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Inhibition of A-Beta Fibrillogenesis by Myelin Basic Protein

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The abnormal accumulation of beta-amyloid in the brain is a key feature of Alzheimer's disease and is believed to be the cause Alzheimer's symptoms. Beta-amyloid is a small fragment of a protein known as amyloid precursor protein (APP). Enzymes digest the protein precursor and release beta-amyloid, which aggregates into larger structures and accumulates in the brain. The larger aggregates may take on one of two forms—a structured form known as a fibril or a more diffuse form known as soluble beta-amyloid. Both of these forms accumulate around neurons and blood vessels of the brain. It is unclear what factors regulate the form and location of beta-amyloid aggregates.

Van Nostrand, Ph.D., and his colleagues have identified a protein, myelin basic protein (MBP), which binds to beta-amyloid and controls its ability to form fibrils. The researchers plan to study the interactions between MBP and the two structural forms of beta-amyloid in the laboratory. Following the laboratory tests, they will examine the same interactions in a mouse model of Alzheimer's disease. The mouse model mimics the accumulation of beta-amyloid as seen in the human form of the disease. The researchers will manipulate the amount of MBP in these mice to see if they can influence the aggregation and accumulation of beta-amyloid. These proposed studies will provide essential, new information concerning the regulation of beta-amyloid accumulation and may lead to the development of novel therapeutic approaches for Alzheimer's disease.