

— Collaboration Highlight —

Vicky Yao, PhD & Rodney Ritzel PhD, 2021 CCAD

Prior to CCAD, we did not know of each other's work. At the time, Rodney was a postdoctoral researcher at the University of Maryland School of Medicine. He has an extensive background in sophisticated experimental techniques for disease modeling and therapeutic development, specializing in brain aging and neuroimmunology. Meanwhile, Vicky had recently started a position in the Computer Science department at Rice University in Houston, with expertise in computational method development for neuroscience. The two of us had completely different backgrounds, but of course both shared an interest in AD.



The suggestion that “collaborations are encouraged” in our initial instructions inspired Rodney to take a deeper look into the attendee profiles, and he immediately noticed that Vicky had the complementary skill set he needed to excel his research. As a preclinical researcher, he is able to experimentally manipulate biological variables and determine how they affect disease outcome, but when it comes to understanding how that outcome cascades through gene networks inside cells, he is less certain. In fact, identifying and validating disease-relevant molecular signatures has been traditionally challenging until the advent of more powerful computational techniques. These are techniques that Vicky is not only trained in, but also actively improving upon using state-of-the-art statistical and machine learning methods designed for biological questions. One of Vicky's main motivations for applying to CCAD was also to identify potential experimental collaborators, and thus, we quickly started discussing potential projects.

Our initial discussions highlighted several directions of common interest: the basis of sex differences in AD (why are women more susceptible?), the role of microglia (the immune cells in the brain), and their potential interplay with epigenetic aging. Epigenetic aging is a mechanism that can explain why somebody's chronological age (calculated based on their birth date) may differ greatly from their “biological age” (the age that organ systems appear to be based on biochemistry). Epigenetics are one of the main ways that the environment and experiences can affect the genetic and molecular states within our cells and may be particularly important for age-related diseases.

Indeed, recent published findings find that the brains of AD patients appear epigenetically older than their chronological ages would suggest, but these studies did not explore how this process might differ with sex and in microglia, the main source of inflammation. Thus, we designed a project that leverages both Rodney's wet lab and Vicky's dry lab expertise: Rodney would experimentally capture the epigenetic profiles of microglia in male and female mice (both healthy and diseased) at several ages. Using this data, Vicky would be able to develop sex-specific epigenetic aging models for microglia. By applying the normal epigenetic model on the diseased microglia, we would be able to determine if there is evidence of accelerated aging (and evaluate whether there are differences with sex) in AD. Furthermore, we would identify dysregulated age-associated pathways and then leverage Rodney's preclinical skillset to conduct drug testing on a small cohort of AD mice to determine whether there are potential therapeutics that can delay or reverse age-related memory loss. Finally, Vicky would be able to computationally predict whether these results would translate well to human studies.

All the discussion and proposal writing were completed remotely, and the first time we met was in Hawaii immediately prior to our project presentations! Even though our proposal was not selected in the end, we both found the experience extremely enriching and eye-opening. Coincidentally, Rodney has since moved to Houston to start his lab at UTHealth, and we are now conveniently located across the street from each other. We are still excited to work together and are now currently looking for other seed funding opportunities to launch our collaboration.