Abstract Information

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Title :	Role of a selenoprotein in the pathophysiology of PD: therapeutic application after intranasal administration

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Abstract :

Oxidative stress is central to the pathogenesis of different diseases affecting the central nervous system, but therapeutic strategies targeting this pathological process have been difficult to design. We have previously demonstrated that selenoprotein T (SELENOT), a new thioredoxin-like protein of the ER, is essential for embryonic development and dopaminergic neuron survival and function. SELENOT exerts its neuroprotective activity by reducing oxidative stress and improving tyrosine hydroxylase activity. In an animal model of PD, targeted SELENOT gene disruption in the brain provoked rapid and severe parkinsonian-like motor deficits. Based on these findings, we designed a 10-amino acid peptide named PSELT as a potential mimic of SELENOT catalytic site to test its activity in PD animal models. PSELT proved to be efficient in protecting dopaminergic neurons in vitro and in vivo and could improve motor skills in animal models of PD. Transcriptomics studies revealed that PSELT acts through an original epigenetic regulatory mechanism. These results uncover the role of SELENOT as a neuroprotective enzyme and indicate that PSELT is a new therapeutic candidate for treatment of neurodegenerative diseases.