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"PARKINSON'S DISEASE AND MIRO1 AS A POTENTIAL MARKER"

Background: Miro1 is an outer mitochondrial membrane protein that recruits microtubule motors to mitochondria to mediate their transport. Miro1 is removed from the surface of depolarized mitochondria to arrest their motility and to facilitate their subsequent clearance via mitophagy. The molecular players that mediate Miro1 removal from damaged mitochondria include Parkinson's-related (PD) proteins—LRRK2, PINK1, and Parkin. Mutations in LRRK2, PINK1, or Parkin cause familial PD and are also associated with the risk of sporadic PD. Therefore, mitophagy may play a key role in Parkinson's pathogenesis and in additional age-dependent neurodegenerative diseases.

We have previously found that Miro1 is resistant to mitochondrial depolarization-induced degradation in fibroblasts from many PD patients and several at-risk individuals. Therefore, Miro1 has the potential to molecularly mark PD populations. We aim to determine whether Miro1 is useful for labeling individuals at risk for PD.

Methods: 87 induced pluripotent stem cells (9 healthy subjects, 30 PD patients bearing mutations in SNCA, LRRK2, or GBA, 42 asymptomatic genetic carriers, and 6 individuals exhibiting prodromal symptoms such as hyposmia, but without PD diagnosis), were cultured with or without carbonyl cyanide chlorophenylhydrazone (CCCP) supplementation. Immunoblotting and ELISA were performed to detect changes in Miro1 protein expression levels.

Results: The Miro1 phenotype is significantly associated with PD risk. Notably, we discovered a unifying impairment in degrading Miro1 at 6 h after CCCP treatment in 25 PD (83.3%) and 36 risk (genetic carriers) lines (85.7%). By contrast, Miro1 was efficiently removed following depolarization in every single control subject (0%).

Conclusion: Miro1 is a promising molecular marker for detecting both PD and at-risk populations. Tracking this Miro1 marker could aid in diagnosis and Miro1-based drug discoveries.