“Our research group is studying how cells live or die in the context of Alzheimer’s disease, Parkinson’s disease, stroke, ischemia, and other degenerative brain disorders, with the ultimate goal of identifying drugs that inhibit cell death and getting them through the initial stages of drug development and on to the clinic.”

There are currently no treatments for the nerve cell death associated with chronic neurological diseases, including Alzheimer’s, Parkinson’s, Huntington’s, and ALS, or the neurological complications of diabetes. There are many reasons for this deficiency, but the main hurdle is the innate complexity of the diseases themselves. In most cases, the nerve cells die from several types of insults, not one specific stress or toxin. Therefore, drugs that effectively treat these conditions will have to block the different pathways that together lead to the nerve cell’s demise.

Because plants lack an immune system, they instead synthesize drug-like molecules to defend themselves against infectious pathogens and insect predators. Most of these molecules have numerous biological activities, and they are the basis of much of the current pharmacopoeia. They have not, however, been exploited for the treatment of chronic neurological diseases.

Schubert’s lab and that of Pamela Maher in the Cellular Neurobiology group are using a series of innovative biological assays to identify plant products that are broadly neuroprotective. They then modify the structure of the compounds through medicinal chemistry to improve their properties as drugs. The goal is to make drugs that inhibit the pathways that cause nerve cell death and are safe because they are based upon edible plant material. To date, they have identified two compounds that meet the above criteria. The first, discovered by Maher, is fisetin, found in strawberries, which is orally active in animal models of memory enhancement, Huntington’s, and Parkinson’s. It is also very active in a rigorous rabbit stroke model. Schubert has made potent synthetic derivatives of curcumin, the major component of the Indian spice turmeric, that work well in rabbit stroke models and memory enhancement.

Currently, this work is being extended in three areas: refinement of the chemical structures, identification of the multiple molecular targets, and testing in additional animal models where they are likely to be effective, such as the complications of diabetes and Alzheimer’s. The ultimate aim is to get these compounds through the initial stages of drug development so they can be advanced to the clinic.

For more information, please visit salk.edu/faculty/schubert.html