



University of Dundee

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# Cells, energy control and Parkinson's: the role of PINK1 and Parkin

Miratul Muqit

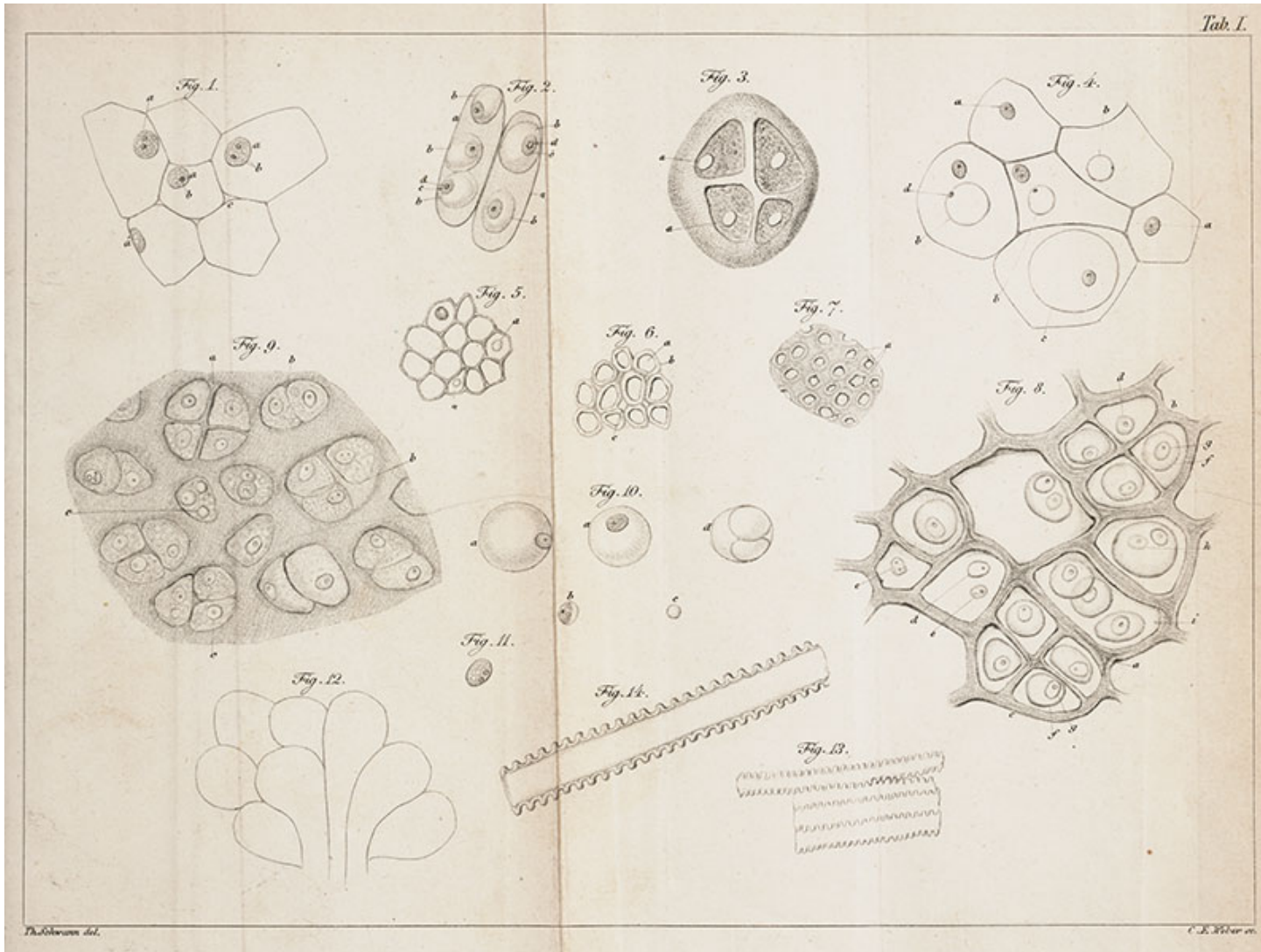
*Dundee Research Interest Group (DRIG) meeting  
26<sup>th</sup> June 2018*

# James Parkinson: “Shaking palsy” 1817

*“Before concluding these pages, it may be proper to observe once more, that an important object proposed to be obtained by them is, the leading of the attention of those who humanely employ anatomical examination in detecting the causes and nature of the diseases, particularly to this malady. By their benevolent labours, its real nature may be ascertained and appropriate modes of relief, or even of cure pointed out.”*

AN  
ESSAY  
ON THE  
SHAKING PALSY.  
BY  
JAMES PARKINSON,  
MEMBER OF THE ROYAL COLLEGE OF SURGEONS.  
LONDON:  
PRINTED BY WHITTINGHAM AND ROWLAND,  
GRAND STREET,  
FOR SHERWOOD, NEELY, AND JONES,  
PATERNOSTER ROW.  
1817.

