Esther Priel et al., J Neurol Neurophysiol 2019, Volume 10
DOI: 10.4172/2155-9562-C1-097

Neuroprotective effects of telomerase increasing compounds in *ex vivo* and *in vivo* animal models of Alzheimer disease

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The telomerase reverse transcriptase protein, TERT, in addition to its role in telomere extension and maintenance, possesses non-canonical functions such as: gene transcription regulation and protection of the mitochondria from oxidative stress. TERT is expressed in the adult brain and its exogenic expression protects neurons from oxidative stress and from the cytotoxicity of amyloid beta (Aβ). Therefore we suggest that increasing the expression of TERT in neurons by pharmaceutical compounds may protect them from the Aβ-induced neurotoxic effects. We used a primary hippocampal cells culture treated with aggregated Aβ as an *ex vivo* model for Alzheimer`s Disease (AD) and examined the effect of telomerase increasing compounds (AGS) on the Aβ neurotoxicity and the expression of various neuronal plasticity genes *in vitro* and *in vivo* in mouse hippocampus. AGS treatment transiently increased TERT expression in hippocampal primary cell cultures in the presence or absence of Aβ and protected neurons from the Aβ induced neuronal degradation. Following AGS treatment, both *in vitro* and *in vivo*, we observed a significant increase in the expression of growth associated protein 43, and feminizing locus on X-3 genes (NeuN), in the presence or absence of Aβ, and synaptophysin in the presence of Aβ. Neurotrophic factors (NGF, BDNF) expressions were also increased in AGS treated mice and the Wnt signaling pathway was activated. This data suggest that increasing TERT by pharmaceutical compounds partially exerts its neuroprotective effect by enhancing the expression of neurotrophic factors and neuronal plasticity genes in a mechanism that involved Wnt signaling activation.

Biography

Esther Priel obtained her DSc in the field of DNA repair from the Technion Institute in Haifa (Israel). She joined the Faculty of Health Sciences at the Ben Gurion University of the Negev in Beer Sheva Israel (1981) and is currently a Full Professor of Molecular Biology; served as the Director of the School of Medical Laboratory Sciences for 9 years at the same university. From 1981 till present she is the Head of the Nucleic Acid Topology Lab. She was a Visiting Scientist at the National Cancer Institute of the National Institute of Health (USA).

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