OMICS Group Conferences
Accelerating Scientific Discovery

3rd World Congress on
Cell Science & Stem Cell Research
November 20-22, 2013 DoubleTree by Hilton Baltimore-BWI Airport, MD, USA

The role of c-Abl in Parkinson's disease

Han Seok Ko
The Johns Hopkins University School of Medicine, USA

Oxidative stress contributes to the pathogenesis of Parkinson's disease (PD). c-Abl kinase activation is a key indicator of oxidative stress and growing evidence indicates that c-Abl activation is associated with the neuronal death in neurodegenerative disorders. Previously, we have identified that c-Abl is activated in the brain of PD patients and in MPTP intoxicated mice. In addition c-Abl tyrosine phosphorylates parkin, leading to loss of parkin's E3 ligase activity, inhibition of its protection function and accumulation of its substrates, AIMP2 and FBP1. Moreover, the c-Abl inhibitor, STI-571 restores parkin's E3 ligase activity and protection function through inhibition of tyrosine phosphorylation of parkin. Conditional knockout of c-Abl in mice protects against MPTP toxicity. Thus, inhibition of c-Abl is an attractive therapeutic target for the treatment of PD. In the present study, we evaluated the *in vivo* efficacy of the selective c-Abl inhibitor, Nilotinib in the MPTP-induced animal model of PD. Our results show that administration of Nilotinib results in protection of DA neuron loss against MPTP toxicity. In addition, our study shows that c-Abl is activated in the A53T α-synuclein Tg mice. Thus, we hypothesis that cellular stress from α-synuclein abnormality causes activation of c-Abl that contributes to DA neuronal cell death *in vivo*. In the present study, we have generated α-synuclein Tg mice where c-Abl gene is overexpressed or deleted in brain to determine the contribution of c-Abl. Evaluation and characterization of the role of c-Abl in bigenic mice suggest that the level of c-Abl activation correlates with the severity of α-synuclein pathology. These studies provide a strong rationale for testing of other c-Abl inhibitors as potential therapeutic agents for the treatment of PD and α-synucleinopathy.

Biography

Han Seok Ko has completed his Ph.D. in pharmacology in 2003 at Hokkaido University in Japan. He then began his postdoctoral fellowship in the Institute for Cell Engineering, Department of Neurology at the Johns Hopkins School of medicine. He became an Assistant Professor in the Department of Neurology at the Johns Hopkins University School of Medicine in 2010. Currently, he is an independent faculty member of the Neuroregeneration Program within the Institute for Cell Engineering, and is a principal investigator of the Morris K. Udall Parkinson's Disease Research Center of Excellence.

hko3@jhmi.edu