NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

School of Biological Sciences
College of Science

Seminar Announcement

In pursuit of bona fide ligands for Nurr1, an orphan nuclear receptor essential for the development and maintenance of midbrain dopaminergic neurons

Date: **13 November 2020, Friday**

Time: **4pm**

Venue: **Classroom 1, SBS**

Nurr1 (NR4A2), an orphan nuclear receptor, plays an essential role in developing, maintaining, and surviving midbrain dopaminergic (mDA) neurons. In line with the nuclear receptor's functional association with Parkinson's disease (PD), postmortem studies showed that its expression and activity are diminished in the PD postmortem brains. Besides, Nurr1 heterozygous null mice behave like an animal model of PD. They exhibit a significant decrease in both rotarod performance and locomotor activities associated with decreased levels of mDA neurons, suggesting that modulation of Nurr1's function may help protect dopaminergic brain cells and slow or modify PD progression. While Nurr1 is currently known as a ligand-independent nuclear receptor, previous studies have identified synthetic Nurr1 ligands for Nurr1 that modulate the Nurr1's transcriptional activation function and improve motor impairments in animal models of PD. In our attempts to identify bona fide ligands of Nurr1, we have newly identified endogenous cellular ligands and determined co-crystal structures of the ligand-binding domain of Nurr1 in complex with the novel ligands, providing insights into Nurr1's ligand-mediated transcriptional activation mechanism. Inspired by our biochemical, structural, cellular, and animal study results, preclinical studies are currently underway to evaluate the therapeutic potential of the Nurr1-activating ligands, which may contribute to achieving improved clinical outcomes than current symptomatic treatments for PD. In this talk, our recent progress in discovering Nurr1's naïve ligands will be discussed.

Speaker:

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