A Probable Treatment for Alzheimer’s Disease: Somewhere Between Confusion and Clarity

The Transthyretin Protein

Alzheimer’s disease currently affects an estimated 4.5 million Americans. The progressive degenerative neurological disorder is commonly associated with memory loss and intellectual impairments concerning speech, skilled movements, and recognition. Discovered in the early 1900s by German psychiatrist Alois Alzheimer, the specific cause of the disease is not known, though the presence of Alzheimer’s disease has been connected to abnormal folding of the amyloid beta (A-beta) protein in the brain. Today, Alzheimer’s disease is the eighth leading cause of death in the United States, with over 63,000 fatalities accounted for. Alzheimer’s disease is also the third most costly disease in the country, costing the U.S. over $100 billion each year.

The A-beta protein and transthyretin are two proteins of interest to scientists trying to understand how Alzheimer’s disease develops. The disease results from the accumulation of a specific fragment of the amyloid precursor protein. When this small piece of protein is cut from the amyloid precursor protein, the smaller piece is referred to as the A-beta protein. The A-beta protein forms plaques by aggregating together (shown in Figure 1), as well as causing neurons in the brain to die, resulting in Alzheimer’s disease. Transthyretin, however, is the “good protein” and prevents the A-beta protein from killing those neurons. Though researchers do not specifically know how the transthyretin does this, it is hypothesized that the transthyretin binds with the A-beta so that it cannot interact with the neurons.

Studies have shown that mice genetically engineered to have higher levels of the A-beta protein also have more transthyretin, therefore preventing Alzheimer’s-like pathology from occurring in the mice. Shown below in Figure 2 are examples from the mouse experiment. Boxes C and E are enlarged from Box A to show portions of the hippocampus (a part of the brain found in the temporal lobe concerned with memory) of the control mouse. Boxes D and F show the enlarged portions of the hippocampus of the mouse that over expressed the mutant amyloid precursor protein and had high levels of A-beta. The brown areas shown in Figure 2 in boxes B, D, and F represent the presence of the transthyretin protein, showing how much the mouse’s brain has increased transthyretin levels to protect itself from the induced A-beta increases and neuronal cell death. This increase in transthyretin, unfortunately, only happens in mice, and has not been seen in humans living with Alzheimer’s disease. Because mice have dramatically increased transthyretin levels, which block the A-beta toxicity, researchers are trying to find ways of increasing that protein in humans.

Mithridion, Inc., is a biopharmaceutical company founded by Dr. Jeffrey Johnson and his colleagues, with the mission of discovering and developing new drugs to treat Alzheimer’s and other neurodegenerative diseases (Figure 3). Having patented findings from the mouse experiment, Mithridion, Inc., aims to develop a drug that will mimic the protein in a mouse’s brain, sAPPalpha, not found in humans, that causes increased transthyretin levels in the mouse brain. This drug could protect humans from the toxicity of A-beta and stop the progression of Alzheimer’s disease. The company hopes to have a drug available to the public within the next few years.