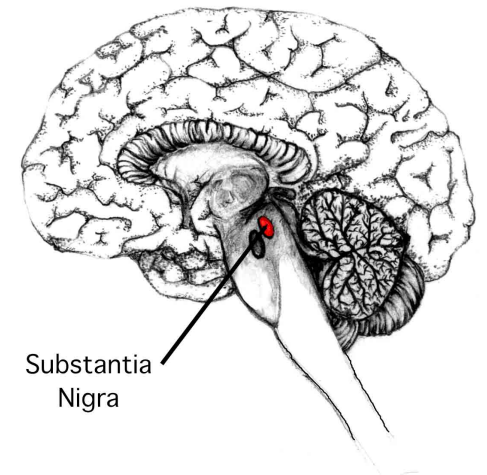
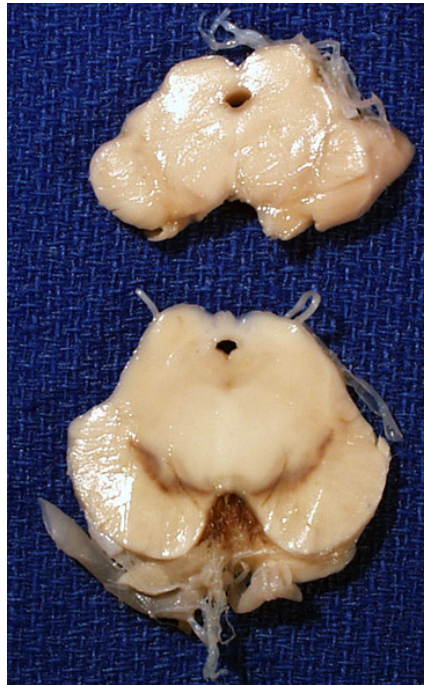
# Theodor Schwann – basic unit of all living tissues are cells



