

*Neuroscience Center of Excellence*

# Chancellor's Award Lecture

*in Neuroscience*



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**12:00 p.m.**

**Friday**

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**8th Floor**

**Neuroscience Center  
of Excellence  
Conference Room**

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## Mechanisms of the Brain Plasticity Under Degeneration of Dopaminergic Neurons With Focus on Dopamine Synthesis by Non-Dopaminergic Neurons

Progressive degeneration of dopaminergic neurons and a dopamine (DA) loss in the nigrostriatal system (NSS) is a key component in the pathogenesis of Parkinson's disease (PD). Motor symptoms first appear in humans many years after the onset of the neurodegenerative process under a threshold loss of about 50% of DA neurons (cell bodies) in the substantia nigra and 70-80% of axons and DA in the striatum. The lack of motor dysfunction during the long development of the disease is believed to be a consequence of brain plasticity compensating the failure of degenerated DA neurons. MPTP-treated mice were used to model and study the following stages of PD: (A) the early pre-symptomatic stage (subthreshold degeneration of axons and DA depletion in the striatum without loss of nigral cell bodies); (B) the advanced pre-symptomatic stage (subthreshold degeneration of striatal axons and DA depletion and a subthreshold loss of nigral cell bodies); (C) the early symptomatic stage (threshold depletion of striatal DA and a loss of DA axons and nigral cell bodies resulting in motor dysfunction). We concluded that: (1) regulation of tyrosine hydroxylase (TH) transcription in DA neurons appears to differ from that of translation; (2) at both stages of PD the TH protein content in DA cell bodies was higher than in the axonal terminals, suggesting an impairment of axoplasmic transport; (3) although TH activity was decreased in the NSS as a whole at both stages of PD, it was increased in compensation in individual neurons; (4) TH activity was not changed in the NSS as a whole and even increased in individual neurons at the symptomatic stage compared to the presymptomatic stage and (5) DA synthesis appears to be increased in striatal non-dopaminergic neurons expressing single enzymes, TH or aromatic L-amino acid decarboxylase. Thus, degeneration of DA neurons is associated with the compensatory functional activation of surviving DA neurons mostly due to the increase of TH activity as well as the increase of DA synthesis in non-dopaminergic neurons.