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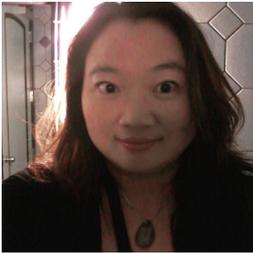
KOLIS Spring Conference

University of California, Berkeley

Minor Hall, School of Optometry



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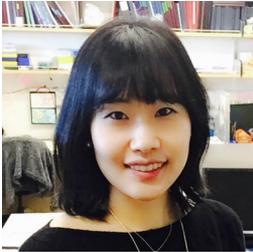


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Agenda

WELCOME

- 10:20 AM - 10:50 AM ————— Registration
- 10:50 AM - 11:00 AM ————— Opening by Narae Lee, Ph.D.
KOLIS President
Rm 491

PLENARY TALKS

- 11:00 AM - 11:45 AM ————— Sona Kang, Ph.D.
Title: Identifying epigenetic basis of adipose metabolism
Rm 491
- 11:45 AM - 12:30 PM ————— Kiho Cho, DVM, Ph.D.
Title: Deciphering intricate and dynamic genome landscapes to decode life forms
Rm 491

- 12:30 PM - 01:15 PM ————— Photo shoot and lunch

- 01:15 PM - 02:00 PM ————— Young-wook Jun, Ph.D.
Title: A mechanogenetic single-cell nano-modules for interrogation of cell signaling in space and time
Rm 491

- 02:00 PM - 02:10 PM ————— Coffee Break

Agenda

SESSION TALKS

	SYMPOSIA I (Rm 491)	SYMPOSIA II (Rm 395)
02:10 PM - 02:40 PM	Soo Young Kim, Ph.D. <i>Title: TGFβ-derived extracellular matrix remodeling following blood-brain barrier disruption is a common denominator for acquired epilepsy</i>	Yoon-A Kang, Ph.D. <i>Title: Myeloid-biased multipotent progenitor expansion by deregulated Notch and Wnt signaling drives myeloid malignancy</i>
02:40 PM - 03:10 PM	Jinkyung Kim, Ph.D. <i>Title: Osmotic control of inner ear endolymphatic hydrops</i>	Mincheol Kang, Ph.D. <i>Title: Effects of placental growth factor in transgenic mice</i>

03:10 PM - 03:20 PM

Coffee Break

03:20 PM - 03:50 PM	Changyang Lee, Ph.D. <i>Title: High frequency ultrasound microbeam in biomedical engineering</i>	Yumi Kim, Ph.D. <i>Title: Reflections on the academic job search</i>
03:50 PM - 04:20 PM	Yong Jin Choi <i>Title: Deficiency of microRNA miR-34a expands cell fate potential in pluripotent stem cells</i>	Kunwoo Lee <i>Title: Genome editing in vivo with the delivery of Cas9 ribonucleoprotein and donor DNA complexed to gold nanoparticles</i>

DINNER & NETWORKING

04:20 PM - 05:20 PM

Sponsors Info Session, Raffle,
Closing Remarks
Rm 491

05:20 PM

Dinner & Networking

Plenary Speakers



Sona Kang, Ph.D.

Assistant Professor

Dept. of Nutritional Sciences and Toxicology, UC Berkeley

Identifying epigenetic basis of adipose metabolism

Complex disorders like type 2 diabetes (T2D) and cancer share many etiological features that are not all attributable to genetic factors. Therefore, other forms of non-genetic variations, such as epigenetic alterations,

should be considered to fully explain the etiology. Epigenetic mechanisms (e.g. histone modification, DNA methylation) provide an important layer of gene regulation at the interface of gene and environment. Emerging evidence indicates a strong epigenetic component in metabolic regulation/dysregulation. For example, the offspring from pregnant mothers who underwent malnutrition have higher risk of developing metabolic disease. Such examples of 'metabolic memory' are predicted to have an epigenetic basis. Recent genome-wide studies report that T2D patients and human subjects with high body mass index have distinct global DNA methylation patterns compared to healthy individuals. By the same token, collective studies have reported site-specific epigenetic alterations at key regulatory metabolic genes in association with certain metabolic states. Despite these notions, the cause-effect relationship of the two remains largely unknown. As an independent investigator, my research goal is to uncover core epigenetic events that play important roles in the metabolic regulation/dysregulation, determine their cause-effect relationship, and alter the phenotype by modulating the key epigenetic events. These studies will greatly help us to understand more accurately the roles of the epigenetic machinery in metabolic processes and may lead to identify novel biomarkers and therapeutic targets in relevant diseases.



