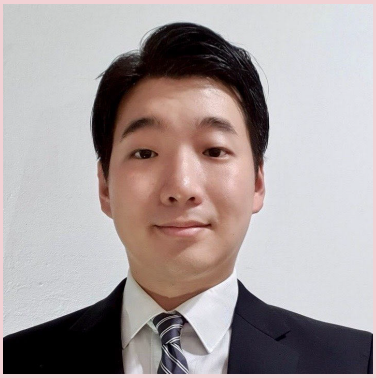
KOLIS-SNUCM Symposium

8/17 Monday 6pm-8pm

Soah Lee, Ph.D.

Stanford

Title:Wnt Activation and Reduced Cell-Cell Contact Synergistically Induce Massive Expansion of Functional Human iPSC-Derived Cardiomyocytes



Kyungoh Jung, Ph.D.

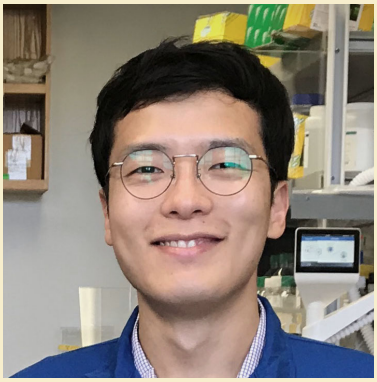
Stanford

Title: Whole-body tracking of single cells via positron emission tomography

Jaekyung Kim, Ph.D.

UCSF

Title: Roles of Sleep Oscillations in Memory Consolidation Versus Forgetting and Recovery after Stroke



Jungwoo Wren Kim, Ph.D.

UC Berkeley

Title: Defects in mRNA translation lead to dysregulation of calcium homeostasis in LRRK2 associated Parkinson's disease

Followed by networking with SNUCM faculty members

Wnt Activation and Reduced Cell-Cell Contact Synergistically Induce Massive Expansion of Functional Human iPSC-Derived Cardiomyocytes

Soah Lee, Ph.D.
Stanford

Modulating signaling pathways including Wnt and Hippo can induce cardiomyocyte proliferation in vivo. Applying these signaling modulators to human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) in vitro can expand CMs modestly (<5-fold). Here, we demonstrate massive expansion of hiPSC-CMs in vitro (i.e., 100- to 250-fold) by glycogen synthase kinase-3β (GSK-3β) inhibition using CHIR99021 and concurrent removal of cell-cell contact. We show that GSK-3β inhibition suppresses CM maturation, while contact removal prevents CMs from cell cycle exit. Remarkably, contact removal enabled 10 to 25 times greater expansion beyond GSK-3β inhibition alone. Mechanistically, persistent CM proliferation required both LEF/TCF activity and AKT phosphorylation but was independent from yes-associated protein (YAP) signaling. Engineered heart tissues from expanded hiPSC-CMs showed comparable contractility to those from unexpanded hiPSC-CMs, demonstrating uncompromised cellular functionality after expansion. In summary, we uncovered a molecular interplay that enables massive hiPSC-CM expansion for large-scale drug screening and tissue engineering applications.

Defects in mRNA translation lead to dysregulation of calcium homeostasis in LRRK2 associated Parkinson's disease

Jungwoo Wren Kim, Ph.D.
UC Berkeley

Summary

The G2019S mutation in leucine-rich repeat kinase 2 (LRRK2) is a common cause of familial Parkinson's disease (PD). This mutation results in dopaminergic neurodegeneration via dysregulated protein translation. How alterations in protein synthesis contribute to neurodegeneration is not known. Here we show using ribosome profiling that mRNAs having complex secondary structure in the 5' untranslated region (UTR) are translated more efficiently in G2019S LRRK2 neurons. This leads to the enhanced translation of multiple genes involved in Ca2+ regulation and to increased Ca2+ influx and elevated intracellular Ca2+ levels. This study reveals a link between dysregulated translation control and Ca2+ homeostasis in G2019S LRRK2 human dopamine neurons, which potentially contributes to the progressive and selective dopaminergic neurotoxicity in PD.

Keywords

Parkinson's disease, LRRK2, ribosome profiling, translatome, calcium homeostasis, 5'UTR, RPS15, uS19

Roles of Sleep Oscillations in Memory Consolidation Versus Forgetting and Recovery after Stroke

Jaekyung Kim, Ph.D.
University of California-San Francisco, San Francisco, USA

Sleep has been implicated in both memory consolidation and forgetting of experiences. However, it is unclear what governs the balance between consolidation and forgetting. We tested how activity-dependent processing during sleep might differentially regulate these two processes. We specifically hypothesized that during NREM sleep, slow oscillations (SO) and delta (δ) waves respectively promote memory consolidation and forgetting. We examined their causal roles using closed-loop optogenetic methods to selectively perturb SO and δ activity. Strikingly, we found that SO and δ waves have dissociable and competing roles in memory consolidation versus forgetting. We further found that changes in the temporal coupling of spindles to SO relative to δ waves (SO/δ-Nesting) could account for such effects. Based on these findings, we examined precisely how activity-dependent processing during sleep is affected by stroke and how to optimally recruit such processing via a pharmacological reduction of tonic GABA to benefit motor memory consolidation and thereby, rehabilitation. My presentation will show that neural activity driven by SO and δ waves have competing roles in sleep-dependent memory consolidation versus forgetting and show that the modulation of SO/δ-Nesting may promote motor recovery after stroke and can be a therapeutic target.

Whole-body tracking of single cells via positron emission tomography

Kyungoh Jung, Ph.D.
Stanford

Abstract

In vivo molecular imaging can measure the average kinetics and movement routes of injected cells through the body. However, owing to non-specific accumulation of the contrast agent and its efflux from the cells, most of these imaging methods inaccurately estimate the distribution of the cells. Here, we show that single human breast cancer cells loaded with mesoporous silica nanoparticles concentrating the 68Ga radioisotope and injected into immunodeficient mice can be tracked in real time from the pattern of annihilation photons detected using positron emission tomography, with respect to anatomical landmarks derived from X-ray computed tomography. The cells travelled at an average velocity of 50 mm s−1 and arrested in the lungs 2–3 s after tail-vein injection into the mice, which is consistent with the blood-flow rate. Single-cell tracking could be used to determine the kinetics of cell trafficking and arrest during the earliest phase of the metastatic cascade, the trafficking of immune cells during cancer immunotherapy and the distribution of cells after transplantation.