Symposium 15: Neural mechanisms of fear memory (Sat July 31, 9-11AM JST)
Chairs: Kenta Hagihara (Friedrich Miescher Inst., Basel) and Takaaki Ozawa (Osaka Univ)

9:00-9:30 Kenta Hagihara (Friedrich Miescher Inst., Basel, Switzerland)
Mutual inhibition between intercalated amygdala clusters orchestrates a switch in fear stat

9:30-10:00 Sung Han (Salk Institute, San Diego, USA)
Encoding multi-sensory threat signals to the amygdala by peptidergic circuits

10:00-10:30 Li-Feng Yeh (RIKEN-CBS, Wako, Japan)
An aversive-sensorimotor neural circuit for instructing associative fear memories

10:30-11:00 Yingxi Lin (SUNY Upstate Medical University)
Functionally distinct active neuronal ensembles

Symposium 15 Speaker 1
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Mutual inhibition between intercalated amygdala clusters orchestrates a switch in fear state

Abstract 1 *(1200 - 2000 characters, with space):
Adaptive behavior necessitates that memories are formed for fearful events, but also that these memories can be extinguished. Effective extinction prevents excessive and persistent reactions to perceived threat, as can occur in anxiety and 'trauma- and stressor-related' disorders. However, while there is evidence that fear learning and extinction are mediated by distinct neural circuits, the nature of the interaction between these circuits remains poorly understood. In the talk, through a combination of in vivo calcium imaging, functional manipulations, and slice physiology, we demonstrate that distinct inhibitory clusters of intercalated neurons (ITCs) located in the amygdala exert diametrically opposing roles during the acquisition and retrieval of fear extinction memory. Furthermore, we find that the ITC clusters antagonize one another via mutual synaptic inhibition and differentially access functionally distinct cortical- and midbrain-projecting amygdala output pathways. Our findings show that the balance of activity between ITC clusters represents a unique regulatory motif orchestrating a distributed neural circuitry regulating the switch between high and low fear states. I will discuss a broader role for the ITCs in a range of amygdala functions and associated brain states underpinning the capacity to adapt to salient environmental demands.

Symposium 15 Speaker 2
Sung Han
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Encoding multi-sensory threat signals to the amygdala by peptidergic circuits

Learning of aversive events is essential for animals' survival. The amygdala is critical for classical threat conditioning that uses electric foot-shock as a threat cue. However, recent studies have shown that innate threat cues from other sensory modalities are independently relayed to other brain areas through parallel pathways from each sensory modality. It has not been tested whether the classical threat conditioning pathways are involved in relaying multi-sensory innate threat cues directly to the amygdala. In this presentation, I will share my group's unpublished results that neurons expressing calcitonin gene-related peptide (CGRP) in the parvocellular subparafasicular thalamic nucleus (SPFp) and external lateral parabrachial nucleus (PBel) that convey unconditioned stimulus to the amygdala, also relay multi-sensory innate threat cues to the amygdala. The discovery of parallel pathways that collectively gate aversive sensory stimuli from all sensory modalities to the amygdala may provide critical circuit-based insights into developing therapeutic interventions for innate fear-related disorders.

Symposium 15 Speaker 3
Li-Feng Yeh

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An aversive-sensorimotor neural circuit for instructing associative fear memories

Learning from aversive experiences is critical for survival. The fear memory, which associates the threat-predicting cues with harmful consequences, induces animals' defensive reactions when in danger. It is unclear how the nervous system transduces innately aversive experiences into neuronal emotional representations which regulate behavior and instruct memory formation. A common view is that emotional responses and memories are activated by the external sensory properties of aversive experiences, yet alternative theories proposed that internal bodily reactions to unpleasant events produce feeling states. Here we identify a brainstem cuneiform (CnF) circuit which conveys both external aversive-sensory and internal aversive-motor information to the lateral/basal nuclei of the amygdala (LA/B), a brain region important in emotional processing, to enhance defensive behaviors and instruct associative memory formation. Glutamatergic CnF neurons project directly to LA/B and receive afferent inputs from aversive-sensory and aversive-motor brain regions. Notably, LA/B neurons encode a defensive sensorimotor state in response to innately aversive stimuli, with both sensory and motor features transmitted through the CnF-to-LA/B pathway. Finally, optogenetic perturbation experiments revealed that during aversive experiences, the CnF-LA/B circuit instructs emotional memory formation and enhances the intensity of ongoing defensive behaviors. These findings reveal how the nervous system constructs an aversive sensorimotor state used for regulating emotional behaviors and driving memory formation. This suggests a clinically relevant brain mechanism for the individual scaling of emotional responding and learning by both the intensity of external traumatic events and the magnitude of the accompanying bodily reactions.

Symposium 15 Speaker 4
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Functionally Distinct Active Neuronal Ensembles

How are transient experiences converted into long-lasting memories? How do experiences modify behaviors? How do similar experiences elicit drastically different behavioral responses in the healthy and disease states? The key to answering these important questions is to understand how sensory information is processed and stored in the brain. Our research aims to address these questions at the molecular and cellular level, by exploring the mechanisms by which experiences are coupled to synaptic modifications of neural circuits that lead to long-term behavioral changes. This is made possible by combining a very wide range of experimental techniques: generating molecular tools to genetically identify the ensembles of neurons in the brain that are activated by a specific sensory and behavioral experience, detecting the learning-induced synaptic changes on the ensemble neurons, dissecting the molecular pathways responsible for the synaptic modulation, and understanding how the ensemble neurons contribute to the neural computations underlying learning and memory. My talk will focus on the recent progress we have made in understanding the mechanisms underlying contextual memory formation in the hippocampus, in particular concurrently activated but functionally distinct neuronal ensembles as well as the various forms of learning-induced synaptic modifications associated with those ensembles.