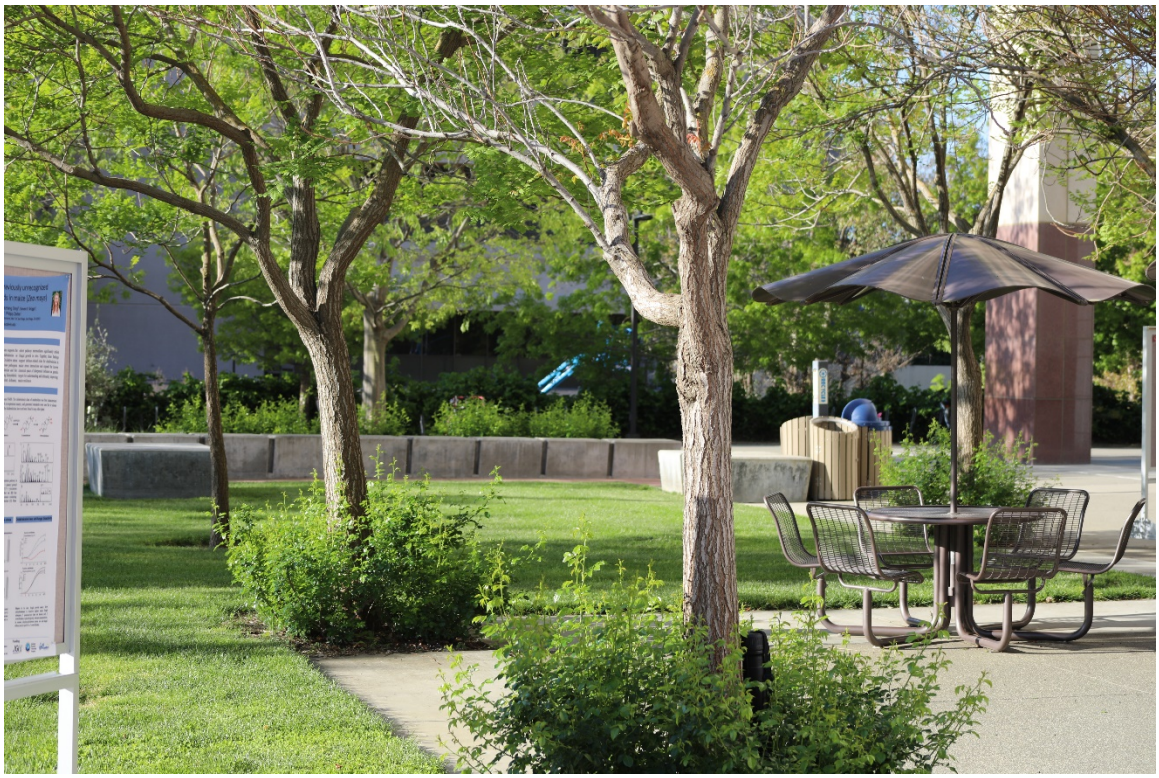
Twenty Eighth Annual

Biotechnology Training Retreat



Saturday,
March 9, 2019

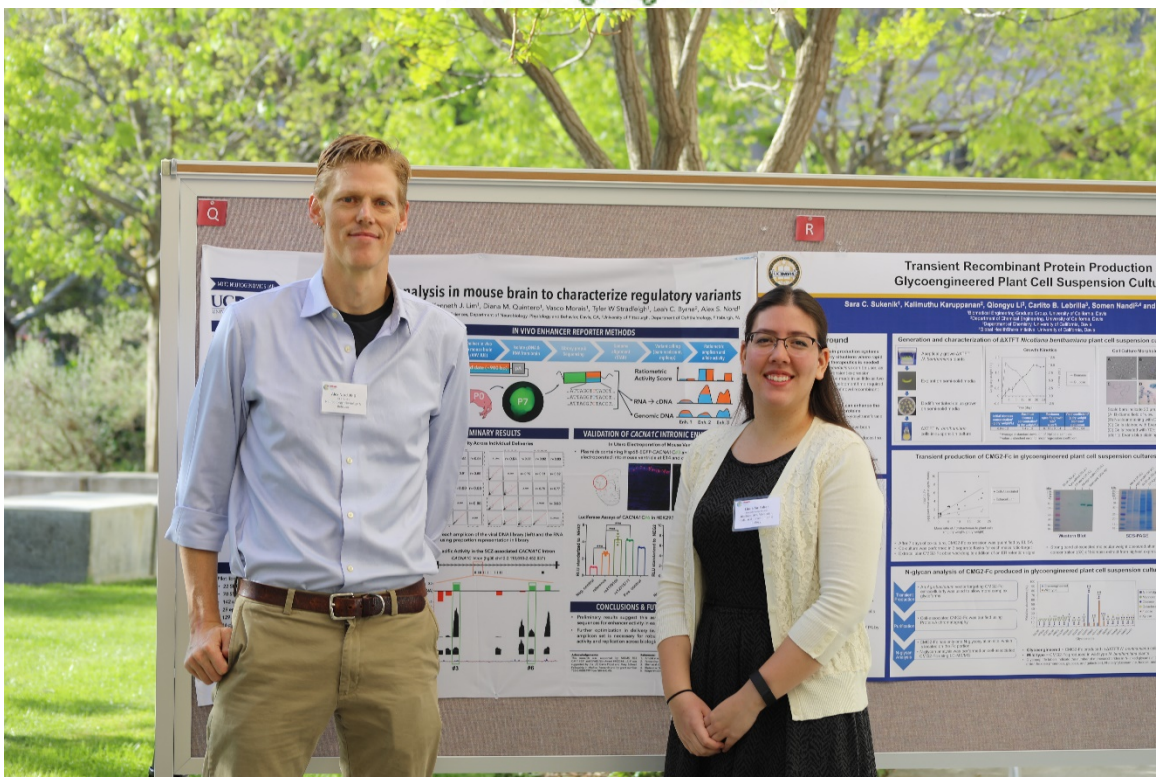
UC Davis Genome Center

Twenty Eighth Annual Biotechnology Training Retreat

Co-sponsored by:

