The PARL-PGAM5-PINK1 axis on mitochondrial homeostasis: implications for Parkinson´s disease.

https://neurodegenerationresearch.eu/survey/the-parl-pgam5-pink1-axis-on-mitochondrial-homeostasis-implications-for-parkinsons-disease/

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The PARL-PGAM5-PINK1 axis on mitochondrial homeostasis: implications for Parkinson´s disease.

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The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

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Research Abstract

24 million people suffer from neurodegenerative disease and these numbers will double in the

next 20 years. Due to their unique metabolism, neurons rely extensively on mitochondria for energy production. Failure of mitochondrial function is connected to Parkinson´s disease (PD) and mutations in genes affecting mitochondria, PINK1 and Parkin, cause PD. PINK1, a mitochondrial kinase, is key for normal activity of mitochondria. PINK1 is under control of proteolitic cleaveage by PARL and phosphatase activity by PGAM5. Here I propose to use two complementary systems to study the regulatory processes of PARL and PGAM5. I will capitalize on the power of Drosophila genetics to discover novel partners regulating PARL-and PGAM5-dependent activity towards PINK1 and I will use primary cortical neurons and patient-derived cybrids to evaluate the evolutionary conservation of the mechanisms I discovered. My work will unveil key regulatory events controlling mitochondrial function relevant to the molecular events that underlie PD.

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