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# New research helps explain genetics of Parkinson's disease

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A new study by Narendra et al. suggests that Parkin, the product of the Parkinson's disease-related gene Park2, prompts neuronal survival by clearing the cell of its damaged mitochondria.

"[This is] an exciting new discovery that links the fields of mitochondrial quality control and the genetics of Parkinson's disease (PD)," writes Heidi McBride of the University of Ottawa Heart Institute. "…This work significantly increases our understanding of PD and provides a new framework for the development of therapeutic interventions."

The study, as well as McBride's commentary, will appear in the December 1, 2008 print issue of the *Journal of Cell Biology (JCB)*. Both articles will be published online Monday, November 24.

Loss-of-function mutations in the gene Park2, which encodes an E3 ubiquitin ligase (Parkin), are implicated in half the cases of recessive familial early-onset Parkinson's disease. Several lines of evidence suggest that Parkin loss is associated with mitochondrial dysfunction, but exactly how was unknown. To learn more about Parkin's role in cells, Narendra et al. examined the protein's subcellular location. They found that Parkin was present in the cytoplasm of most cells, but translocated to mitochondria in cells that had undergone mitochondrial damage such as membrane depolarization.

Damaged mitochondria can trigger cell death pathways; indeed, dysregulation of mitochondrial health was already thought to be a

possible cause of the neuronal cell death associated with Parkinson's disease. The relocation of Parkin to damaged mitochondria, the team showed, sends these defunct organelles to autophagosomes for degradation. Parkin may thus prevent the damaged mitochondria from triggering cell death. Because neurons are not readily replicable, disposing of damaged mitochondria may be especially important in the adult brain.

Citation: Narendra, D., et al. 2008. J. Cell Biol. doi:10.1083/jcb.200809125. (www.jcb.org)

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