# Pathological insights: Trettiakof 1919



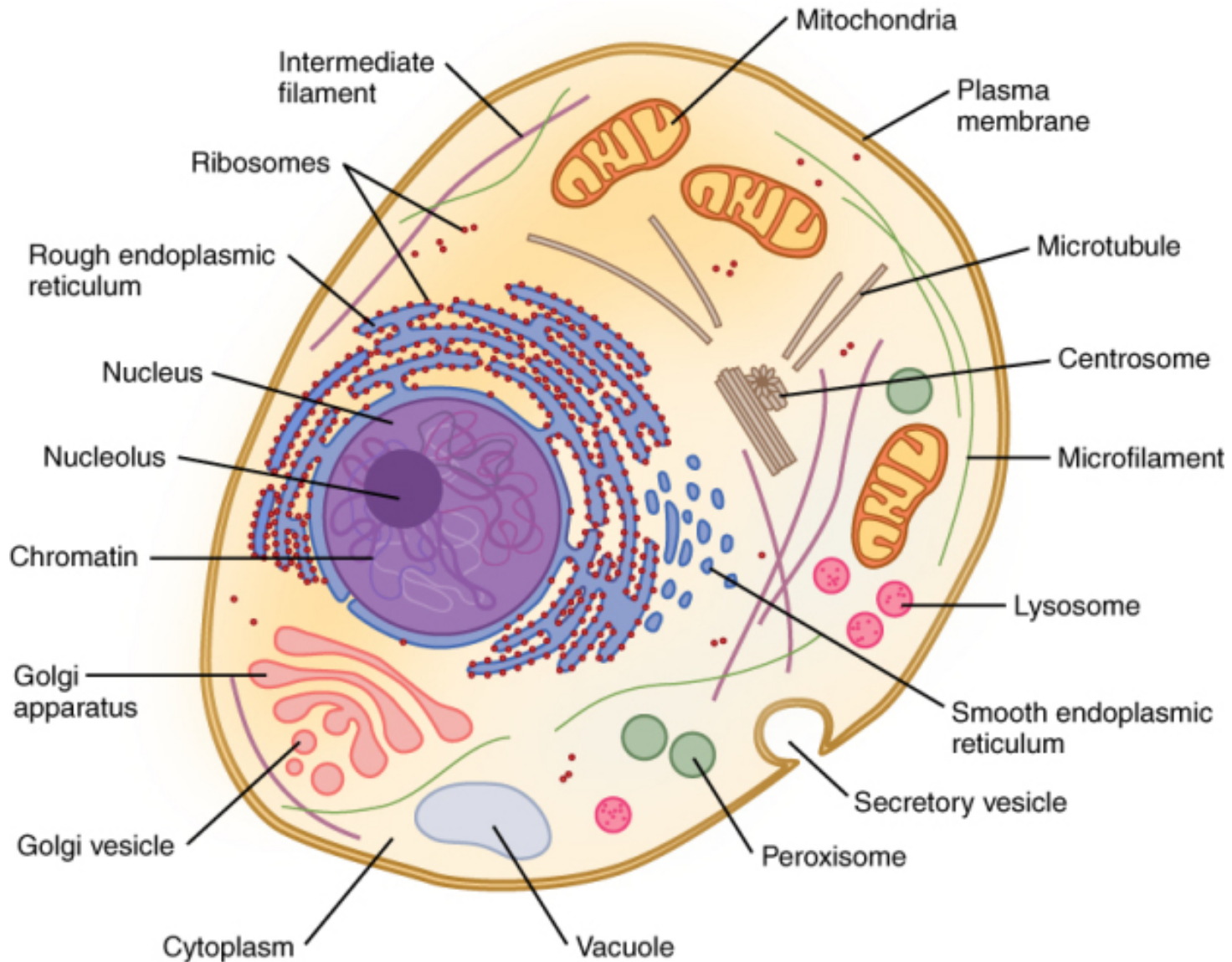
Konstantin Tretiakoff



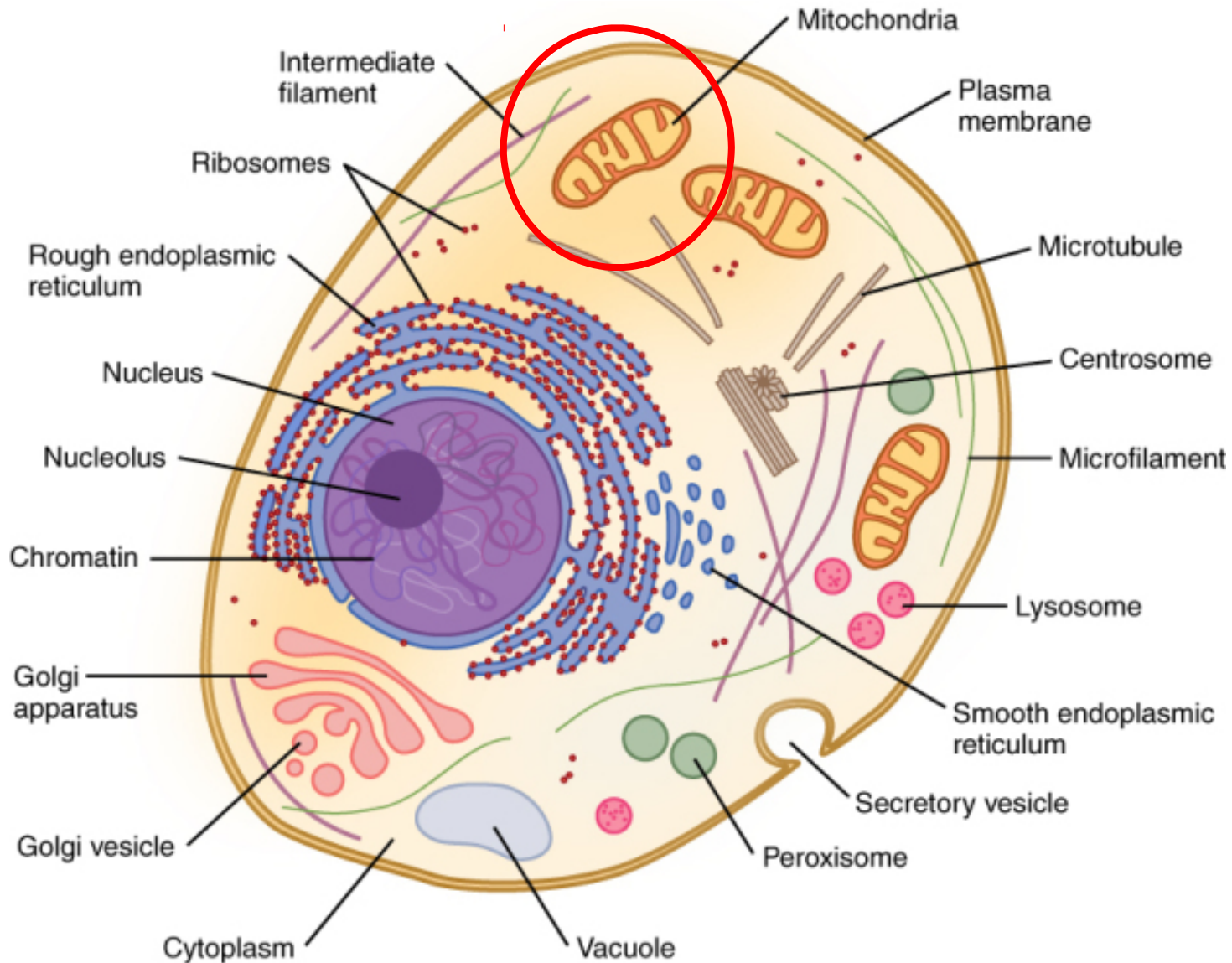
Substantia Nigra

