

INNOVATE

EVIDENCE-BASED MENTAL HEALTH RESEARCH



The Brain's Response to Inflammation

The immune system keeps the body healthy by maintaining balance and fighting off infection. The brain has many lines of defense to protect itself against infection including the skull and meninges, as well as the blood-brain barrier and an immune system led by cells called microglia.

Microglia

There are two main types of cells in the brain: neurons and glial cells. Although glial cells were dismissed for many years as simply the “glue” holding the brain together, research has shown glia to be key contributors to essential brain function. Microglia are immune cells found in the brain. They constantly monitor the cells around them and are

often the first to respond to problems. Like garbage collectors, they take out the trash and consume sick, dead or invasive cells. Cellular debris activates microglia to begin digestion. What they do requires precise monitoring. Imagine what would happen if the garbage in your home were never collected or collected so often that things that weren't trash were getting picked up. The same is true for microglia in the brain. Their function is essential to the health of the central nervous system, but what determines the balance between helpful and harmful?

Until recently, microglia were thought to only respond in response to inflammation, but new research has shown their importance in brain development and homeostasis (Frick et al., 2013). Marie Burns, professor in the Center for Neuroscience and Department of Cell Biology and

Human Anatomy at UC Davis, studies neuroinflammation associated with mental illness and the molecular mechanisms of microglia activation and regulation through gene therapy.

Burns received one of 23 Research Pilot Awards from the Behavioral Health Center of Excellence at UC Davis for the study, “New Technologies for Assessing Neuroinflammation in vivo” to look at the inflammatory response in live cells and determine the efficacy of new treatments.

The Retina

The team identified the retina as an ideal model for developing tools to routinely monitor neuroinflammation non-invasively. The retina is an accessible and convenient target for research because it is part of the central nervous system, and yet located at the back of a natural transparent window, the eye.

“The retina is a window to the brain, viewed through the lens of the eye. A successful outcome in Dr. Burns’ research will lead to new ways to identify inflammation in brain tissue and monitor the effects of therapies for common disorders of the brain.”

*-Cameron Carter, M.D.
Director, Behavioral Health Center of Excellence*



Dr. Burns prepares slides for microscopy in her lab at UC Davis.

Because the retina is an extension of the brain that can be visualized non-invasively in an individual over months or years, it creates an opportune target for neuroscience research. Burns and her team are developing novel techniques to visualize interactions between immune cells and neurons within their native environment.

Broad Impact on Disease

Burns described the relevance of her work in relation to brain health. “Neuroinflammation has been proposed to underlie many prevalent diseases of the central nervous system, including neurodevelopmental disorders like autism, psychiatric illnesses like schizophrenia and depression, and to go awry in neurodegenerative diseases of aging like Parkinson’s and Alzheimer’s,” she said.

Inflammation of the nervous system is a relatively new area of research and much remains to be known about the processes involved in the brain’s immune response. One obstacle is the difficulty in studying microglia in typical lab experiments because microglia rapidly become activated and

transform into cell-eating machines when removed from their native environment. Burns’ lab is one of only a handful of labs in the world capable of imaging microglia non-invasively while monitoring their movements and characterizing their behavior in relationship to functioning neural circuits and the rest of the immune system.

The ability to study microglia in their native environment has promising implications for assessment and treatment of neurological disorders. Burns and her team aim to develop new technologies for rapid, low-cost, non-invasive assessment of neuroinflammation. The long term-goal for these technologies is to facilitate diagnosis and quantify disease progression and response to therapeutic interventions. Our understanding of the molecular underpinnings that determine brain health and the corresponding mental illnesses that result is rapidly evolving. New technologies, like those being developed by Burns and her team, have the potential for widespread impact on brain health.

The research team includes: Robert Zawadzki, Ph.D.; Ed Pugh, Ph.D.; Helen Wang, M.D., Ph.D.; and Eric Miller, B.S.

Luciana Romina Frick, Kyle Williams, and Christopher Pittenger, “Microglial Dysregulation in Psychiatric Disease,” *Clinical and Developmental Immunology*, vol. 2013, Article ID 608654, 10 pages, 2013. doi:10.1155/2013/608654

Behavioral Health Center of Excellence at UC Davis

UC Davis launched the Behavioral Health Center of Excellence in October 2014 to advance mental health research and policy with initial funding from the Mental Health Services Act. The Innovate series highlights the Center’s \$4.3 million Research Pilot Award program.

www.behavioralhealth.ucdavis.edu
@UCDBrainHealth

UC DAVIS
BEHAVIORAL HEALTH CENTER
OF EXCELLENCE