UC Davis Designated Emphasis in Biotechnology
Graduate Program (DEB)

UC Davis Biotechnology Program



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UCDAVIS
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UC Davis Twenty Eighth Annual Biotechnology Training Retreat
March 9, 2019
UC Davis Genome Center Auditorium

8:30 – 9:00 am	**Registration/Continental Breakfast**
9:00 – 9:15 am	**Welcome** **Prasant Mohapatra, PhD** Vice Chancellor for Research
9:15 – 10:30 am	**Presentations** 9:15 Noah Goshi, 2018-19 Biotech Fellow — Biomedical Engineering 9:30 Matt McNulty, DEB Student..... — Chemical Engineering 9:45 Katie Beglinger, DEB Student..... — BMCDB 10:00 Mary Xiong, DEB Student ..... — Chemical Engineering 10:15 Maika Malig, DEB Student..... — Integrative Genetics & Genomics
10:30 – 10:45 am	**Break/Poster Viewing**
10:45 – 12:00 pm	**Presentations** 10:45 Anita Rajamani, DEB Student ..... — Biomedical Engineering 11:00 Linda Su Feher, DEB Student..... — BMCDB 11:15 Jackie Whitehead, DEB Student ..... — Biomedical Engineering 11:30 Dan Lewis, DEB Student..... — Genetics 11:45 Morgan Matson, DEB Student..... — Chemistry
12:00 – 1:00 pm	**Lunch/Poster Viewing/Voting on STEM-Talks and Biotech Posters**
1:00 -1:30 pm	**Gene Editing and Synthetic Biology – Bioethics Discussion**
1:30 – 1:45 pm	**Winners Announced and Closing Remarks** **Denneal Jamison-McClung, PhD** Director, Biotechnology Program

For social media, use #BiotechRetreat

2019 Poster Titles

A. **"Quantifying Autophagy Following Perturbation by Dengue Virus"**
Nitin Sai Beesabathuni[1*], Priya Shah[1,2]
Department of Chemical Engineering[1], University of California, Davis
Department of Microbiology and Molecular Genetics[2], University of California, Davis

B. **"Analysis of Eukaryotic Translation Initiation Factor (Eif) Phosphorylation by Mass Spectrometry"**
Katherine Beglinger*, Armann Andaya, Julie Leary, Christopher Fraser
Department of Molecular and Cellular Biology, University of California, Davis

C. **"Developing Host Cell Death Assays As Readouts for Amoebic Trogoytosis"**
Akhila Bettadapur* and Katherine S. Ralston
Department of Microbiology and Molecular Genetics, University of California, Davis

D. **"Delivery of Biomolecules into Model Membranes Using Nanolipoprotein Particles"**
Amanda T. Dang[1*], Matthew A. Coleman[2], Tonya L. Kuhl[3]
Department of Materials Science and Engineering[1], University of California, Davis
Department of Radiation Oncology[2], University of California, Davis Comprehensive Cancer Center
Department of Chemical Engineering[3], University of California, Davis

E. **"How *Entamoeba Histolytica* Goes Vampire: The Hunt for New Genes in the Conserved Process of Trogocytosis"**
Shea E. Feeney* and Katherine S. Ralston
Department of Microbiology and Molecular Genetics, University of California, Davis

F. **"Biocompatible Mesoporous Monoliths for Immobilization of Membrane-Bound Proteins"**
Sukriti Gakhar* and Marjorie L. Longo
Department of Chemical Engineering, University of California, Davis

G. **"Role of Somatostatin in Preserving Beta Cell Function"**
Jessica L. Huang* and Mark O. Huising
Department of Neurobiology, Physiology and Behavior, University of California, Davis

H. **"A New Method for Taxonomic Classification Using Minhash and Sequence Bloom Trees"**
Luiz Irber*, Philip Brooks, Taylor Reiter, C. Titus Brown
Department of Population Health and Reproduction, University of California, Davis

I. **"The Actin Sun-Kash Enhancer Pathway and its Regulation of Nuclear Migration Through Constricted Spaces"**
Linda Ma* and Daniel Starr
Department of Molecular and Cellular Biology, University of California, Davis

J. **"A Simplified Bioreactor Process for Recombinant Butyrylcholinesterase Production in Transgenic Rice Cell Suspension Cultures"**
Kantharakorn Macharoen*[1], Karen McDonald[1,2] and Somen Nandi[1,2]
[1]Department of Chemical Engineering, University of California, Davis
[2]Global HealthShare® Initiative, University of California, Davis

K. **"Characterization of R-Loop Structures in the Human Genome Using SMRF-seq"**
Maika Malig*, Stella Hartono, Jenna Giafaglione, Lionel Sanz, Frédéric Chédin
Department of Molecular and Cellular Biology, University of California, Davis