Kiho Cho, D.V.M., Ph.D.

Professor

Dept. of Surgery, UC Davis

Deciphering intricate and dynamic genome landscapes to decode life forms

The sum of conventional genes (exons) is estimated to represent less than ~2% of the reference human genome, which has not been fully sequenced yet. Current genetic identification-surveillance protocols focus on polymorphism and/or function of small sets of genes, small RNAs, and/or microsatellites on a static genome platform, underestimating the enormous genome diversity within each individual as well as each species. The genetic identification-surveillance information, which is derived from genes/small RNAs/microsatellites, might be too myopic and static for sustainable studies of decoding normal and disease phenotypes of life forms.

We developed a suite of genome-landscaping technologies which enable high-resolution and tunable genetic identification-surveillance of both static and dynamic (temporal and spatial) genomes of life forms, ranging from plants to humans. Using our surveillance technologies, we also demonstrated that the gene/small RNA/microsatellite-focused approaches are unable to provide adequate information for the design, execution, and interpretation of certain studies. The landscaping-based genetic identification-surveillance technologies would be applicable to a broad range of species and fields, such as forensics, animal/plant breeding, pharmacogenomics, monitoring of radiation therapy, cell typing, diagnostics, and the biology of normal and disease states.

Plenary Speakers



Young-wook Jun, Ph.D.

Assistant Professor

Dept. of Otolaryngology; Chemistry and Chemical Biology Program, UC San Francisco

A mechanogenetic single-cell nano-modules for interrogation of cell signaling in space and time

Spatial segregation, clustering, scaffolding, and compartmentalization of receptors as well as ligand-receptor interactions play critical means of controlling the molecular structures, and activities of receptors, and thus signaling of cells. In mechanical signaling that senses and responds to physical properties of extracellular environments, mechanical force resulting from cell-matrix and cell-cell interactions additionally serves as a key regulator of signaling. These spatial, molecular (i.e. ligand-receptor interaction), and mechanical cues often interplay either concurrently or consecutively in many mechanical signaling processes. This enables a vast diversity of signaling outcomes, orchestrating complex multicellular behaviors and functions in developmental, physiological, and pathological processes. Despite our increased understanding of mechanical signaling via recent advances in imaging and force-sensing tools, much is still unknown about the interplay between spatial, molecular, and mechanical cues and how they are integrated to potentiate mechanical signaling. To address this unmet need, my lab develops single-cell perturbation modules based on nanoparticles capable of localizing, visualizing, and mechanically activating mechanosensitive membrane proteins at the single cell or molecule level. The key to our approach is the ability to quantitatively deliver a specific spatial, biochemical, and mechanical cue to any desired location and at any given time. In this talk, I will discuss about design, fabrication, and utility of the nanoprobe as a perturbative tool. I will further discuss about applications of nanoprobe systems to dissect, interrogate, and understand the mechanisms underlying cell-cell communication processes via Notch and E-cadherin.

Session Speakers



Soo Young Kim, Ph.D.

