THE CHALLENGE
Although Alzheimer’s disease has been described for more than a century, there is currently no effective treatment. There are also no drugs to prevent the progression of Parkinson’s disease, Huntington’s disease or amyotrophic lateral sclerosis (ALS). The causes and symptoms of neurodegenerative diseases, particularly those associated with old age, are extremely complex and not well understood, making the discovery of drug candidates especially challenging.

THE APPROACH
Dave Schubert is taking a different approach to finding drugs for neurodegenerative disorders. Many labs and companies focus on the molecules that cause the diseases and then develop targeted drugs that turn these molecules on or off. In contrast, members of the Schubert lab have created a way to screen many chemical compounds for their ability to prevent the type of nerve cell death that is found in the aging human brain. Using assays developed by Schubert, the researchers can sift through thousands of possible drugs and pick out those that show potential to protect or help recover brain cells without having to pick a specific, predetermined drug target.

Schubert’s lab can then home in on what these potential drugs do, how they help or protect neurons, and, in some cases, make them even more therapeutic by tweaking their structure and chemical properties. By screening molecules derived from plants, the lab has uncovered a handful of drug candidates that were modified through medicinal chemistry to improve their pharmacological properties and make them more potent. Several of these synthetic drug candidates are being studied for their potential benefit to humans and are in various processes of being evaluated for clinical use.

Schubert is also creating additional screening techniques and refining the approaches to optimize drugs after identifying candidate molecules. Since several of their drug candidates have the ability to slow down the aging process and extend life span in rodents, another major focus of the Schubert lab is to identify and study safe compounds that extend the period of healthy human aging.

THE INNOVATIONS AND DISCOVERIES
• Drug candidates identified or synthesized based upon Schubert’s novel screening techniques are effective in rodent models of neurodegenerative diseases, including Parkinson’s, Huntington’s and ischemic stroke.
• The Schubert lab discovered that the natural plant compound fisetin—found in strawberries and other fruits and vegetables—prevents cognitive and kidney damage associated with rodent models of diabetes as well as memory and learning deficits in mouse models of Parkinson’s and Alzheimer’s diseases—it also showed promise in treating the symptoms in an autism model.
• Schubert and his colleagues have shown that a synthetic derivative of the curry spice curcumin, called J147, improves behavioral and pathological symptoms associated with Alzheimer’s, traumatic brain injury and stroke. This compound is currently in Phase 1 clinical trials for the treatment of Alzheimer’s.