

DANDRITE LECTURE

A synaptic energy crisis entangled in neurodegeneration

The brain is a vulnerable metabolic organ that suffers acute functional decline when fuel delivery is compromised. We previously showed that CNS nerve terminals are one of the likely loci of metabolic vulnerability as they rely on efficient activity-dependent upregulation of ATP synthesis to sustain function, but failure to do so leads to abrupt synaptic collapse. To understand what steps in fuel combustion might be limiting at nerve terminals, we carried out a genetic suppressor expression screen of the glycolytic enzymes to determine, which, if any, might allow synapses to function under very low fuel conditions. Remarkably we found that modest changes in the abundance of the first ATP producing enzyme allows synapses to function under extreme hypometabolic conditions and that increasing this enzyme's activity leads to profound protection of mid-brain dopamine neurons in vivo and is able to reverse phenotypic defects driven by PARK20 mutations in vitro. This data points to exciting possibilities for how to confer resilience to vulnerable neuronal populations.

Host: Chao Sun



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Time: 12:30 – 13:30
Venue: Nucleus (1871-120)
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OPEN TO ALL INTERESTED.