*Postdoctoral Fellow at Kaufer Lab
Dept. of Integrative Biology, UC Berkeley*

TGF β -derived extracellular matrix remodeling following blood-brain barrier disruption is a common denominator for acquired epilepsy

Despite well-known risk factors such as stroke and head trauma, it has not been clinically effective to prevent acquired epilepsy. To do so, it is crucial

to understand what commonly drives neural hyperexcitability. Using comparative transcriptome analyses with different models of acquired epilepsy, we show that TGF β signaling activation following blood-brain barrier (BBB) disruption commonly occurs regardless of brain region and insult types, accompanied by the strong upregulation of genes relevant to inflammation and extracellular matrix (ECM) modulation. We found the chronic degradation of perineuronal nets (PNNs), a protective and nourishing ECM structure around fast-spiking parvalbumin (PV)-expressing interneurons in the epileptogenic regions of rodents. Losartan, a drug that prevents epilepsy via TGF β signaling suppression, blocked the degradation of PNNs elicited by BBB breakdown. These findings suggest TGF β -derived ECM remodeling following vascular injury and in turn, the chronic loss of PNNs around PV(+) interneurons as a common denominator for acquired epilepsy.



Jinkyung Kim, Ph.D.

*Postdoctoral Fellow at Oghalai Lab
Dept. of Otolaryngology-Head and Neck Surgery, Stanford*

Osmotic control of inner ear endolymphatic hydrops

Endolymphatic hydrops, which is a typical pathology in Meniere's disease, is a disorder of inner ear accompanied by vertigo, tinnitus, fluctuating hearing loss, imbalance and aural fullness. Despite numerous studies, the cau-

se and the fundamental cure of the hydrops, most commonly, are unknown. Here we investigated the root causes of endolymphatic hydrops and developed approaches to regulate endolymphatic hydrops. Noninvasive 3D *in vivo* cochlear imaging revealed that perilymph osmolality regulated endolymph volume. Endolymphatic hydrops, or a progressive bulging of Reissner's membrane, was induced by blast exposure. Post-traumatic outer hair cell loss is defined immediately, although the cells progressively died within the first 7 days after the blast. After complete perfusion of gold nanoparticles through the perilymph, *in vivo* imaging showed no penetration of the particles into the endolymph, indicating no significant tears between endolymph and perilymph barrier. Furthermore, we found no endolymphatic hydrops after the blast within TectaC1509G/C1509G, Tyr-DT-A and furosemide-treated mice. It suggested that stereociliary deflection by tectorial membrane initiated post-traumatic endolymphatic hydrops under the condition of K⁺ within the endolymph. Finally, we eliminated endolymphatic hydrops by modulation of perilymphatic osmolality. It partially rescued synaptic ribbon loss, but not outer hair cell loss. The progressive hearing loss associated with Meniere's disease may be in part treatable by controlling endolymph volume.

Session Speakers



Yoon-A Kang, Ph.D.

Postdoctoral Fellow at Passequé Lab

The Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research, Dept. of Medicine, UC San Francisco

Myeloid-biased multipotent progenitor expansion by deregulated Notch and Wnt signaling drives myeloid malignancy

Myeloproliferative neoplasms (MPN) are characterized by the deregulated production of myeloid cells. Despite clinical successes with tyrosine kinase inhibitors (TKI), much remains to be learned about the mechanisms driving aberrant myeloid cell output in MPNs to develop better treatment options, especially for patients with TKI resistances. Myeloid cell production is entirely controlled by the differentiation rates of the self-renewing hematopoietic stem cells (HSC). HSCs give rise to non self-renewing multipotent progenitors (MPP), which differentiate into either myeloid- or lymphoid-committed progenitors. We recently identified MPP3 as a novel myeloid-biased MPP subset that is functionally distinct from the lymphoid-primed MPP4, and is specialized in producing myeloid cells with low contribution to the lymphoid lineage. We also demonstrated that MPP3 is part of an inducible myeloid regeneration pathway that is activated in HSCs, and leads to both the transient overproduction of MPP3 and the myeloid reprogramming of MPP4 to rebuild the myeloid lineage in various regenerative settings. Here, we show that transient myeloid regeneration pathways are constitutively activated in myeloid malignancies, and directly contribute to the deregulated output of myeloid cells observed in a variety of MPN mouse models. Strikingly, we find that transformed HSCs with leukemia-initiating stem cell (LSC) activity have consistently decreased Notch and increased Wnt signaling activity. Using both pharmacological and genetic approaches, we demonstrate that a combination of high Wnt and low Notch activities directly activates myeloid regeneration pathways from normal HSCs, with overproduction of MPP3 and myeloid-reprogramming of MPP4. Moreover, we show that re-balancing Wnt and Notch activities in LSCs can block the aberrant activation of myeloid regeneration pathways, and extend survival by restoring proper lineage output in MPN mice. Our results illuminate new features of myeloid malignancies linking deregulated signaling activities in LSCs to the aberrant production of multipotent progenitors that drive myeloid cell output. They also suggest that targeting the abnormal Notch and Wnt activities could be used to develop new HSC-based anti-differentiation therapies for the treatment of a broad range of MPNs.