L. **"Optogenetic Regulation of Autophagy in Chinese Hamster Ovary Cells for Increased Production of Therapeutic Proteins"**
Shiaki A. Minami[1]* and Priya S. Shah[1,2]
[1]Department of Chemical Engineering, University of California, Davis
[2]Department of Microbiology and Molecular Genetics, University of California, Davis

M. **"Chemical Modifications of Anti-microRNAs to Enhance Binding Interactions with the MicroRNA-Argonaute2 Complex"**
Kevin M. Pham*, Scott R. Suter, Shannon S. Lu, and Peter A. Beal
Department of Chemistry, University of California, Davis

N. **"Development of Exosome Mimics for Vascularization in Ischemic Wound Sites"**
Lalithasri Ramasubramanian*[1,2], Priyadarsini Kumar[1], Dake Hao[1], Diana L. Farmer[1,3], Aijun Wang[1,2,3]
[1]Surgical Bioengineering Laboratory, Department of Surgery, University of California, Davis
[2]Department of Biomedical Engineering, University of California, Davis
[3]Institute for Pediatric Regenerative Medicine, Shriners Hospitals for Children – Northern California

O. **"Multiple Factors Regulated D-Loops in DNA Repair by Homologous Recombination"**
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Department of Microbiology and Molecular Genetics, University of California, Davis

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Shahin Shams*, Justin Madrigal, Roberta Stilhano, and Eduardo Silva
Department of Biomedical Engineering, University of California Davis

Q. **"Parallel Analysis of Regulatory Variants in Mouse Brain"**
Linda Su-Feher*, Jessica L. Haigh, Jason Lambert, Sarah J. Morse, Alex S. Nord
Department of Neurobiology, Physiology, and Behavior, University of California, Davis

R. **"Transient Production of an Anthrax Decoy Fusion Protein in Glycoengineered Plant Cell Suspension Cultures"**
Sara C. Sukenik*[1], Kalimuthu Karuppanan[1], Qiongyu Li[2], Carlito B. Lebrilla[2], Somen Nandi[1,3] and Karen A. McDonald[1,,3]
[1]Department of Chemical Engineering, University of California, Davis
[2]Department of Chemistry, University of California, Davis
[3]Global HealthShare® Initiative, University of California, Davis

S. **"Effects of ADAR Homodimerization on dsRNA Substrate Specificity"**
Alexander Thuy-Boun*, Peter Beal
Department of Chemistry, University of California, Davis

T. **"Evaluating the Developmental Toxicity of Halogenated Pyrroles in Zebrafish"**
Bianca Yaghoobi*, Isaac N. Pessah, and Pamela J. Lein
Department of Molecular Biosciences, School of Veterinary Medicine, University of California, Davis

U. **"Production of a Plant Alkaloid in a Microbial Host"**
Angela Zhang* and Shota Atsumi
Department of Chemistry, University of California, Davis

V. **"Actin-Based Pathway for Nuclear Migration in P. Cells of C. Elegans"**
Jamie Ho*, Linda Ma*, and Daniel A. Starr
Department of Molecular and Cell Biology, University of California, Davis

***DEB Graduate Student**

2019 Presentation Titles

1. **"Analysis of Eukaryotic Translation Initiation Factor (eIF) Phosphorylation by Mass Spectrometry"**
   Katie Beglinger*, Armann Andaya, Christopher Fraser
   Department of Molecular and Cellular Biology, University of California, Davis

2. **"Mechanisms of Neuronal Transmission of Inflammation to Distal Neuroanatomical Regions"**
   Noah Goshi*[1], Rhianna Morgan[2], Pamela Lein[2], and Erkin Seker[3]
   [1]Department of Biomedical Engineering, University of California, Davis
   [2]Department of Molecular Biosciences, University of California, Davis
   [3]Department of Electrical and Computer Engineering, University of California, Davis

3. **"Stochastic Resonance in Bacterial Growth under Antibiotic Treatment"**
   Daniel D. Lewis*[1], Xuanwei Yu[2], and Cheemeng Tan[1]
   [1]Department of Biomedical Engineering, University of California, Davis
   [2]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD

4. **"Characterization of R-Loop Structures in the Human Genome Using SMRF-seq"**
   Maika Malig*, Stella Hartono, Jenna Giafaglione, Lionel Sanz, and Frédéric Chédin
   Department of Molecular and Cellular Biology, University of California, Davis

5. **"Developing Production of a Plant Alkaloid in a Microbial Host"**
   Morgan Matson*, Angela Zhang*, Nicole Nozzi*, and Shota Atsumi
   Department of Chemistry, University of California, Davis

6. **"Re-Thinking Pharmacological Life Support for Human Habitation on Mars"**
   Matthew J. McNulty*, Jesse Delzio, Kalimuthu Karuppanan, Somen Nandi, and Karen McDonald
   Department of Chemical Engineering, University of California, Davis

7. **"Dietary Lipoprotein Composition Modulates Endothelial Expression of VCAM-1, an Early Marker of *Atherosclerosis*"**
   Anita Rajamani*[1], Kamil Borkowski[2], Samir Akre[1], Andrea Fernandez[1], John W. Newman[2], Scott I.Simon[1], and Anthony G. Passerini[1]
   [1]Department of Biomedical Engineering, University of California, Davis
   [2]Department of Nutrition, University of California, Davis