*First to recognise degeneration within substantia nigra*

# Basic components of cells



# Energy producers of the cells - mitochondria



# Energy production in the mitochondria

Oxygen

Fat

Sugar

Protein



**ENERGY**



# Impact of damage on Energy production



Oxygen

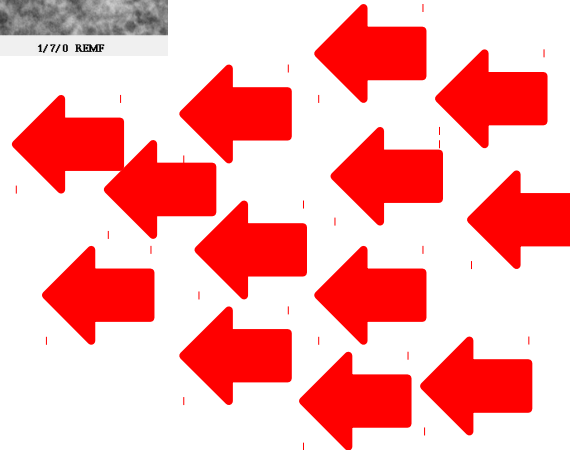
Fat

Sugar

Protein

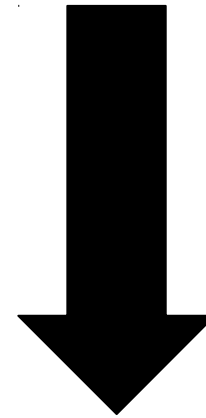
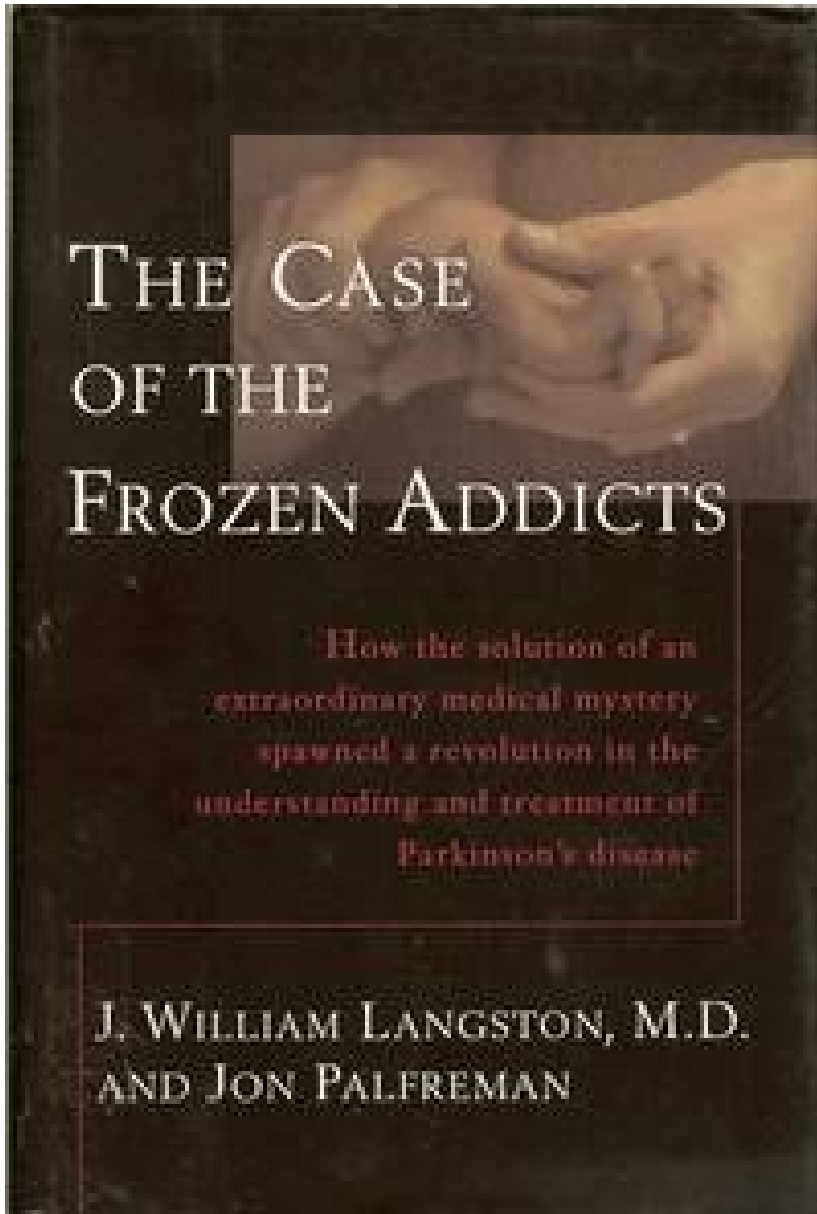