Mincheol Kang, Ph.D.

Postdoctoral Fellow at Adamopoulos Lab

Dept. of Internal Medicine, UC Davis

Effects of placental growth factor in transgenic mice

Angiogenesis is an important biological process during development, reproduction and in immune responses. Placental growth factor (PlGF) is a member of vascular endothelial growth factor (VEGF) that is critical for angiogenesis and vasculogenesis. I generated transgenic mice over-expressing PlGF in specifically T-cells using the human CD2 promoter to investigate the effects of PlGF over-expression. Transgenic mice were difficult to obtain owing to high lethality; for this reason, I investigated why gestational loss occurred in these transgenic mice. Here I report that placenta detachment and inhibition of angiogenesis occurred in PlGF transgenic mice during the gestational period. Moreover, even when transgenic mice were born, their growth was restricted. Conclusively, PlGF over-expression prevents angiogenesis by inhibiting Braf, ERK activation and down-regulation of HIF-1 α in the mouse placenta. Furthermore, it affected regulatory T-cells, which are important for maintenance of pregnancy.

Furthermore, I investigate the role of the PlGF during the inflammatory process associated with rheumatoid arthritis (RA) and type II diabetes. I findings demonstrate that PlGF plays a critical role in rheumatoid inflammation and the development of inflammatory type II diabetes by promoting production of pro-inflammatory cytokines. For this reason, the use of anti-PlGF peptides may be an effective therapeutic strategy for diseases associated with inflammation.

Session Speakers



Changyang Lee, Ph.D.

*Postdoctoral Fellow at Marcu & Yankelevich Lab
Dept. of Biomedical Engineering, UC Davis*

High frequency ultrasound microbeam in biomedical engineering

Ultrasound has been used as diagnostic imaging tools in medicine for a long time due to its real-time capability and mobility as well as nonionizing radiation and safety. High frequency ultrasound (above 30 MHz) has opened up new ultrasound biomedical applications thanks to its fine spatial resolution by sacrificing the depth of penetration due to increasing attenuation. Design and fabrication of transducers in the high frequency range 100 MHz – 1 GHz is a challenge. Ultrasound with frequency beyond 100 MHz may find many other potential biomedical applications. Shung's group has shown the potential of high frequency at biomedical engineering fields such as micro-particle manipulation, cellular mechanism study by applying high frequency ultrasound, and characterization of cell and tissue using backscattering. These new approaches can be potentially powerful tools in the biology and medicine.



Yong Jin Choi

*Ph.D. Candidate at He Lab
Dept. of Molecular and Cell Biology, UC Berkeley*

Deficiency of microRNA miR-34a expands cell fate potential in pluripotent stem cells