8. **"Parallel Analysis of Regulatory Variants in Mouse Brain"**
   Linda Su-Feher*, Jessica L. Haigh, Jason Lambert, Sarah J. Morse, and Alex S. Nord
   Department of Neurobiology, Physiology, and Behavior, University of California, Davis

9. **"Nanoparticle-Mediated Morphogen Delivery to Instruct Mesenchymal Stem Cell Spheroids"**

Jackie Whitehead*, Alefia Kothambawala, and J. Kent Leach
Department of Biomedical Engineering, University of California, Davis

10. **"Effects of N-Glycosylation on the Properties and Molecular Dynamics of a Plant-Made Fc-Fusion Anthrax Decoy Protein"**

Yongao Xiong[1], Qiongyu Li[2], Austen Bernardi[1], Vally Kommineni[2], Abhaya Dandekar[3], Carlito Lebrilla[2], Roland Faller[1], Karen McDonald[1], and Somen Nandi[1]
[1]Department of Chemical Engineering, University of California, Davis
[2]Department of Chemistry, University of California, Davis
[3]Department of Plant Sciences, University of California, Davis

*DEB Graduate Student

UCDAVIS
Biotechnology Program

Oral Presentation Abstracts

1. Katie Beglinger

ANALYSIS OF EUKARYOTIC TRANSLATION INITIATION FACTOR (EIF) PHOSPHORYLATION BY MASS SPECTROMETRY

Presenter: Katie Beglinger
Authors: Katie Beglinger*, Armann Andaya, Christopher Fraser
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Chris Fraser

Translation initiation is the rate-limiting step of protein synthesis and is highly regulated by eukaryotic initiation factors (eIFs), which work together to recruit a mRNA to the ribosome and locate the initiation codon. An additional layer of regulation of this pathway is likely influenced by post-translational modifications of initiation factors, specifically phosphorylation. While several global studies have identified extensive numbers of phosphorylation sites on eIF3 and eIF4F, it is still unclear which sites are important in regulating translation. The objective of my research is to identify which phosphorylation sites are key in regulating translation initiation and to determine how phosphorylation regulates the function of translation initiation factors.

We have started to determine which phosphorylation sites on the cap binding complex, eIF4F, are important in regulating translation. To build on our previous work, we have expressed and purified this complex from HeLa cells that have been treated with the kinase inhibitor torin. We are now quantifying site-specific phosphorylation stoichiometries using a novel cerium oxide dephosphorylation and tandem mass tagging method followed by nanoLC-MS/MS. Identified phosphorylation sites that change in response to kinase inhibitors will be characterized using *in vitro* functional assays.

*DEB Graduate Student

2. Noah Goshi

MECHANISMS OF NEURONAL TRANSMISSION OF INFLAMMATION TO DISTAL NEUROANATOMICAL REGIONS

Presenter: Noah Goshi
Authors: Noah Goshi*, Rhianna Morgan, Pamela Lein, and Erkin Seker
Graduate Group: Biomedical Engineering
Preceptor: Erkin Seker

Chronic neuroinflammation is a major factor in a number of neurological conditions including neuropathic pain, foreign body response to therapeutic neural implants, neurodegeneration and a number of psychiatric disorders. An interesting phenomenon observed in many of these conditions is that regions anatomically remote, but synaptically connected to the initial insult site also show signs of neuroinflammation. Our hypothesis is that neuroinflammation is transmitted not only by extracellular soluble factors, but also via axonal transport and electrophysiological signals. There are a number of *in vivo* studies supporting the propagation of neuroinflammation via these putative mechanisms, including clinical observations and rodent models demonstrating histological evidence of inflammatory changes in remote neural populations following a focal cerebral ischemia. However the highly complex and interconnected processes that dictate neuroinflammation *in vivo* make it extremely challenging to determine the extent to which neurons are responsible for the observed propagation of neuroinflammation. We will present our progress in developing an *in vitro* model to better study the transmission of neuroinflammation through axonal and electrophysiological mechanisms. We have engineered a cell culture platform consisting of two culture chambers connected via a microchannel array. The microchannel array allows for the synaptic connection of the two chambers via axonal projections between the chambers, while maintaining chemical isolation due to the high fluidic resistance within the microchannels and

the development of a hydrostatic pressure flow. Using this platform, we have developed and characterized a protocol to culture rat neurons, astrocytes and microglia together, which is important as these are the three main cell types involved in neuroinflammation. Ultimately, our goal is to use this *in vitro* model to better understand the mechanisms that regulate the transmission of inflammation within the central nervous system.

*DEB Student

3. Daniel Lewis

STOCHASTIC RESONANCE IN BACTERIAL GROWTH UNDER ANTIBIOTIC TREATMENT

Presenter: Daniel Lewis
Authors: Daniel Lewis*, Xuanwei Yu[2], and Cheemeng Tan
Graduate Group: Integrative Genetics & Genomics
Preceptor: Cheemeng Tan

Biological noise or heterogeneity is generally thought to decrease the efficiency of biotechnological processes and the efficacy of biomedical treatment. The noise manifests in the variation of protein level, phenotype, and growth of cells. Here, we present a new paradigm in which noise may be exploited to enhance the efficacy of antibacterial treatment. In this work, we demonstrate how bacteria can exploit noise in the expression of resistance enzyme to improve their growth in a noisy environment under antibiotic treatment. The phenomenon, called stochastic resonance, occurs when the levels of the resistance enzyme and the rate of bacterial growth fluctuate at the same frequency, producing resonance. We construct a computational model and provide experimental results to show that bacteria are responding to a given frequency of noise in their environment. This work has important implications for the design of antibiotic treatment by taking advantage of the natural variability of biological systems. Our results suggest the dosage and half-life of new or existing drugs may be optimized to take advantage of stochastic resonance, inhibiting the growth of resistant bacteria by taking advantage of noise rather than trying to override it.