ENERGY



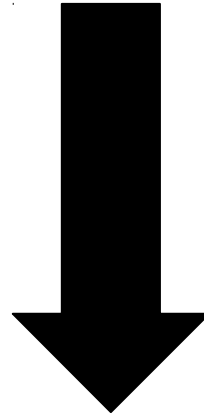


# Damage to mitochondria can lead to Parkinson's



**Parkinson's**

# Damage to mitochondria can lead to Parkinson's – How?



**Parkinson's**

# Genetic Breakthrough in 2004



**PINK1 Gene**



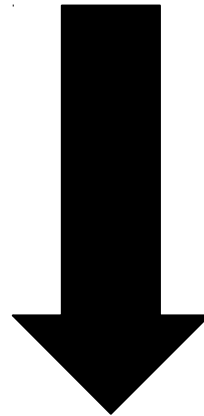
50 nm 08LungTEM 1/7/0 REMF



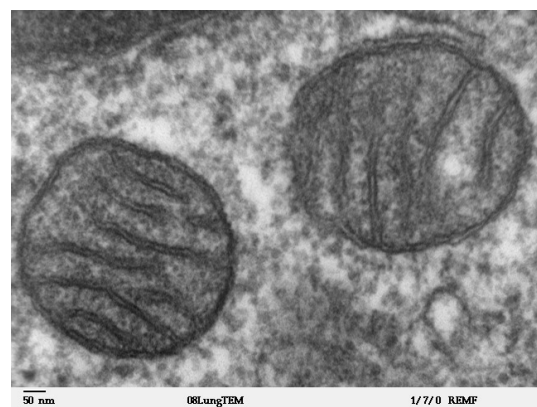
**Parkinson's**

# Genetic Breakthrough in 2004

**PINK1 Gene**

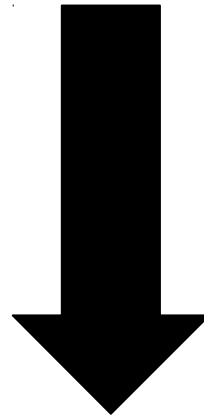


**Parkinson's**

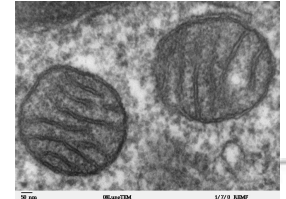


# PINK1 is a sensor of mitochondrial damage

**PINK1 Gene**

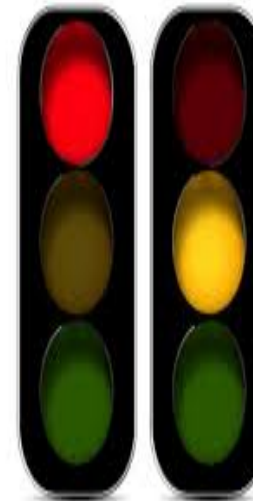
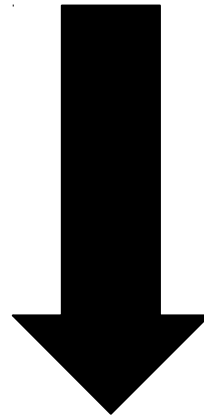


**Pathway inactive**



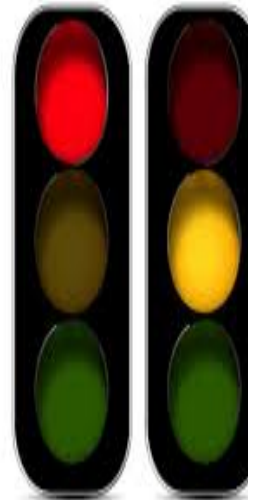
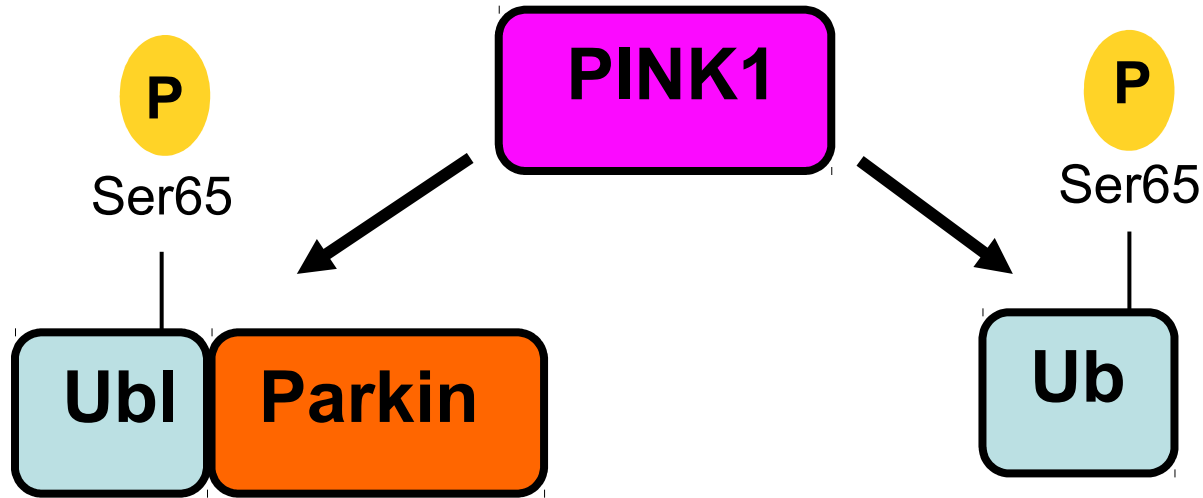
# PINK1 is a sensor of mitochondrial damage