Mouse embryonic stem cells (ESCs) and induced pluripotent stem cells possess pluripotent cell fate potential, efficiently contributing to all embryonic cell types, but rarely to extra-embryonic lineages. Here, we identify a microRNA, miR-34a, whose deficiency in mouse pluripotent stem cells expands their developmental potential. In a variety of in vitro and in vivo functional assays, miR-34a-deficient pluripotent stem cells exhibit totipotent-like cell fate potential both at the population level and at the single cell level, giving rise to both embryonic and extra-embryonic cell lineages. The expression profiles of miR-34a^{-/-} pluripotent stem cells are characterized by a strong yet specific induction of MuERV-L (MERV L) family endogenous retrovirus, a unique molecular hallmark of totipotent 2-cell stage blastomeres and totipotent-like ESCs. We demonstrate that miR-34a represses MERV L expression through transcriptional regulation, at least in part by directly repressing the transcription factor GATA-binding protein 2 (Gata2). Consistent with the strong correlation between MERV L activation and totipotent-like fate potential, the miR-34a/Gata2 pathway that represses MERV L expression also restricts the acquisition of totipotency in pluripotent stem cell culture. Taken together, our findings provide novel insights into the molecular basis for totipotent-like cell fate potential, and highlight the functional importance of miRNAs in regulating cell fate plasticity in pluripotent stem cell culture.

Session Speakers



Yumi Kim, Ph.D.

*Postdoctoral Fellow at Dernburg Lab
Dept. of Molecular and Cell Biology, UC Berkeley*

Reflections on the academic job search

Throughout a six-month period in 2015-2016, I applied and interviewed for tenure-track assistant professor positions in the general area of cell biology. In this talk, I will share my recent experiences on this exciting journey. I will discuss the timeline, the application and interview process, and what to expect after the job offer.



Kunwoo Lee

*Ph.D. Candidate at Murthy Lab
Dept. of Bioengineering, UC Berkeley & UC San Francisco*

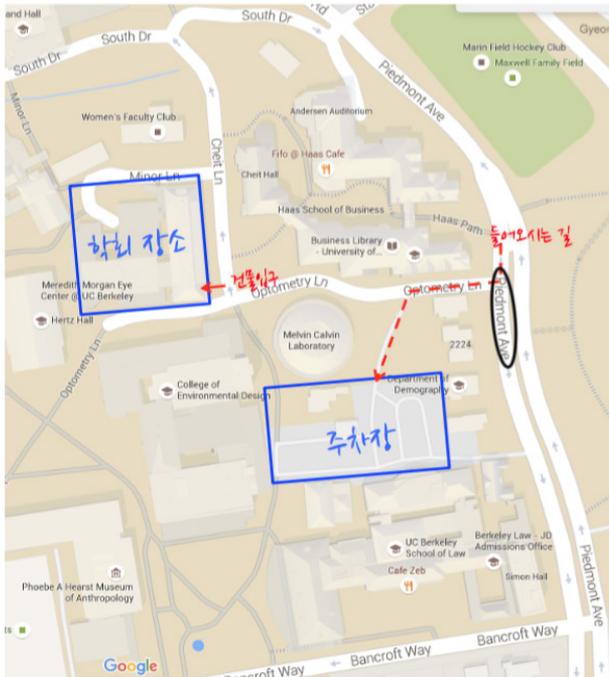
Genome editing in vivo with the delivery of Cas9 ribonucleoprotein and donor DNA complexed to gold nanoparticles

CRISPR/Cas9-mediated genome editing has the potential to revolutionize the treatment of genetic diseases and the development of cell-based therapies. However, gene editing with Cas9 is still challenging in vivo, because it requires simultaneous and efficient delivery of Cas9, guide RNA, and donor DNA into cells. In this presentation, we present a gold nanoparticle-based delivery vehicle, termed CRISPR-Gold, which can directly deliver Cas9 protein, guide RNA (gRNA), and donor DNA in vitro and in vivo and efficiently induce homology directed repair (HDR). CRISPR-Gold is composed of gold nanoparticles assembled with the Cas9-gRNA ribonucleoprotein (RNP) complex, donor DNA, and an endosomal disruptive polymer. Notably, we show that CRISPR-Gold can correct a nonsense mutation in the dystrophin gene that causes Duchenne muscular dystrophy in mdx mice, and restore dystrophin protein expression in mouse muscle after a single injection. CRISPR-Gold is the first example of a non-viral delivery vehicle that can induce HDR in vivo and has the potential to treat a wide spectrum of genetic diseases.

Directions

<찾아오시는 길>

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