*DEB Graduate Student

4. Maika Malig

CHARACTERIZATION OF R-LOOP STRUCTURES IN THE HUMAN GENOME USING SMRF-SEQ

Presenter: Maika Malig
Authors: Maika Malig*, Stella Hartono, Jenna Giafaglione, Lionel Sanz, and Frédéric Chédin
Graduate Group: Molecular and Cellular Biology
Preceptor: Frédéric Chédin

R-loops are non-B DNA structures formed during transcription upon reannealing of the nascent RNA to the template DNA, causing the non-template DNA strand to be displaced and single-stranded. These structures are prevalent in mammalian genomes and form over conserved genic hotspots. R-loops are associated with contrasting cellular processes. R-loops plays a key role in controlling gene expression and are involved in Immunogloblulin (Ig) class-switch recombination and efficient transcription termination. However, deregulation of these structures, primarily attributed to their aberrant formation and persistence, have been associated to genomic instability, a phenomenon linked to a growing number of human disorders such as neurodegenerative disorders and cancers.

Most genome-wide R-loop profiling studies have relied on short-read sequencing technology resulting in a population average view of R-loop formation. Here we present a high-throughput, high-resolution R-loop footprinting method, SMRF-seq (single-molecule R-loop footprinting sequencing). This method leverages third generation single-molecule, real-time (SMRT) sequencing coupled to non-denaturing bisulfite treatment. Under non-denaturing conditions, sodium bisulfite leads to the conversion of cytosine to uracil on inherently single-stranded regions such as the patches found on the looped out strand of R-loops. Following

PCR amplification and sequencing, long stretches of cytosine (C) to thymine (T) conversions are indicative of the presence of an R-loop. This technique was applied to a variety of R-loop forming hotspots and resulted in the most comprehensive characterization of R-loops at the single-molecule level. Long, contiguous C to T footprints were observed specifically on the looped out strand but not on the RNA-paired DNA strand, as expected. SMRF-seq confirmed that R-loops form at promoter regions and validates extensive R-loop hotspots over gene bodies and terminal regions. Given that individual footprints often extend past exon/intron boundaries, the data further suggests that R-loops form on pre-mRNA. Examination of R-loop lengths showed median lengths ranging from 250 to 450 bp at most loci, making R-loops the longest non-B DNA structures known to date. At almost all loci, a small fraction of R-loops reached kilobase lengths, with the largest continuous R-loop known to date covering 2.7 kb. The data also revealed that individual R-loops often pile up over larger R-loop-prone regions following non-random and partially overlapping molecular clusters. This data enabled us to annotate at near-base pair resolution, the starts and ends of individual R-loop structures. While no clear sequence motifs could be identified, we observed a weak trend towards G-rich sequences within footprints, which is consistent with previous requirements to form R-loops.

We expect the application of SMRF-seq to enable a big step forward in our understanding of R-loop formation under a variety of conditions, including disease states.

*DEB Graduate Student

5. Morgan Matson

DEVELOPING PRODUCTION OF A PLANT ALKALOID IN A MICROBIAL HOST"

Presenter: Morgan Matson
Authors: Morgan Matson*, Angela Zhang*, Nicole Nozzi*, and Shota Atsumi
Graduate Group: Chemistry
Preceptor: Shota Atsumi

The level of chemical complexity encompassed by plant-derived natural products has made them a rich source for the discovery of novel scaffolds for pharmaceuticals or industrial applications. The tropane alkaloid scopolamine is a natural product that acts as a muscarinic antagonist and has a variety of different clinical applications. Obtaining a commercially viable supply of scopolamine, as well as other natural products, can be an enormous challenge that often leads to overharvesting. Due to its nature as secondary metabolite, scopolamine is produced by its native plants in extremely minute quantities. This makes extraction laborious and costly. Total chemical synthesis of scopolamine is not industrially viable as the schemes are prohibitively long and low-yielding due to chemoselectivity issues. A relatively new third option to produce scopolamine that is rapidly gaining interest is production of the target compound via an engineered microbial host. While traditional chemical synthesis struggles to achieve reliable stereospecificity, enzymatic biosynthesis has evolved precise stereospecificity over millennia. Our design for an artificial biosynthetic pathway to produce scopolamine in the model host organism *Escherichia coli* is based on what is known or hypothesized about the native nightshade biosynthetic pathway. We propose a chemoenzymatic approach that utilizes

chemical synthesis to form the tropane ring moiety and an enzymatic pathway from glucose to build the acyl aromatic moiety.

