

Seminar

Disturbed neural cell networks in neurodegenerative conditions: from the molecular level to the system level

Dr. Jinyoung Kim

Department of Biomedical Sciences, City University of Hong Kong

Plasticity at the synapse and beyond

Prof. Ying Li

Department of Biomedical Sciences, City University of Hong Kong

Date: 22 March 2018 (Thursday)
Time: 12:00 nn – 1:30 pm (Reception with light sandwiches at 11:45am, talks start at 12nn. To facilitate the order of sandwiches, please register through email chchung33@cityu.edu.hk.)
Venue: B6605, Yeung Kin Man Academic Building, City University of Hong Kong

Two Presentations of 30 min each, followed by a 30 min discussion on collaboration activities

Neural Plasticity

1. Disturbed neural cell networks in neurodegenerative conditions: from the molecular level to the system level - Dr. Jinyoung Kim

Neurodegenerative diseases in the central nervous system (CNS) such as Alzheimer's (AD) and Parkinson's disease (PD) are complex because toxic insults to the brain affect not only neurons but also glial cells like astrocytes. In a similar context, pathological conditions induce not only neurodegeneration but also neuroprotective pathways to minimize damages since regeneration of the CNS neurons is extremely rare. For example, several pro-inflammatory cytokines like TNF α released by activated microglia have the dose-dependent effects on neurons through activation of either neuroprotective or neurotoxic signaling pathways. Reactive astrocytes, active forms of astrocytes, also have both neuroprotective and neurotoxic effects through their molecular (e.g. gene expression), cellular (e.g., structure), and functional (e.g. proliferation) changes. However, underlying mechanisms how neural cells communicate each other to switch their functions in neurodegenerative conditions are not clearly understood. The circadian clock is an endogenous oscillator that drives daily biological rhythms in biochemical, physiological, and behavioral levels. The core of the circadian clock is a transcriptional/translational negative feedback loop controlling a large group of gene expression (~40% of all protein coding genes). A growing body of epidemiological studies suggests that the circadian clock is closely related with diverse human diseases including neurodegenerative diseases because the circadian clock is intrinsic to the brain and all peripheral tissues and regulates diverse cellular processes and signaling pathways. Although abnormal circadian rhythms are frequently observed in patients with AD and PD, there is not enough molecular evidence to support that abnormal circadian phenotypes are driven by altered circadian clocks in the molecular level. In our lab, using cell and molecular biological approaches, we have observed that neurotoxic stimuli altered circadian clocks in most neural cells. Neurodegenerative conditions induced by glutamate excitotoxicity or activated microglia altered the circadian clock in both neurons and astrocytes but majority of pathways changed in these conditions were not overlapped. This suggests that the altered circadian clocks induced by similar toxic stimuli might have distinct roles in different neural cell types to decide their functions in the neurodegenerative conditions. Based on these results, our lab is currently studying roles of the circadian clocks in neural cells to understand how neural cells communicate each other through the circadian clocks to control their functions and effects of the altered circadian clocks on neurodegeneration.

Seminar

2. Plasticity at the synapse and beyond - Prof. Ying Li

From the traditional perspective of associative learning theory if a presynaptic neuron repeatedly played a role in firing a postsynaptic neuron that fire together wire together (Hebbian synapses). We have showed long-lasting potentiation of local field potential (LFP) in the medial thalamus (MT)-anterior cingulate cortex (ACC) synapses in the rats with chronic visceral pain (VP). Theta burst stimulation (TBS) in the MT reliably induced long-term potentiation (LTP) in the MT-ACC pathway in normal rats, but was occluded in the VP state. Further, repeated tetanization of MT increased ACC neuronal activity and visceral pain responses of normal rats, mimicking VP rats suggested that a mechanistic overlap between TBS-LTP and ACC synaptic strengthening. The occlusion of LTP was observed in the basolateral amygdala (BLA)-ACC synapses in VP rats, and also in the rats prolonged treated with chemotherapeutic agents, Cisplatin. However, most of these studies exploring the mechanism of induction of LTP made use of artificial stimulation protocols which may not exactly replicate the normal physiological circumstances.

It has been recognized that large scale neural oscillation plays a core role in dynamical coordination between brain areas and fundamental cognitive functions. We explore neuronal spike-field coherence (SFC), and synchronization between regions in the brain. Using VP, Cisplatin treated, and infraorbital nerve chronic constriction injury model our published and ongoing studies showed occlusion of LTP in various synapses, and altered SFC within and between brain areas associated with cognitive deficits. Lastly, utilizing a multiple flavor-place paired associate (PAs) behavioral paradigm we characterized the potentiated SFC within hippocampus (HPC) and within ACC, and increases in the coherent ACC spikes and HPC theta oscillation upon PAs memory acquisition and consolidation. These cumulative evidences suggest a parallel conceptual framework beyond the Hebbian synapse within which neuroscientists approach the study of learning mechanisms in the brain.

Biography



Dr Kim received her M.S. degree at SungKyunKwan University in South Korea, where she studied the role of aminoacyl-tRNA synthetase complex under the mentoring of Prof. Sunghoon Kim. Then, she moved to USA for her next step and obtained PhD degree from Department of Neuroscience and Cell Biology at Rutgers University in 2009. During this period, she discovered the novel mechanism of neurodegeneration under the guidance of Prof. Patrizia Casaccia, and her work was featured in several leading journals because of its new perspectives in the field. In 2010, she joined Prof. Charles J. Weitz lab in Department of Neurobiology at Harvard Medical School for her postdoctoral training. Her work about the regulatory mechanism of circadian clocks was also highlighted.



Prof. Li is a leading investigator in the area of brain target of visceral pain. Developing a viscerally hypersensitive animal model to mimic the patient with irritable bowel syndrome, his team characterized the functional changes of thalamus, amygdala and anterior cingulate cortex interactions contributed to pain perception, emotional and cognitive deficits. In early 90's Prof. Li's group has discovered the "CCK releasing peptide" (CCK-RP) that mediated release of CCK secreted into the intestine of the rat. They identified for the first time both cholecystokinin and serotonin released from enteroendocrine cells acting as paracrine agents on the terminals of vagal afferents in responses to a number of luminal signals to regulate gastrointestinal functions.