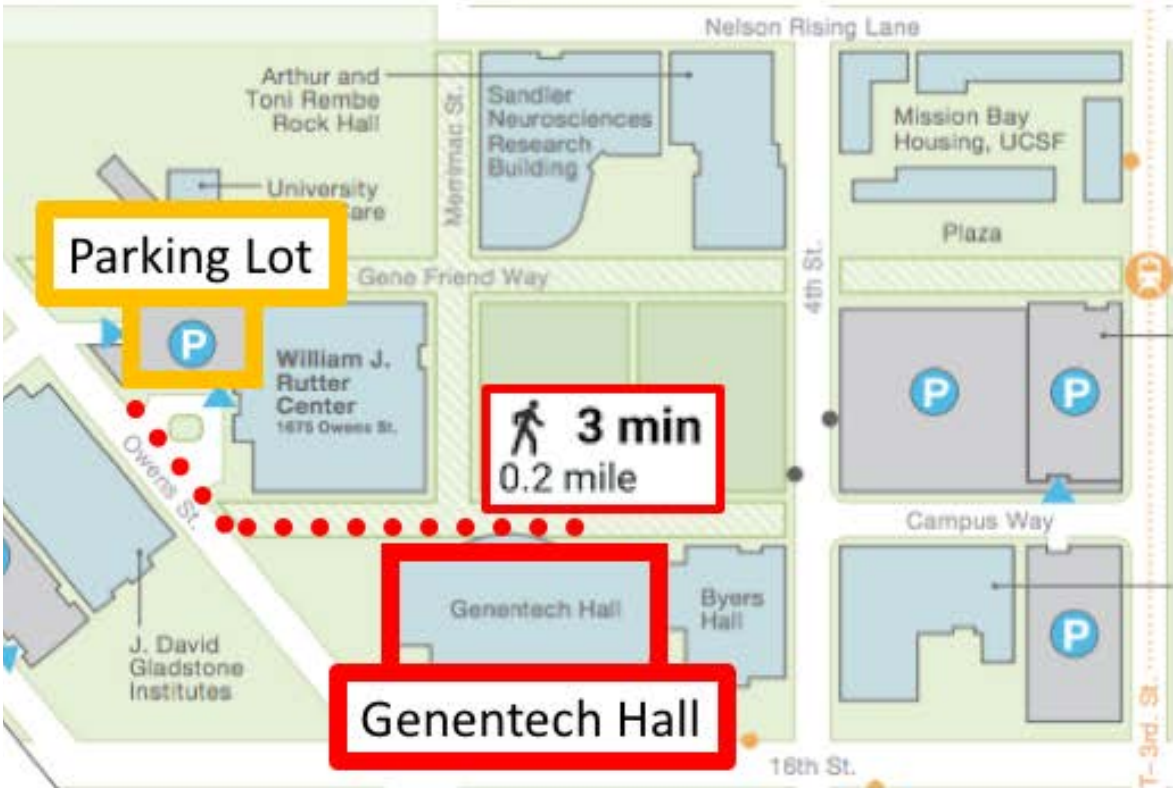
KOLIS 2017

KOLIS

2017 Winter Conference

UCSF Genentech Hall
December 9th, 2017

KOLIS



Genentech Hall (UCSF)
600 16th Street
San Francisco, CA 94158
https://goo.gl/maps/bNLZjK8iVJu
(Google Maps link to the main entrance of the building)

Community Center Garage
1625 Owens Street
San Francisco, CA 94158
https://goo.gl/maps/RjzLTC71mw12
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Parking Instructions
Park at the Community Center Garage.
A parking voucher will be given to you upon request during registration.
Please submit the voucher to cashier along with the garage ticket upon exit.

KOLIS

KOLIS 2017 Winter Conference

PROGRAM

9:20 – 9:50 AM

Registration
Coffee & Breakfast
Lobby, UCSF Genentech Hall

9:50 – 10:00 AM

Opening Remarks
Hyun Yong Jin, KOLIS President

Academic Session I

10:00 – 10:30 AM

Kicheol Kim, Ph.D.
Postdoctoral Associate, *UCSF*
Transcriptomic analysis of $CD4^+$, $CD8^+$ and $CD14^+$ cells in newly diagnosed multiple sclerosis patients

10:30 – 11:00 AM

Hyunsun Jo (Joe), Ph.D.
Co-founder and CEO, *Pin Therapeutics*
Targeted protein degradation as an emerging platform modality

11:00 – 11:30 AM

Jong Chan Yeo, Ph.D.
Postdoctoral Associate*, UC Berkeley*
In Vivo Biochemistry: Single-cell dynamics of cyclic di-GMP in *E. coli* in response to zinc overload

11:30 – 12:00 PM

Hak Kyun Kim, Ph.D.
Research Scientist, *Stanford University*
A transfer-RNA-derived small RNA is a target for the treatment of hepatocellular carcinoma by regulating ribosome biogenesis

12:00 – 1:00 PM

Photo & Lunch

Industry Session

1:10 – 2:00 PM

Danny Joh, Ph.D.
Co-founder and COO, *Pin Therapeutics*

Sehyun Kim, Ph.D.
Senior Scientific Researcher, *Genentech*
Do you really want to work in the industry?

