

# Inhibition of BAX-mediated apoptosis to treat neuronal cell death in Parkinson's disease

## The Problem

- Loss of dopaminergic (DA) neurons in the *substantia nigra* is a defining pathological feature of Parkinson's disease. This process is largely driven by apoptotic cell death.
- Inhibition of BAX-mediated apoptosis blocks DA death, thus preventing a key pathophysiological feature of PD.
- BAK is expressed in very low levels in DA neurons, making BAX a unique target for apoptosis inhibition in Parkinson's Disease.

## The Solution

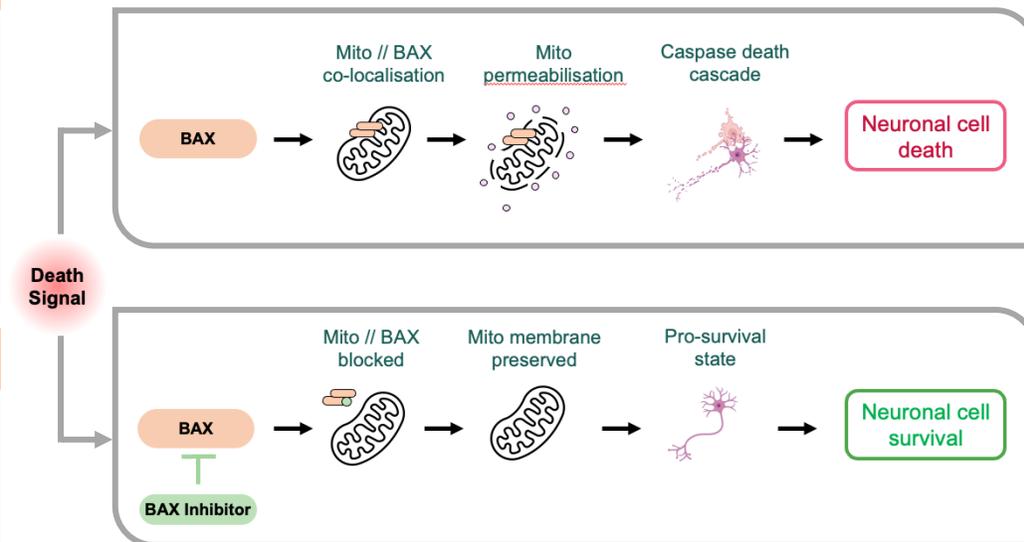
- Through our novel and potent tool compound WEHI-3773 we have demonstrated proof-of-concept protection of DA neurons in response to death stimuli.
- We have also shown that WEHI-3773 disrupts the BAX–VDAC2 interface, a key checkpoint in apoptosis execution.
- Our approach demonstrates that selective BAX inhibition offers neuroprotection and preserves apoptosis in non-neuronal cells.
- Our series of novel BAX inhibitor compounds is ready to progress through Hit-to-Lead

## Our Program

### Next steps:

- Our compounds will be assessed in disease-relevant studies to assess their impact on neuronal survival and function.
- Assess the *in vivo* PK profiles of selected compounds in mice to select candidates to be tested in disease-relevant models of neurodegeneration.

Seeking **partnerships and funding** to progress drug discovery and pre-clinical activities



## Our Team

Prof. Guillaume Lessene, Medicinal chemistry  
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