

Pathoprofile **ALZHEIMER'S**

Alzheimer's disease is an age-related neurodegenerative disorder characterized by gradual cognitive decline. With 44 million people affected worldwide, it is one society's most prevalent degenerative diseases¹ The number of Canadians suffering from Alzheimer's or a related form of dementia is estimated to double to around 1.3 million people within the next generation.²⁻⁴ This could be due to the repercussions of chronic stress over longer life expectancies.

NEUROLOGICAL FEATURES

There are two types of Alzheimer's: early-onset (familial) Alzheimer's and late-onset (sporadic) Alzheimer's. Despite its enigmatic etiology, a growing body of research has noted several hallmark symptoms of familial Alzheimer's including loss of neurons, general atrophy of the brain, such as amyloid- β plaques and neurofibrillary tangles (NFTs).⁵ Two of the most prominent pathological features of the disease, A β 42 peptide plaques and hyperphosphorylated tau tangles, are integral to understanding the progressive cognitive decline associated with familial Alzheimer's.^{3,5}

APP CLEAVAGE

The APP gene encodes an amyloid precursor protein (APP), an inactive protein that must undergo modifications before its conversion to an activated form. While the function of APP remains elusive, growing research suggests that it may play a role in neuronal growth and repair.⁵ Normally, APP is initially cleaved by the enzymes, α -secretase and β -secretase, forming an α -stub and a β -stub, respectively.⁴ These cleavage products are further cleaved by γ -secretase, an enzyme complex comprised of four proteins - Nicastrin, Aph1, Pen-2, and the catalytic core presenilin.⁶ Following cleavage, the α -stub generates a p3 peptide, and the β -stub produces an extracellular C-terminal fragment, an intracellular domain fragment, and a variable amyloid- β (A β) peptide.^{6,7} This peptide can exist in different forms with lengths ranging from 39 to 49 residues; in particular, the peptide most commonly exists as A β 40 or A β 42.^{7,8} Accumulation of the more toxic A β 42 isoform instigates the aggregation of amyloid plaques.^{7,8}

