CBI Toulouse
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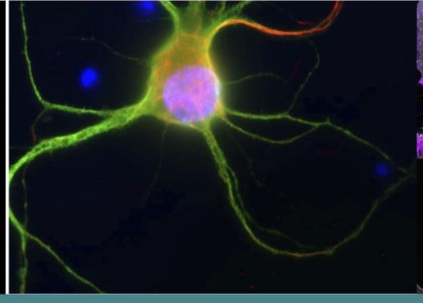
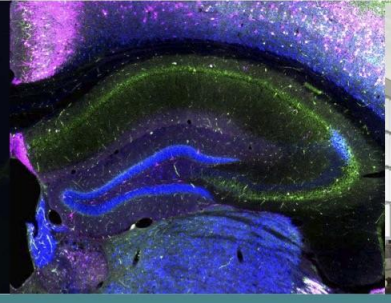
NEURO





MOLECULAR AND CELLULAR NEUROBIOLOGY

12h15 A.M

TUESDAY
OCTOBER 26TH
2021

Federico Miozzo, PhD

Institute of Neuroscience – MILAN

http://www.in.cnr.it/index.php/it/people-it/793-federico-miozzo

Maintenance of mitochondrial integrity in midbrain dopaminergic neurons governed by a conserved developmental transcription factor

The degeneration of dopaminergic (DA) neurons in the substantia nigra is a hallmark of Parkinson's disease (PD). Dysregulation of developmental transcription factors is implicated in dopaminergic neurodegeneration, but the underlying molecular mechanisms remain largely unknown. *Drosophila Fer2* is a prime example of a developmental transcription factor required for the birth and maintenance of midbrain DA neurons. Using an approach combining ChIP-seq, RNA-seq, and genetic epistasis experiments with PD-linked genes, here we demonstrate that *Fer2* controls a transcriptional network to maintain mitochondrial structure and function, and thus confers dopaminergic neuroprotection against genetic and oxidative insults. We further show that conditional ablation of *Nato3,* a mouse homolog of *Fer2*, in differentiated DA neurons results in locomotor impairments and mitochondrial abnormality in aged mice. Our results reveal the essential and conserved role of *Fer*2 homologs in the mitochondrial maintenance of midbrain DA neurons, opening new perspectives for modelling and treating PD.

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