For the past 25 years, neurodegenerative drug discovery has focused on a small number of targets. Despite years of effort and billions of dollars invested drug development pipelines for neurodegenerative diseases have a 99.6% attrition rate — underscoring both the futility of the approach as well as the need for novel druggable targets.

To address both the need for new targets and new drugs to modulate those targets, research in the Gaffney lab focuses on the interface between target identification, computational drug design, synthetic chemistry, and pharmacology.

Using these approaches, we have designed and developed a series potent small molecule activators of the renin-angiotensin-system. By mimicking the biological action of the natural ligand for Mas these molecules are able to amplify both the regenerative and protective capacity of this system.

Given these compounds ability to target multiple features of the neurodegenerative process, we are assessing the therapeutic utility of these molecules in models of Alzheimer’s, Parkinson’s, Multiple Sclerosis, and ALS.

In parallel, we are targeting pathways involved in neuroinflammation. A hallmark across neurodegenerative diseases, less than 10% of molecules in clinical trials for Alzheimer’s disease target these pathways.

Using proteomic and chemical biology approaches we are identifying new neuroinflammatory targets. These discoveries will be followed by the design of new molecules against these targets, ultimately translating these discoveries into the clinic to deliver new therapies to patients suffering from the neurodegenerative disorders.