Our research group is using a novel drug discovery paradigm developed in our laboratories to make drugs for Alzheimer’s and Parkinson’s diseases, stroke and diabetic complications. The goal is to get these new drugs through the initial stages of development and into the clinic as rapidly as possible.

There are currently no effective treatments for any age-associated neurological disease, including Alzheimer’s, Parkinson’s or the neurological complications of diabetes. There are many reasons for this deficiency. One is the innate disease complexity, for in most cases the nerve cells die from multiple stresses and toxins. Therefore, drugs to treat these conditions must block the different pathways that together kill cells, not just a single target.

Plants synthesize drug-like molecules to defend themselves against pathogens and predators. Most of these molecules have numerous biological activities, but they have not yet been exploited for the treatment of neurodegenerative diseases. Scientists in the Schubert laboratory are using a series of innovative biological assays to identify plant products that are broadly neuroprotective. They then use medicinal chemistry to improve their drug-like properties. To date, they have identified two lead compounds that meet the above criteria and have synthesized a series of much more potent derivatives that maintain the multiple biological activities of the parents.

The first is fisetin, which is found in strawberries and is orally active in animal models of Alzheimer’s, Huntington’s and Parkinson’s. It is also very active in rodent models of stroke. Fisetin has a unique ability to protect from the vascular inflammation that is associated with all neurodegenerative conditions. Schubert’s team also has made potent synthetic derivatives of curcumin, the major component of the Indian spice turmeric, that work extremely well in animal models of Alzheimer’s and ischemic stroke. Some members of both groups of compounds are ready to start the FDA drug approval process, pending funding.

This work is being extended in three areas: refinement of the chemical structures to improve their pharmacological properties, characterization of the multiple molecular pathways that are responsible for the exceptionally neuroprotective properties, and testing in additional animal disease models. The ultimate goal is to get these compounds to the clinic to treat diseases for which there are currently no cures.

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