Amyloid precursor protein (APP) is a key focus of research into the causes of Alzheimer’s disease because it is the precursor to beta-amyloid, a fragment of APP that forms amyloid plaque, a characteristic feature of Alzheimer pathology. Once APP is made inside a cell, it is transported to different locations within that cell by specialized transport proteins. The final destination of APP strongly influences whether it is cut to form beta-amyloid, so scientists are working to understand the proteins and mechanisms that control the transport of APP.

Catherine Collins, Ph.D. and colleagues are studying an APP transport pathway that involves a protein called JIP1. JIP1 is known as a “scaffolding” protein, providing support and transport activity for nerve cells. JIP1 interacts with other proteins called JNKs (jun-N-terminal kinases) which perform important signaling functions within the cell. The JNK protein is of particular interest because it is known to be activated in Alzheimer’s disease, in which it might be part of a signaling pathway leading to cell death.

Dr. Collins and colleagues proposed to study APP and its interactions with JIP1 and JNK using a common genetic model, the fruit fly. They plan to use imaging and biochemical studies to examine how signaling through the JNK pathway affects the transport of APP. Because the genetics of the fruit fly are so well characterized and accessible, the researchers will be able to insert genes that will be used to visualize the activity of the JNK signaling pathway. This method will allow the researchers to determine if JNK signaling controls the transport of APP, or alternatively, if excess APP causes activation of the JNKI pathway leading to cell death. These studies will shed light on the mechanisms leading to APP-associated toxicity in nerve cells, and may help to identify potential targets for the development of treatments for Alzheimer’s disease.