2:00 – 2:30 PM **Kwang-Ai Won, Ph.D.**
Scientific Advisor, *LG Chem*
Drug R&D and Career

2:30 – 3:00 PM **Coffee break with Special Networking Sessions**
Women in Science
Life in Industry
Careers in Academia

Academic Session II

3:00 – 3:30 PM **Karam Kim, Ph.D.**
Assistant Project Scientist, *UC Davis*
Alpha-actinin anchors PSD-95 and AMPA receptors at postsynaptic sites

3:30 – 4:00 PM **Kunwoo Lee, Ph.D.**
CEO, *Genedit*
Non-viral CRISPR/Cas delivery

4:00 – 4:30 PM **Hyun Eui Kim, Ph.D.**
Postdoctoral Associate, *UC Berkeley*
Lipid-mediated communication between mitochondria and cytosol in protein homeostasis

4:30 – 4:50 PM **Year End Summary of KOLIS 2017**

4:50 – 5:10 PM **Raffle**
Ara Hwang, KOLIS Treasurer &
Min Kang, KOLIS Planning Manager

5:10 – 5:20 PM **Introduction of KOLIS 2018 Board**

5:20 – 5:30 PM **Closing Remarks**
Kyung Duk Koh KOLIS Vice President

5:30 – 6:30 PM **Dinner and Networking**

KOLIS WINTER CONFERENCE 2017

ACADEMIC SESSION I

Academic Session I **10:00 – 10:30 AM**
Presentation 1

Transcriptomic analysis of $CD4^+$, $CD8^+$ and $CD14^+$ cells in newly diagnosed multiple sclerosis patients

Kicheol, Ph.D.
Postdoctoral Associate
UC San Francisco

Multiple Sclerosis (MS) is an autoimmune condition of the central nervous system characterized by demyelination and neurodegeneration. The exact cause of MS remains unknown and there is no cure. Many MS-associated genes are primarily expressed in immune cells such as T-cells and dendritic cells. Gene expression profiles from whole tissue or peripheral blood mononuclear cells have been reported, however, they consist of many different cell types. Therefore, cell-type specific gene expression can be more informative. Total RNA was purified from $CD3^+CD19^-CD4^+$ and $CD3^+CD19^-CD8^+$ T-cells and $CD14^+$ monocytes collected from MS patients (n=75) participating in the UCSF MS EPIC/ORIGINS studies. 3' mRNA-seq was performed on cell subsets to test for differentially expressed genes (DEGs) between disease courses (RR, PP, CIS) and disease-modifying treatments (DMTs: glatiramer acetate, dimethyl fumarate, natalizumab, fingolimod). DEG analysis was performed using DESeq2. There were 5,198 DEGs when comparing T-cells and monocytes of MS patients, and 172 DEGs between $CD4^+$ and $CD8^+$ T-cells (FDR < 0.05, Log2FC >< ∓1.5, baseMean > 1). A disease course comparison in treatment naïve patients further identified DEGs (7 genes in $CD4^+$, 15 in $CD8^+$, and 2 in $CD14^+$ between PPMS and RRMS; 8 in $CD4^+$, 14 in $CD8^+$, 2 in $CD14^+$ between RRMS and CIS; 12 in $CD4^+$, 54 in $CD8^+$, 10 in $CD14^+$ between PPMS and CIS). While most of all the DEGs were down-regulated in PPMS with respect to RRMS and CIS, in turn, RRMS patients showed mainly up-regulated transcripts when compared to CIS. Specifically, *EIF2S3L* and *SNORD8* were significantly regulated in both $CD4^+$ and $CD8^+$ T-cells in RRMS when compared to PPMS or CIS. In addition, *CHI3L2* was down-regulated in PPMS compared to CIS in $CD4^+$. *CHI3L2* is in the same family as *CHI3L1* which has been suggested as a biomarker of MS. When comparing treatment-naïve patients to those on DMTs, *HLA-DQB1* and *PRSS21* were significantly decreased in $CD14^+$ in patients treated with dimethyl fumarate. In contrast, 38 transcripts including those for immune-related genes *S100B* and *MS4A1* were differentially expressed in $CD8^+$ of patients treated with fingolimod. We analyzed gene expression in T-cells and monocytes from newly diagnosed MS patients and observed cell-specific transcriptional changes in both untreated patients and in response to different DMTs. These findings provide important insights into cell-specific gene expression changes in subtypes of MS and in response to DMTs.