*DEB Graduate Student

6. Matthew McNulty

RE-THINKING PHARMACOLOGICAL LIFE SUPPORT FOR HUMAN HABITATION ON MARS

Presenter: Matthew McNulty
Authors: Matthew J. McNulty*, Jesse Delzio, Kalimuthu Karuppanan, Somen Nandi, and Karen McDonald
Graduate Group: Chemical Engineering
Preceptor: Karen McDonald

The pharmaceutical supply chain for a Mars mission is severely constrained by accelerated radiation-induced degradation and multiple month transit from Earth to Mars; not only are the drugs we bring with us at high risk, but re-supply of those drugs is also exceedingly costly. Any emergency medical countermeasures to unanticipated threats are also severely limited with an Earth-reliant supply chain. For these reasons, *in situ* production of biopharmaceuticals under the available resources of a Martian environment will be key in securing stable long-term crew member health.

Plants have been long recognized as high potential organisms for space exploration life support – capable of harnessing light, producing food, closing the loop on human waste streams, and buoying crew member mental health. However, this potential has expanded in recent decades to include pharmacological life support as we have established expression of recombinant proteins *in planta* as a versatile supply of complex pharmaceuticals. While drug delivery modalities like oral administration are inherently compatible with *in planta* production and the resource-limited Martian surface, these modalities can be incompatible with some important pharmaceutical targets, such as antibodies, a growing class of biopharmaceuticals here on Earth. For these targets, we need to be able to purify drugs to

>95% for intravenous or subcutaneous injection without access to complex manufacturing equipment and facilities.

We propose that plant viruses presenting coat protein display of epitopes with affinity to the fragment crystallizable (Fc) region of antibodies is a high potential platform technology for purification of antibodies and Fc-fusion proteins in a Martian environment, particularly when coupled with plant-based biopharmaceutical production. We have successfully produced virus-based immunosorbent nanoparticles in a plant host and used them to purify antibodies. We will describe the process development of this novel strategy for virus-based immunosorbent nanoparticle purification of pharmaceuticals in limited resource environments.

*DEB Graduate Student

7. Anita Rajamani

DIETARY LIPOPROTEIN COMPOSITION MODULATES ENDOTHELIAL EXPRESSION OF VCAM-1, AN EARLY MARKER OF *ATHEROSCLEROSIS*

Presenter: Anita Rajamani
Authors: Anita Rajamani*, Kamil Borkowski, Samir Akre, Andrea Fernandez, John W. Newman, Scott I. Simon, and Anthony G. Passerini
Graduate Group: Biomedical Engineering
Preceptor: Anthony Passerini

Atherosclerosis, a maladaptive inflammation of arteries, underlies numerous cardiovascular diseases (CVD). CVD accounts for 2300 deaths every day in United States alone and is the leading cause of death and disability worldwide. Over half of CVD related deaths are attributable to modifiable risk factors, yet there is a lack of reliable early stage clinical markers to gauge an individual's disease progression. Among the earliest changes that precede atherosclerosis is an increase in endothelial surface expression of vascular cell adhesion molecule (VCAM-1), and subsequent capture of monocytes to the inflamed endothelium. Our lab has developed cell-based models to investigate the fundamental mechanisms that regulate arterial inflammation. Using these tools we dissect the individual and combined effects of different physiological factors that elicit endothelial VCAM-1 expression, including shear stress (flow conditions), cytokines, and dietary lipoproteins. In this study, we incubated cytokine-stimulated human aortic endothelial cells (HAEC) with triglyceride rich lipoprotein (TGRL), part of *bad cholesterol*, isolated from subjects after a standard western high fat

breakfast meal, and quantified the change in VCAM-1 in response to TGRL. Subjects were stratified into different risk categories based on the relative inflammatory potential of their TGRL. TGRL from *pro-atherogenic* responders increased VCAM-1 from baseline cytokine-stimulated levels, whereas TGRL from the *anti-atherogenic* group reduced VCAM-1 expression in cytokine-stimulated HAEC. Further investigation into the composition of TGRL distinguishing these two groups revealed enrichment in certain classes of fatty acids and their metabolites that were unique to pro-atherogenic responders. A mathematical model generated using the concentration of these signature metabolites accurately classified the subjects by their inflammatory response. Additional validation of these findings may result in identification of novel biomarkers in circulation that better reflect an individual's inflammatory state and risk for sub-clinical atherosclerosis.

*DEB Graduate Student

8. Linda Su-Feher

PARALLEL ANALYSIS OF REGULATORY VARIANTS IN MOUSE BRAIN

Presenter: Linda Su-Feher
Authors: Linda Su-Feher*, Jessica L. Haigh, Jason Lambert, Sarah J. Morse, and Alex S. Nord
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Alexander Nord

Regulatory DNA elements known as enhancers play critical roles in the regulation of gene expression during brain development. Sequence variation in enhancers is hypothesized to contribute to genetic risk for neurological disorders such as epilepsy and schizophrenia. The advancement of massively parallel reporter assays, which can screen thousands of DNA sequences at a time for enhancer activity, has enabled the functional characterization of enhancers in both *in vitro* and *in vivo* models, but few of these assays have been applied to the brain. We adapted an enhancer reporter assay known as STARR-seq for *in vivo* delivery into the mouse brain. We developed a pilot library of genomic candidates containing common non-coding sequence variants, including those associated with epilepsy and schizophrenia, in order to identify whether these variants contribute to altered gene expression in the brain. We also tested a library of ~800 *de novo* sequence variants identified in individuals with autism spectrum disorders. Results from preliminary deliveries of these libraries to the postnatal mouse brain via adeno-associated virus suggest that this method is able to identify sequences capable of acting as enhancers. We validated a schizophrenia-associated regulatory element and show that it drives reporter gene expression in developing mouse brain. By utilizing this approach, we hope to identify how non-coding sequence variation in human populations contributes to brain development and neurological disorders.

