

## Activation of Mitophagy and Autophagy in Familial Forms of Parkinson's Disease, as a Potential Strategy for Cell Protection

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**Abstract :** Parkinson's disease (PD) is a progressive neurodegenerative disorder which is induced by the loss of dopaminergic neurons in the midbrain. The mechanism of neurodegeneration is associated with the aggregation of misfolded proteins, oxidative stress, and mitochondrial dysfunction. Considering this, the process of removal of unwanted organelles or proteins by autophagy is vitally important in neurons, and activation of these processes could be protective in PD. Short-time acidification of cytosol can activate mitophagy and autophagy, and here we used sodium pyruvate and sodium lactate in human fibroblasts with PD mutations (Pink1, Pink1/Park2,  $\alpha$ -syn triplication, A53T) to induce changes in intracellular pH. We have found that both lactate and pyruvate in millimolar concentrations can induce short-time acidification of cytosol in these cells. It induced activation of mitophagy and autophagy in control and PD fibroblasts and protected against cell death. Importantly, the application of lactate to acute brain slices of control and Pink1 knockout mice also induced a reduction of pH in neurons and astrocytes that increase the level of mitophagy. Thus, acidification of cytosol by compounds which play important role in cell metabolism also can activate mitophagy and autophagy and protect cells in the familial form of PD.

**Keywords :** Parkinson's disease, mutations, mitophagy, autophagy

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