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Gabriele Saretzki

Newcastle University, UK

Telomerase activators improve motor function and protein degradation in a mouse model of Parkinson's Disease (PD)

While telomerase maintains telomeres in dividing cells, its protein component TERT (Telomerase reverse transcriptase) has various non-canonical functions such as localisation to mitochondria resulting in decreased oxidative stress, apoptosis and DNA damage. The TERT protein persists in adult neurons while telomerase activity is downregulated early during development (Ishaq et al., 2016). We recently demonstrated increased mitochondrial TERT protein in hippocampal neurons from Alzheimer's disease (AD) brains and mutual exclusion of pathological tau and TERT protein. Transduction of mutated tau into cultivated neurons confirmed that TERT decreases mitochondrial oxidative stress and lipid oxidation (Spilsbury et al., 2015). Mitochondrial dysfunction is also involved in the development of other neurodegenerative diseases. Treatment of PD model mice (Masliah et al., 2000) overexpressing human wild-type alpha-synuclein with 2 telomerase activators (TA Science Inc., USA) resulted in increased TERT expression in brain and amelioration of PD symptoms by significantly improving balance, gait and motor function as well as mitochondrial function. Analysing levels of total, phosphorylated and aggregated alpha-synuclein we found a substantial decrease of all these protein forms in the hippocampus and neocortex suggesting a better protein degradation after telomerase activator treatment. Interaction of TERT with proteasomal and autophagy pathways has been described recently. Accordingly, we have preliminary data showing a decrease in poly-ubiquitinated proteins and the autophagy receptor p62 and analyse the involvement of these degradation pathways currently. Thus, our results suggest that telomerase activators might form a novel treatment option for better degradation of toxic proteins in neurodegenerative diseases such as PD and AD.

Speaker Biography

Gabriele Saretzki has completed her PhD in 1990 at Humboldt University Berlin and performed most of her postdoctoral studies at the Institute for Ageing and Health in Newcastle upon Tyne (UK) where she is a Lecturer in Ageing Research since 2002. Her main interests are telomeres, telomerase, senescence, ageing, oxidative stress, mitochondria, stem cells and brain. She has pioneered work on non-canonical functions of the telomerase protein TERT shifting her focus recently to brain ageing and neurodegenerative diseases. She has published more than 88 papers in peer-reviewed journals and is an editorial board member of BMC Biology, PloS One and Oxidative Medicine and longevity.

e: gabriele.saretzki@ncl.ac.uk

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