**PINK1 Gene**

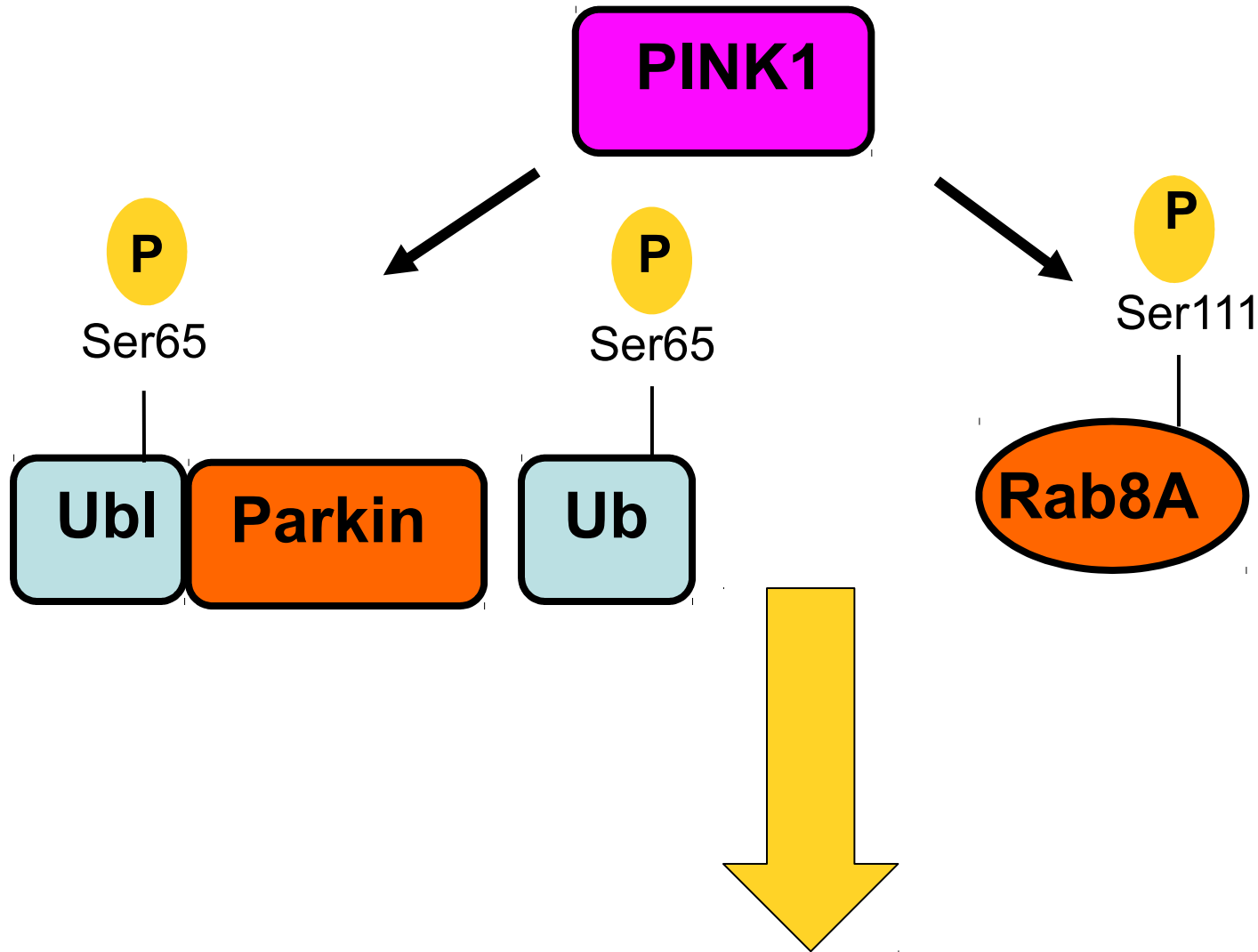


**Pathway Active**

# PINK1 pathway Active



# PINK1 pathway Active

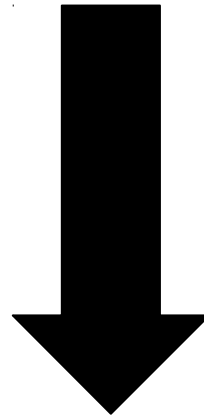


**Elimination of bad mitochondria**

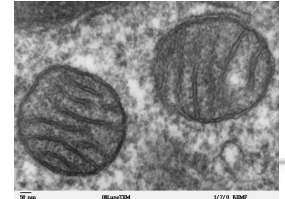


# PINK1 pathway Inactive

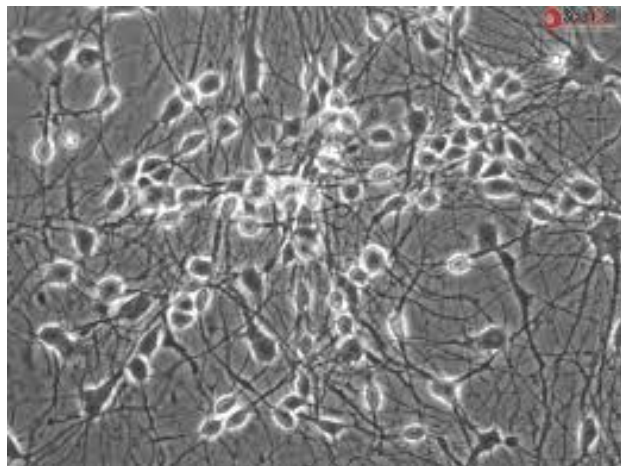
**PINK1 Gene**



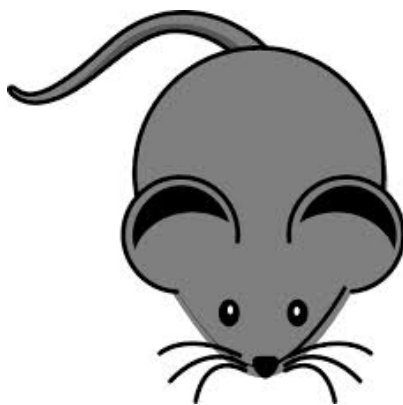
**Pathway inactive**



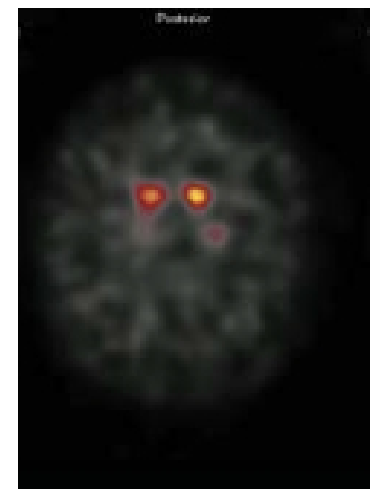
# Showing our findings are important for Parkinson's



