IDENTIFICATION OF IRON-ASSOCIATED SIDEROFLEXIN 1 AS A POTENTIAL DOWNSTREAM EFFECTOR OF PTEN-INDUCED KINASE 1

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PTEN-induced kinase 1 (PINK1) is a protective mitochondrial serine/threonine kinase; many Parkinson’s disease-associated mutations have been identified that exhibit recessive inheritance. There is still limited knowledge of substrates and mode of action for this enzyme.

We have established inducible stably transduced BE2-M17 cell lines expressing PINK1 using a lentiviral expression system. The mitochondrial proteome for cells with and without induction of PINK1 gene expression were compared. Following PINK1 induction, two dimensional protein gel electrophoresis followed by mass spectrometry identified a new protein gel spot of 35 kDa identified as Sideroflexin 1.

Sideroflexin 1 is a five transmembrane putative transporter of unknown function; deficiency has been linked with mitochondrial iron accumulation and anaemia in erythrocytic precursors and flexed-tail phenotype in mice$^1$. To investigate Sideroflexin 1 tissue distribution, mouse brain tissue expression of Sideroflexin 1 was examined by western analysis. This revealed mitochondrial expression with increased expression with aging and moderate increase in brains of an alpha-synuclein transgenic mouse line.

Further investigations will explore potential interaction and potential phosphorylation of Sideroflexin 1 by PINK1. This may yield important insight into function of these proteins and their role in Parkinson’s disease.

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