Abstract

Telomerase, a ribonucleoprotein enzyme, maintains the protective ends of eukaryotic chromosomes called telomeres. It has been known that telomerase is involved in the process of senescence and tumorigenesis. Recently, catalytic subunit of telomerase (TERT) has also been shown to protect neurons against amyloid beta peptide induced apoptosis. Here we studied novel functions of TERT in brain using telomerase overexpressing mice \textit{in vivo}. The injury volume induced by ischemia in brain of mouse overexpressing telomerase decreased about three fold compared to wildtype. Furthermore, neuron cells originated from TERT overexpressing mice are more resistant to NMDA, the agonist of glutamate-gated ion channel receptor which causes excitotoxicity. During ischemia, large amount of glutamate are released in brain and cause neuronal cell death through NMDA receptor mediated pathway. Therefore the resistance of brain of TERT overexpressing mice to ischemic injury may partly be explained by the reduced sensitivity of primary neurons to NMDA. In contrast, no difference for kinate excitotoxicity and serum dependency has been found. Furthermore, telomerase overexpressing mice may have defects in motor coordination and long term memory. The molecular mechanisms of telomerase in these behavioral defects are unknown yet. These results imply that telomerase may function in neuronal cell survival in brain.

Key words: Telomerase, Ischemia, Apoptosis, NMDA, Behavior