***DEB Graduate Student**

9. Jackie Whitehead

NANOPARTICLE-MEDIATED MORPHOGEN DELIVERY TO INSTRUCT MESENCHYMAL STEM CELL SPHEROIDS

Presenter: Jackie Whitehead
Authors: Jackie Whitehead*, Alefia Kothambawala, and J. Kent Leach
Graduate Group: Biomedical Engineering
Preceptor: J. Kent Leach

Cell-based tissue engineering is a promising alternative to autologous grafts to treat large bone defects. Human mesenchymal stem cells (MSCs) are a promising cell-type for such therapies. These benefits can be further enhanced by aggregating MSCs into spheroids. Osteogenic differentiation may be influenced through several approaches. Growth factors are potent instructors for differentiation; however, short half-lives and nonspecific delivery can limit the efficacy of their use in cell-based therapies. Therefore, the development of effective strategies that utilize smaller concentrations of inductive growth factors to induce differentiation or retain an induced phenotype upon transplantation would be advantageous for advancing cell-based therapies. To augment osteogenic differentiation of MSC spheroids, we formed spheroids in the presence of bone morphogenetic protein-2 (BMP-2)-loaded hydroxyapatite (HA) nanoparticles. We hypothesize that the presentation of internal instructive cues to MSC spheroids will enhance their osteogenic potential. We examined the ability of BMP-2-laden incorporated HA to increase the induction of the osteogenic phenotype, as well as the retention of the acquired phenotype when soluble cues were removed. HA nanoparticles were incorporated into MSC spheroids. Spheroid diameter increased as a function of incorporated HA concentration. BMP-2 was effectively adsorbed onto HA nanoparticles. The dose of BMP-

2 did not vary based on HA concentration, but rather, by the BMP-2 concentration initially presented to the HA. This approach resulted in greater localized delivery of BMP-2 to MSCs when BMP-2 is loaded onto HA versus freely soluble in media. After 14 days in culture, MSC spheroids containing BMP-2-loaded HA nanoparticles induced greater alkaline phosphatase (ALP) activity and *RUNX2* expression compared to spheroids with native HA nanoparticles or an equivalent dose of soluble BMP-2. In addition, the osteogenic phenotype was retained to a greater degree with BMP-2-laden HA incorporated into the spheroid compared to spheroids with an equivalent dose of soluble BMP-2. These data confirm that BMP-2 can be delivered to MSC spheroids using HA nanoparticles as a delivery vehicle. These findings demonstrate a promising strategy for simultaneous delivery of osteoconductive and osteoinductive cues for enhancing MSC participation in bone formation.

*DEB Graduate Student

10. Yongao Xiong

EFFECTS OF N-GLYCOSYLATION ON THE PROPERTIES AND MOLECULAR DYNAMICS OF A PLANT-MADE FC-FUSION ANTHRAX DECOY PROTEIN

Presenter: Yongao Xiong
Authors: Yongao Xiong*, Qiongyu Li, Austen Bernardi, Vally Kommineni, Abhaya Dandekar, Carlito Lebrilla, Roland Faller, Karen McDonald, and Somen Nandi
Graduate Group: Biomedical Engineering
Preceptor: J. Kent Leach

Protein N-glycosylation is a critical post-translational modification and has influences on variety of biological processes at cellular and molecular level, making glycosylation a major study aspect for glycoprotein based therapeutics. To obtain an in-depth understanding on how N-glycosylation impacts on protein properties, a Fc-fusion anthrax decoy protein, namely rCMG2-Fc, was expressed in *Nicotiana benthamiana* plant with three types of N-glycosylation profiles (plant complex type:APO; oligomannose type: ER and aglycosylated: Agly). The decoy protein binds to the protective antigen (PA) or anthrax through its CMG2 domain and inhibits toxin endocytosis. The protein expression, N-glycosylation profiles, binding kinetics to PA, toxin neutralization efficiency, and thermostability were determined experimentally. In parallel, we performed molecular dynamics (MD) simulations of the predominant full-length rCMG2-Fc glycoform for each of the three N-glycosylation profiles to understand the effects of glycosylation at the molecular level. The expression levels of APO and ER variants were 2-fold higher than the Agly variant, suggesting stabilizing effects of N-glycans on rCMG2-Fc during *in planta* production. To confirm protein function, a cell-based toxin neutralization assay (TNA) was developed to determined the EC_{50} values of variants, where the APO and

Agly variants yielded lower EC_{50} than the ER variant. The binding kinetics between rCMG2-Fc and PA were determined by biolayer interferometry (BLI), where the binding affinities of all variants were in sub-nanomolar range regardless of N-glycosylation. The protein thermostability was examined utilizing the PA binding ELLISA, where the fraction of functional ER variant decayed after overnight incubation at 37°C. This finding is consistent with the higher EC_{50} for the ER variant in TNA. In MD simulation, MAN8 (ER) glycoform showed higher hydrophobic solvent accessible surface areas, indicating a possibly higher aggregation tendency.

