SFXN3

The mitochondrial protein SFXN3 is a neuronally-enriched protein expressed in synaptic terminals and regulated by key synaptic proteins, including α-synuclein. We first show that SFXN3 uses the carrier import pathway to insert into the inner mitochondrial membrane. Using high-resolution proteomics on Sfxn3-KO mice synapses, we then demonstrate that SFXN3 influences proteins and pathways associated with neurodegeneration and cell death (including CSPα and Caspase-3), as well as neurological conditions (including Parkinson's disease and Alzheimer's disease). Over-expression of SFXN3 orthologues in Drosophila models of Parkinson's Disease significantly reduced dopaminergic neuron loss. In contrast, the loss of SFXN3 was insufficient to trigger neurodegeneration in mice, indicating an anti- rather than pro-neurodegeneration role for SFXN3. Taken together, these results suggest a potential role for SFXN3 in the regulation of neurodegeneration pathways [1].

1)
Ledahawsky LM, Eirini Terzenidou M, Edwards R, Kline RA, Graham LC, Eaton SL, van der Hoorn D, Chaytow H, Huang YT, Groen EJN, Motyl AAL, Lamont DJ, Tokatlidis K, Wishart TM, Gillingwater TH. The mitochondrial protein Sideroflexin 3 (SFXN3) influences neurodegeneration pathways in vivo. FEBS J. 2022 Jan 28. doi: 10.1111/febs.16377. Epub ahead of print. PMID: 35092170.