Academic Session I **10:30 – 11:00 AM**
Presentation 2

Targeted protein degradation as an emerging platform modality

Hyunsun Jo (Joe), Ph.D.
Co-founder and CEO
Pin Therapeutics

Pin is aiming at creating therapeutic products based on the PROTAC technology, which utilizes bifunctional compounds to degrade target proteins within the cell. The typical antibody or small molecule drug exerts its efficacy by binding to the target protein and inhibiting the function of the protein. Antibodies can bind to only cell surface targets and are unable to bind to intracellular proteins. While small molecule inhibitors have been effective with targets like kinase inhibitors, researchers are realizing that it is very difficult to inhibit many types of proteins with small molecule inhibitors. The PROTAC approach can allow us to target these proteins that are currently considered undruggable.

The PROTAC compounds can hijack the E3 ligase system to degrade target proteins. Over the last couple of years, the literature has demonstrated the concept. Moreover in vivo efficacy of PROTAC compounds have been published by a few groups, strengthening the applicability and raising the clinical potential.

Academic Session I **11:00 – 11:30 AM**
Presentation 3

In Vivo Biochemistry: Single-cell dynamics of cyclic di-GMP in *E. coli* in response to zinc overload

Jong Chan Yeo, Ph.D.
Postdoctoral Associate
UC Berkeley

Intracellular signaling enzymes drive critical changes in cellular physiology and gene expression, but their endogenous activities in vivo remain highly challenging to study in real-time and for individual cells. Here we show that flow cytometry can be performed in complex media to monitor single-cell population distributions and dynamics of cyclic di-GMP signaling in E. coli, which controls the bacterial colonization program. These in vivo biochemistry experiments are enabled by our second-generation RNA-based fluorescent (RBF) biosensors, which exhibit high fluorescence turn-on in response to cyclic di-GMP. Specifically, we demonstrate that intracellular levels of cyclic di-GMP are repressed with excess zinc, but not with other divalent metals. Furthermore, in both flow cytometry and fluorescence microscopy set-ups, we monitor the dynamic rise in cellular cyclic di-GMP levels upon zinc depletion and show that this response is due to de-repression of the endogenous diguanylate cyclase DgcZ. In the presence of zinc, cells exhibit enhanced cell motility and increased sensitivity to antibiotics due to inhibited biofilm formation. Taken together, these results showcase the application of RBF biosensors to visualize single-cell dynamic changes in cyclic di-GMP signaling in direct response to environmental cues such as zinc, and highlight our ability to assess whether or not observed phenotypes are related to specific signaling enzymes and pathways.

Academic Session I **11:30 – 12:00 PM**
Presentation 4

A transfer-RNA-derived small RNA is a target for the treatment of hepatocellular carcinoma by regulating ribosome biogenesis

Hak Kyun Kim, Ph.D.
Research Scientist
Stanford University

Transfer-RNA-derived small RNAs (tsRNAs; also called tRNA-derived fragments) are an abundant class of small non-coding RNAs whose biological roles are not well understood. Here we show that inhibition of a specific tsRNA, LeuCAG3¢tsRNA, induces apoptosis in rapidly dividing cells *in vitro* and in a patient-derived orthotopic hepatocellular carcinoma model in mice. This tsRNA binds at least two ribosomal protein mRNAs (*RPS28* and *RPS15*) to enhance their translation. A decrease in translation of *RPS28* mRNA blocks pre-18S ribosomal RNA processing, resulting in a reduction in the number of 40S ribosomal subunits. These data establish a post-transcriptional mechanism that can fine-tune gene expression during different physiological states and provide a potential new target for treating cancer.

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INDUSTRY SESSION

Industry Session **1:10 – 2:00 PM**
Presentation 1

Do you really want to work in the industry?

Danny Joh, Ph.D.
Co-Founder and COO
Pin Therapeutics
Se Hyun Kim, Ph.D.
Senior Research Scientist
Genentech

This session is intended to help those who are contemplating a career in the biopharma industry. The session will be divided into two presentations. The first presentation will provide a brief overview of the industrial drug development process and describe various roles (e.g. research, pre-clinical, regulatory, manufacturing, and etc) that may be considered for PhDs in biological sciences. The second presentation will focus more on practical tips on how one might approach cover letter/resume-writing, networking, and interview preparation.

Industry Session
Presentation 2

2:00 – 2:30 PM

Drug R&D and Career

Kwang-Ai Won, Ph.D.
Scientific Advisor
LG Chem

I led multiple drug candidates into the clinic and FDA-approved drugs onto the market, and worked with scientists and business people in academia and pharmaceutical companies in the USA and Korea. In my presentation, I will provide an update on one of those drugs, cabozantinib, known as COMETRIQ for the treatment of thyroid cancer and CABOMETYX for the treatment of kidney cancer and liver cancer. I will also share my thoughts on how your career can be advanced based on my own experiences in drug research and development.

