New insight into Parkinson's disease

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New research provides crucial insight into the pathogenic mechanisms of Parkinson's disease (PD), a prevalent neurodegenerative disorder. The study appears in the April 19 issue of the *Journal of Cell Biology*.

The identification of inherited mutations in genes such as Parkin and PINK1 (PTEN-induced putative kinase 1) has revealed key factors in the development of familial forms of the disease. Parkin adds ubiquitin molecules to other proteins to trigger their degradation, while PINK1 regulates mitochondrial quality control. But how these two genes work together remains a mystery.

Now, Keiji Tanaka and colleagues show that PINK1 is rapidly and continuously degraded under steady-state conditions when mitochondria are healthy, and that a loss in mitochondrial membrane potential stabilizes PINK1's accumulation. Furthermore, PINK1 recruits Parkin from the cytoplasm to mitochondria with low membrane potential to initiate the disposal of damaged mitochondria.

Interestingly, the ubiquitin ligase activity of Parkin is repressed in the cytoplasm under steady-state conditions; however, PINK1-dependent mitochondrial localization liberates the latent enzymatic activity of Parkin. Some pathogenic mutations of PINK1 and Parkin interfere with the aforementioned events, suggesting they play a role in causing the disease.

More information: Matsuda, N., et al. 2010. J. Cell Biol. doi:10.1083/jcb.200910140

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