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## PAPER OF THE MONTH • DECEMBER 2020



### Joseph Flores, PhD

Research Associate, Lady Davis Institute



### Andréa C. LeBlanc, PhD

Professor, Department of Neurology & Neurosurgery, McGill University  
Senior Investigator, Lady Davis Institute (1993-2019)



## nature communications

### “Pre-symptomatic Caspase-1 inhibitor delays cognitive decline in a mouse model of Alzheimer disease and aging,”

Joseph Flores, Anastasia Noël, Bénédicte Foveau, Olivier Beauchet, Andréa C. LeBlanc

Early therapeutic interventions are essential to prevent Alzheimer Disease (AD). To this point, however, the outcomes of basic and clinical research exploring different pathways to prevent or reverse its ravages have proven disappointing, thus compelling novel approaches to attacking the onset of AD. To this end, Dr. Andréa LeBlanc’s lab has been investigating approaches to inhibit the onset of neurodegeneration in AD and to identify novel plausible therapeutic targets.

The LeBlanc team identified the activation of the inflammasome Nlrp1-Caspase-1- Caspase-6 neurodegenerative pathway in early cognitive impairment and Alzheimer disease brain neurons. This paper shows that a Caspase-1 inhibitor, delays the onset of cognitive deficits in an AD mouse model and raises hope that VX-765, previously approved in the United States by the Food and Drug Administration for central nervous system clinical trials in humans, may be a useful drug to prevent the onset of cognitive deficits and brain inflammation in AD.

The data indicates that, without a sustained administration, VX-765 effectively delays cognitive deterioration in an AD mouse model. A 1-month pre-symptomatic administration of the drug delays cognitive impairment by at least 5 months in Swedish/Indiana mutant amyloid precursor protein (APPSw/Ind) J20 mice. Conversion of mice age and time of treatment to human age suggests that a 3-4-year pre-symptomatic treatment in humans could prevent age-dependent cognitive deficits for 10 to 15 years.

The editors at *Nature Communications* featured this paper on an Editors’ Highlights webpage of recent research on “From Brain to Behaviour.”

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