Neuroscience Seminar Calendar – Fall 2017

Tuesday, September 12th

CU-Boulder – Interdepartmental Neuroscience Seminar Series

Muenzinger Psychology, Room E214, 4-5 pm

Colleen McClung, Associate Professor, Department of Psychiatry, University of Pittsburgh Medical School

Circadian genes and psychiatric disorders; insights from mice and men

Nearly all people suffering from psychiatric disorders have significant disruptions in circadian rhythms and the sleep/wake cycle. Furthermore, disruptions to circadian rhythms including shift work, overseas travel, and irregular social schedules tend to precipitate or exacerbate mood and psychotic episodes. However, the role of the genes that control circadian rhythms in the development of these disorders has remained unclear. This seminar will summarize recent data from our lab using human postmortem tissue to understand how molecular rhythms in specific brain regions, and cell types within those regions, are altered in subjects with psychiatric diseases like bipolar disorder and schizophrenia. Moreover, I will discuss our work in mouse models which implicates the circadian system as a vital regulator of neuronal signaling and communication between circuits in the brain that control mood and reward. I will discuss the molecular, cellular and electrophysiological changes that might underlie the regulation of mood and switch to different mood states with disruption of the circadian gene function or the sleep/wake cycle. This combination of human and rodent studies provides better understanding of how circadian genes in multiple regions of the brain contribute to the development and progression of psychiatric diseases.
"Listening" and "Talking" to Neurons

Non-neuronal cells amplify pain and drug reward

~ Pathways from basic science to clinical trials ~

Work over the past 25 years has challenged classical views of pain and opioid actions as being mediated solely by neurons. This challenge to classical views has now extended to effects of multiple drugs of abuse as well. Glia (microglia & astrocytes) in the brain and spinal cord are key players in chronic pain, compromising the efficacy of opioids for suppressing pain, contributing to opioid tolerance and dependence/withdrawal, and potently contributing to the rewarding qualities of opioids, cocaine, methamphetamine, and alcohol. All these effects arise by glially-created neuroinflammation. Glial reactivity can also be “primed” so to create enduring, amplified neuroinflammation, thereby contributing to the transition of acute-to-chronic pain. Intriguingly, the activation receptor on glia that creates neuroinflammation under conditions of chronic pain is one and the same receptor that is activated by opioids and other abused drugs. Importantly, this glial activation receptor is not the neuronal opioid receptor that suppresses pain. Indeed, clinically-relevant therapeutics targeting this glial activation receptor in particular, or glially-driven neuroinflammation, more generally can act as stand-alone treatments for neuropathic pain, improving the clinical utility of opioids, and suppressing drug reward. Translation of laboratory findings to clinical trials with human and veterinary pain populations is rapidly approaching.
**Tuesday, October 10**
CU-Boulder – Interdepartmental Neuroscience Seminar Series
Muenzinger Psychology, Room E214, 4-5 pm

**Shelly Flagel**, Associate Professor, Dept. of Psychiatry, University of Michigan

**“Chasing ghosts”: The search for the neural mechanisms underlying aberrant cue-driven behavior**

Stimuli or cues in the environment can guide behavior in adaptive ways, bringing one closer to valuable resources (e.g. food) or leading one away from danger (e.g. predator). However, such cues can also gain inordinate control over one’s behavior and lead to maladaptive or pathological behavior. For example, addicts tend to relapse when they come into contact with people, places or paraphernalia previously associated with the drug-taking experience; and relapse occurs despite the desire to remain abstinent. Using an animal model that captures individual variation in response to cues associated with reward, we are able to study the neural mechanisms underlying cue-motivated psychopathologies, like addiction. The utility of the “sign-tracker”/”goal-tracker” animal model in elucidating these mechanisms will be discussed, as will the progress we have made using pharmacological, neuroanatomical and chemogenetic tools.
Tuesday, October 24th

CU-Boulder – Interdepartmental Neuroscience Seminar Series

Muenzinger Psychology, Room E214, 4-5 pm

Thomas Finger, Professor, Vice-Chair, Dept. of Cell and Developmental Biology, University of Colorado Denver School of Medicine

Chemical synapses without synaptic vesicles: purinergic neurotransmission in taste buds