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ACADEMIC SESSION II

Academic Session II **3:00 – 3:30 PM**
Presentation 1

Alpha-actinin anchors PSD-95 and AMPA receptors at postsynaptic sites

Karam Kim, Ph.D.
Assistant Project Scientist
UC Davis

The vast majority of synapses in the brain are glutamatergic, and PSD-95 is a major scaffolding protein in excitatory glutamatergic synapses. Despite the central role PSD-95 plays in anchoring postsynaptic AMPARs, how PSD-95 itself is tethered to postsynaptic sites remained unknown. Here we show that the F-actin binding protein α-actinin binds to the very N-terminus of PSD-95. Knock-down (kd) of α-actinin phenocopies kd of PSD-95. Mutating lysine at position 10 or lysine at position 11 of PSD-95 to glutamate impairs in parallel PSD-95 binding to α-actinin and postsynaptic localization of PSD-95 and AMPARs. Also, expression of mutant α-actinin which cannot interact with PSD-95 showed similar phenotype. These experiments unequivocally identify α-actinin as a critical PSD-95 anchor tethering the AMPAR - PSD-95 complex to postsynaptic sites.

Academic Session II **3:30 – 4:00 PM**
Presentation 2

Non-viral CRISPR/Cas delivery

Kunwoo Lee, Ph.D.
GEO
Genedit

Cas9 based therapeutics have the potential to revolutionize the treatment of genetic diseases because of their ability to generate homologous DNA recombination (HDR) and correct DNA mutations. However, viral gene therapy is currently the only delivery technology available for generating HDR *in vivo* with Cas9, and is challenging to bring into clinical trials because of off-target DNA damage and immunogenicity. We present a non-viral Cas9 delivery vehicle, termed CRISPR-Gold, which can for the first time induce HDR *in vivo* by directly delivering Cas9 protein, gRNA, and donor DNA. CRISPR-Gold is composed of gold nanoparticles assembled with the Cas9/gRNA ribonucleoprotein (RNP) complex, donor DNA, and an endosomal disruptive polymer. We show here that CRISPR-Gold can correct the DNA mutation that causes Duchenne muscular dystrophy (DMD) in mdx mice via HDR. Additionally, other engineering approaches for CRISPR system will be discussed.

Academic Session II **4:00 – 4:30 PM**
Presentation 3

Lipid-mediated communication between mitochondria and cytosol in protein homeostasis

Hyun Eui Kim, Ph.D.
Postdoctoral Associate
UC Berkeley

Defects in mitochondrial metabolism have been increasingly linked with age-onset protein misfolding diseases such as Alzheimer's, Parkinson's, and Huntington's. In response to protein folding stress, compartment-specific unfolded protein responses (UPRs) within the endoplasmic reticulum, mitochondria, and cytosol work in parallel to ensure cellular protein homeostasis. While perturbation of individual compartments can make other compartments more susceptible to protein stress, the cellular conditions that trigger cross-communication between the individual UPRs remain poorly understood. We have uncovered a conserved, robust mechanism linking mitochondrial protein homeostasis and the cytosolic folding environment through changes in lipid homeostasis. Metabolic restructuring caused by mitochondrial stress or small molecule activators trigger changes in gene expression coordinated uniquely by both the mitochondrial and cytosolic UPRs, protecting the cell from disease-associated proteins. Our data suggest an intricate and unique system of communication between UPRs in response to metabolic changes that could unveil new targets for diseases of protein misfolding.

KOLIS Board Members 2017

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Vice President	Kyung Duk Koh	UC San Francisco
Treasurer	Ara Hwang	UC San Francisco
Planning Manger	Minjung Kang (Winter) Jonghoon Chang (Spring)	Stanford University UC San Francisco

Campus Representatives 2017

UC Berkeley	Hong Sik Yoo Jong Chan Yeo
UC Davis	Jai Woong Seo
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PROGRAM AT A GLANCE

9:20 – 9:50 AM	**Registration** **Coffee & Breakfast**
9:50 – 10:00 AM	**Opening Remarks**
10:00 – 12:00 AM	**Academic Session 1**
12:00 – 1:00 PM	**Photo & Lunch**
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4:30 – 4:50 PM	**Year End Summary of KOLIS 2017**
4:50 – 5:10 PM	**Raffle**
5:10 – 5:20 PM	**KOLIS 2018 Board Committee**
5:20 – 5:30 PM	**Closing Remarks**
5:30 – 6:30 PM	**Dinner and Networking**