The role of mitochondrial calcium in PINK1/Parkin related Parkinson's disease

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Résumé

Mitochondrial dysfunction has long been implicated in the pathogenesis of Parkinson's disease (PD). Loss of function mutations in *parkin* and *PINK1* cause the majority of early onset PD which can be elegantly modelled in *Drosophila*. Genetic studies in *Drosophila* established that PINK1 and Parkin act in a common pathway to maintain mitochondrial homeostasis, and impinge on the mitochondrial fission/fusion machinery. Substantial *in vitro* evidence has implicated PINK1-Parkin in regulating mitochondrial autophagy (mitophagy), however, the *in vivo* relevance and cause of cell death remains unclear. We have recently generated mitophagy reporter lines with show a surprising lack of impact of PINK1/Parkin on basal mitophagy raising questions about the physiological regulation of mitophagy. Considering a potential pathogenic cause we assessed the impact of mitochondrial calcium overload. Generating new mutants in the mitochondrial calcium uniporter (MCU) complex components we found that limiting mitochondrial calcium uptake can prevent some of the *Pink1/parkin* phenotypes. These findings support calcium overload as a contributing factor in PINK1/Parkin pathogenesis.

Mots-Clés: Parkinson's disease, drosophila, mitochondrial calcium

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