A synapse, defined originally in 1897 by Foster & Sherrington, is a point of cell-to-cell contact specialized for rapid signalling between cells. The synapse linking taste receptor cells to the taste nerves shows unusual functional properties suggestive of a unique structural organization. Conventional chemical synapses in the nervous system involve a presynaptic accumulation of neurotransmitter-containing vesicles, which upon activation, fuse to the plasma membrane to release neurotransmitter which activates receptors on the postsynaptic cell. In taste buds, taste receptor cells (Type II sensory cells) exhibit no conventional synaptic features but nonetheless show regulated release of their afferent neurotransmitter ATP -- not via fusion of synaptic vesicles to the membrane but rather through a large-pore, voltage-gated channel, CALHM1. Ultrastructural and super-resolution light microscopy show that the specialized points of contact between the receptor cells and sensory nerve fibers display no synaptic vesicles, but rather distinctive, large (1-2μm) mitochondria spaced 20-40 nm from the presynaptic membrane with the CALHM1 channel tightly localized to the subjacent plasma membrane. These mitochondria have unusually large intermembrane spaces suggesting the capability of storing relatively large amounts of ATP. Further, pharmacological disruption of the mitochondrial respiratory chain limits the ability of the taste cells to release ATP. Thus the specialized mitochondria serve as the site of both synthesis and storage of releasable ATP. The juxtaposition of the large mitochondrion to the areas of membrane displaying CALHM1 also define a restricted compartment that limits the influx of Ca2+ upon opening of the non-selective CALHM1 channels. These findings reveal a distinctive organelle signature and functional organization for regulated, focal release of purinergic signals in the absence of synaptic vesicles.
Tuesday, November 7th

CU-Boulder – Interdepartmental Neuroscience Seminar Series

Muenzinger Psychology, Room E214, 4-5 pm

Steve Ramirez, Assistant Professor, Department of Psychology and Brain Science, Boston University

Artificially modulating positive and negative memories in healthy and maladaptive states

Memories thread and unify our overall sense of being. With the accumulation of our knowledge about how memories are stored, retrieved, and updated, neuroscience has reached a point where brain cells active during these discrete processes can be identified and manipulated at rapid timescales. Here, I present our recent advances in memory research that combine transgenic and optogenetic approaches to reveal underlying neuronal substrates sufficient for activating mnemonic processes. Our studies’ conclusions are threefold: (1) a defined subset of hippocampus cells are sufficient to elicit the neuronal and behavioral expression of positive, neutral, and negative memory recall, as well as sufficient to modify existing memories; (2) artificially activated memories can be leveraged to acutely suppress psychiatric disease-related states; (3) chronic activation of positive or negative memories is sufficient to induce lasting changes in memory, social, and hedonic-related behaviors. We propose that hippocampus cells that show activity-dependent changes during learning construct a cellular basis for processing memory engrams and that directly activating these endogenous neuronal processes may be an effective means to correct maladaptive behaviors.
Tuesday, December 5th

CU-Boulder – Interdepartmental Neuroscience Seminar Series

Muenzinger Psychology, Room E214, 4-5 pm

Lisa Brenner, Associate Professor, Depts of Psychiatry, Neurology, and Physical Medicine and Rehabilitation, Univ. Colorado Denver School of Medicine; and Christopher Lowry, Associate Professor, Dept. of Integrative Physiology, Univ. Colorado Boulder

The microbiome and mental health

Novel prevention and treatment strategies are urgently needed to reduce the burden of stress-related psychiatric disorders, including posttraumatic stress disorder (PTSD) and major depressive disorder (MDD). Both preclinical and clinical studies suggest that inflammation increases vulnerability to development of anxiety and affective disorders. Consequently, immunoregulatory strategies to decrease inflammation have potential for the prevention and treatment of these disorders. Using a murine model of chronic psychosocial stress, the chronic subordinate colony housing (CSC) model, we found immunization with a heat-killed preparation of Mycobacterium vaccae, a bioimmunomodulatory agent previously shown to activate regulatory T cells (Treg) and to increase production of anti-inflammatory cytokines, prevented development of a PTSD-like syndrome. Immunization with M. vaccae antigen induced a more proactive emotional coping style during exposure to a dominant aggressor, and, in association with suppression of proinflammatory cytokine secretion, prevented stress-induced development of spontaneous colitis and aggravation of colitis in a model of inflammatory bowel disease. Analysis suggests that the protective effects of M. vaccae immunization are due to protection from a stress-induced proinflammatory gut microbial community. Consistent with this hypothesis, protective effects of immunization were absent following Treg depletion. These data provide a hypothetical framework for development of novel strategies for prevention of stress-related psychiatric disorders in vulnerable individuals. Clinical trials investigating the potential health benefits of treatment with immunoregulatory probiotics in Veterans with PTSD are ongoing.