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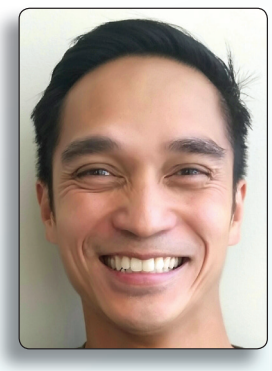

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nature COMMUNICATIONS

Caspase-1 inhibition alleviates cognitive impairment and neuropathology in an Alzheimer's disease mouse model

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This research reveals that a drug reverses memory deficits and stops Alzheimer disease pathology (AD) in an animal model. Importantly, this drug has already proven to be non-toxic for humans in a clinical setting and could, therefore, be brought quickly to trials in humans against AD.

Dr. LeBlanc had discovered that the Caspase-6 enzyme is highly activated in Alzheimer disease brain lesions and associated with loss of memory, pursuing the hypothesis that stopping Caspase-6 might stop progressive dementia. Since there are no specific Caspase-6 inhibitors, her research moved upstream, ultimately discovering that Caspase-1 was responsible for activating Caspase-6.

This was a significant revelation because Caspase-1 inhibitors had been developed for treating inflammatory diseases. Her team tested the effects of a particular Caspase-1 inhibitor, called VX-765, against memory loss and brain pathologies in a mouse model of Alzheimer disease and discovered that it has an unprecedented beneficial effect in Alzheimer mice. The drug rapidly reverses memory loss, eliminates inflammation, and stops Alzheimer's prototypical amyloid peptide accumulation in the mouse brains. In addition to being safe for humans at relatively high doses for extended periods of time, it is capable of crossing the blood-brain barrier, a significant challenge in the development of drugs against disorders of the brain. Having identified the Caspase-1/Caspase-6 neurodegenerative pathway in human neurons and in human Alzheimer brains, there is a chance that VX-765 will prove effective in humans.

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