

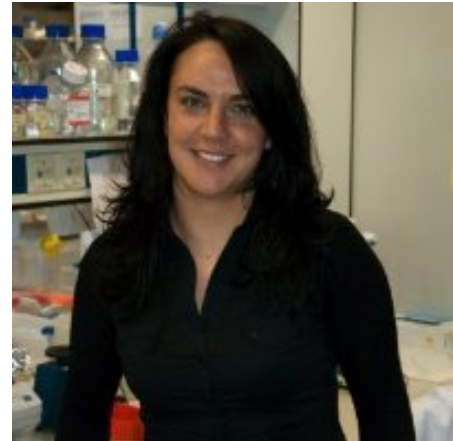
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### Keywords

Mitochondria - Parkinson's Disease - PINK1 – Complex I

### Science

Parkinson's Disease (PD) is a common progressive neurodegenerative disorder, characterized by postural instability, rigidity, tremor and bradykinesia. The pathological hallmark of PD is the loss of dopaminergic neurons in the substantia nigra region of the brain. New data revealed that at least ten different mutations in the gene encoding for PTEN-induced putative kinase 1 (PINK1) are associated with recessive forms of early onset PD. The PINK1 gene encodes a 581 amino acid protein with a N-terminal mitochondria targeting peptide and a putative serine/threonine kinase domain. The targeting of PINK1 to the mitochondria suggests that this protein may phosphorylate mitochondrial target(s) that might play a role in regulating mitochondria function. This hypothesis brings forward a possible link between this gene and the clinical and experimental evidence that implicate the involvement of mitochondrial dysfunction and oxidative stress in PD.

Our approach will allow us to further investigate the functional properties of PINK1 and will clarify the mechanism by which PINK1 regulates Complex I activity. We are also confident that identification of PINK1 substrates will give us more insight into role of PINK1 in regulating ETC functionality.

Therefore, we believe that further studies of the fundamental roles of PINK1 in mitochondrial functions could not only reveal the biological function of this protein, but could additionally lead to a better understanding of the mechanistic link between mitochondrial dysfunction and PD, a key pathogenic factor in a number of neurodegenerative disorders, in particular PD.

### Selected publications

**Morais, V.A.**<sup>#</sup>, Haddad, D., Craessaerts, K., De Bock, P., Swerts, J., Vilain, S., Aerts, L., Overbergh, L., Grünewald, A., Seibler, P., Klein, C., Gevaert, K., Verstreken, P., De Strooper, B. <sup>#</sup> (2014) PINK1 Loss of Function Mutations Affect Mitochondrial Complex I Activity via NdufA10 Ubiquinone Uncoupling. *Science. In press*

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