Harvard Stem Cell Institute, Boston, Massachusetts, USA

Purpose: The localization and function of telomerase (mTert) expressing cells in adult kidney is unknown. In this study we sought to identify cells in kidney that express mTert and determine their function.

Methods: We used a novel mTert-GFP transgenic mouse in which the mTert promoter drives GFP to define the localization and regulated expression of telomerase within the adult mammalian kidney.

Results: mTert-GFP localized to collecting duct epithelia in the inner medulla and papilla but not in cortex in kidneys from mTert-GFP mice. Consistent with this, we amplified endogenous mTert mRNA from renal papilla but not from cortex. At baseline, only 5-10% of collecting duct epithelial cells expressed GFP, suggesting that telomerase expression might be dynamically regulated. We further reasoned that telomerase could function to repair damaged telomeres in the harsh environment of the inner medulla and papilla. To test this hypothesis, we administered furosemide to mTert-GFP mice. Abrogation of the medullary concentrating gradient with furosemide is known to activate the ATM/p53 DNA repair pathway in collecting duct cells both *in vitro* and *in vivo*. We observed a dramatic increase in both mTert-GFP and mTert mRNA expression both 4 and 8 hours after furosemide administration. mTert mRNA was also rapidly induced by subjecting a collecting duct cell line to rapid changes in osmolality, a stimulus that activated the ATM/p53 DNA repair pathway in parallel.

Conclusion: Telomerase is expressed in collecting duct and is induced by rapid changes in osmolality *in vitro* and *in vivo*, consistent with a role for telomerase in the epithelial DNA repair response.