NEUROPROTECTIVE POTENTIAL OF DJ-1 RELATED PEPTIDES IN MODELS OF PARKINSON’S DISEASE

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Background: Parkinson’s disease (PD) is one of the most common neurodegenerative diseases caused by both environmental and inherited factors. DJ-1 mutations were identified as a cause of familial PD. The function of DJ-1 is still unknown; however, it is associated with response to oxidative stress. Using in vitro cellular platform expressing various DJ-1 levels and transgenic DJ-1 mice we found that DJ-1 has a key role in the resistance to oxidative and neurotoxic insults.

Aim: We have developed DJ-1 related peptides in order to asses whether they could exert neuroprotection.

Methods and results: Based on our knowledge on DJ-1 structure and function and a thorough bioinformatics survey we have designed DJ-1 related peptides and tested their ability to rescue from oxidative and neurotoxic insults. We found that short peptides based on DJ-1 significantly augmented cellular resistance of various cell lines and primary CNS cultures to various toxins. Furthermore, by using in vivo models of Parkinson’s disease, MTPT and 6-hydroxydopamine hemiparkinsonian mice models, we found that the peptides had significant neuroprotective properties. Peptide treated mice demonstrated significant abrogation of the disease in both behavioral and biochemical tests.

Conclusions: These studies indicate that DJ-1 has a neuroprotective potential, and may be used as a platform for developing therapies. DJ-1 related peptides demonstrated protective effects in \textit{in vitro} and \textit{in vivo} models. These promising peptides might serve as the basis for development of a novel neuroprotective therapy for PD.