Discovery Science
Emerging Scholars Lecture

"The Role of Optineurin in Neuronal Mitophagy"

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Mitophagy, the selective removal of damaged mitochondria, is thought to be critical to maintain neuronal homeostasis. Mutations in proteins implicated in mitophagy, including PINK1, Parkin, OPTN, and TBK1, cause Parkinson's disease or ALS, suggesting defective mitochondrial turnover contributes to neurodegeneration. To test this hypothesis, we used mild oxidative stress to induce low levels of mitochondrial damage in hippocampal neurons. We observed the sequential recruitment of Parkin, TBK1, and OPTN to depolarized mitochondria followed by their sequestration into autophagosomes, and determined this pathway was compartmentally restricted to the soma. Further, acidification of mitophagosomes was remarkably slow in neurons and overall was a rate-limiting step in the mitophagy pathway. Expression of an ALS-linked OPTN mutation disrupted the integrity of the mitochondrial network and this effect was exacerbated by oxidative stress. We propose that the slow kinetics of mitophagy enhance neuronal susceptibility to disease-associated mutations in the pathway, leading to neurodegeneration.

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December 3, 2019
4:00 p.m.

206 Preston Research Building

Refreshments will be served!

This lecture series features the most promising young scientists who are making notable discoveries as postdoctoral fellows or early career faculty.

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