**Brain cells in a dish**

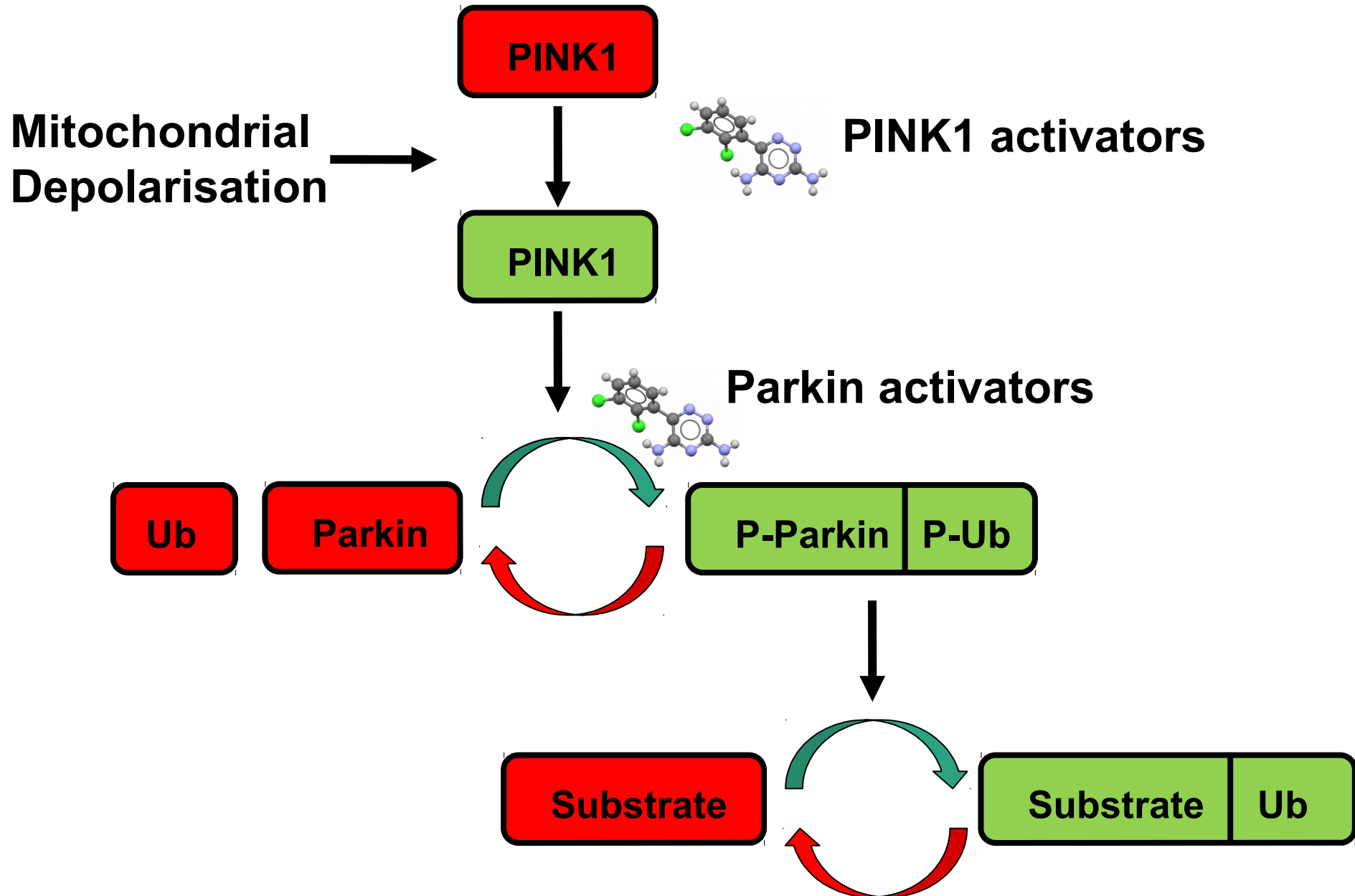


**Mouse models**

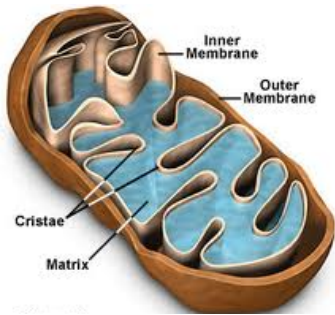
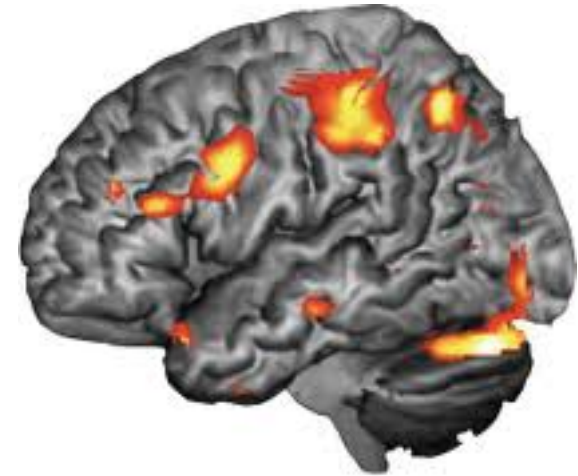
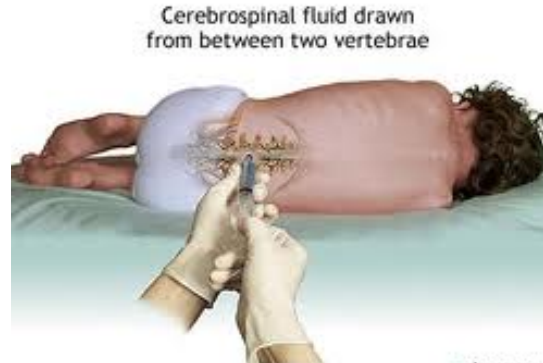
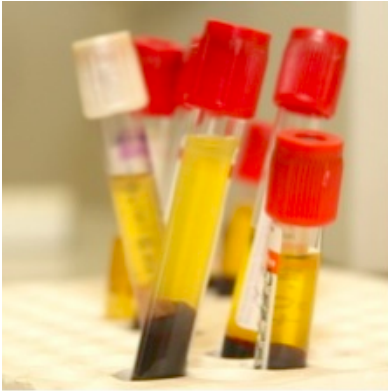


**Human Patients**

# Targeting the PINK1 pathway in Parkinson's



# Developing Biomarkers of PINK1 pathway



**MITOCHONDRIAL STRESS**



**Parkinson's disease**

**Antibody Probes**



In collaboration with Sandy Chou, Abcam

# Acknowledgments



Odetta Antico  
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**DNA sequencing – Nick Helps and team**  
**Mass spectrometry – David Campbell, Bob Gourlay, Joby Varghese**

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