*DEB Graduate Student

UCDAVIS
Biotechnology Program

Bioethics Discussion

ETHICS QUESTION

"HUMAN GENOME EDITING HAS ARRIVED"

Written and Presented by

Denneal Jamison-McClung, PhD
Interim Director of the Biotechnology Program

INTERIM DIRECTOR: Denneal Jamison-McClung, PhD

HUMAN GENOME EDITING HAS ARRIVED

In the fall of 2018, the global scientific community was stunned to learn that genome-editing of embryos had been performed by Dr. He Jiankui, leading to the birth of twin girls with changes in the CCR5 gene, which encodes a chemokine receptor expressed by T cells and macrophages. In its active state, this protein acts as a co-receptor of HIV-1, allowing the virus to infect human cells. An allelic, inactive forms of CCR5 has been characterized, delta32, and confers HIV-resistance in homozygotes. The rationale for Dr. He's research was to create homozygous delta32 babies who would be resistant to HIV-1 infection and unable to become infected through contact with their HIV-1 positive father.

"He Jiankui: China condemns 'baby gene editing' scientist"
- BBC News - January 21, 2019
https://www.bbc.com/news/world-asia-46943593?ocid=socialflow_twitter

In the process of investigating the research program that led to these births, it was discovered that ethical review documents had been forged, institutional/governmental oversight was avoided by raising private funding for the research, participants were not properly consented and actions violated China's regulations on gene-related research. The actions of this scientist have been condemned by the international scientific community and by the Chinese government.

As the story unfolds, it turns out that several renowned researchers, including those in the US, had been contacted by Dr. He and knew of his potential research plans. Most have stated that they counseled against the proposed research activity, but did not proceed with reporting the discussions to governing or scientific bodies.

Discussion Questions:

1) What responsibility do researchers have to report potential ethics violations by their local and global colleagues?

2) How best can the scientific community establish, communicate, monitor and enforce agreed-upon bioethical norms of behavior?

3) If human genome-editing technologies reach a point when there are no safety concerns related to off-target or unexpected genomic changes, will ethical oversight still be needed? Why or why not?

4) Which stakeholders in society should be involved in setting the regulatory parameters around genome editing technologies? Only scientists who understand the technologies? Patients and families who will benefit? Clinicians? Educators? General public? Policy makers? Insurance companies? Clergy?

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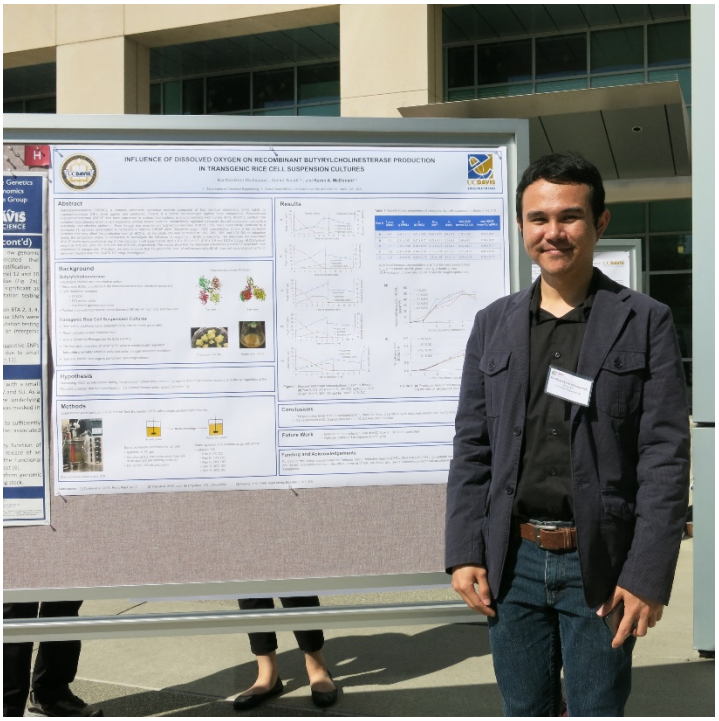
Poster Abstracts



A. Quantifying Autophagy Following Perturbation by Dengue Virus

Nitin Sai Beesabathuni[1*], Priya Shah[1,2]
[1]Department of Chemical Engineering[1], University of California, Davis
[2]Department of Microbiology and Molecular Genetics[2], University of California, Davis

Photo: Nitin Sai Beesabathuni
Graduate Group: Chemical Engineering
Preceptor: Priya Shay

Autophagy is a multi-step intracellular process by which cells recycle their misfolded proteins and damaged organelles into primary building blocks for biosynthesis. The cellular materials are sequestered by double-membrane vesicles called autophagosomes, which fuse with lysosomes to degrade the material. Autophagy is linked to many diseases, including cancer and infectious diseases. Quantifying autophagy through scalable properties such as instantaneous rates and turnover time allows fundamental understanding of autophagy and will be useful for biomedical and biotechnology applications. However, many current methods only estimate autophagosome pool size which is insufficient in characterizing the dynamic nature of autophagy. We are quantifying autophagy rates using high-throughput single-cell microscopy techniques.

We are using an instantaneous rate approach to measure autophagy by tagging a tandem green and red fluorescent protein reporter to MAP1LC3, a protein associated with autophagosomes. Following the chemical inhibition of autophagosome degradation, the initial accumulation rate of autophagosomes will be measured at different time points. The absolute formation and degradation rates contributing to the overall observed rate can be evaluated, thus characterizing the change in the functional state of the system over time. Additionally, the turnover time of autophagosomes at steady-state can be utilized for direct comparison between different cellular systems during various perturbations.

We are applying this method to study autophagy upon perturbation by dengue virus (DENV). DENV infects nearly 400 million people annually and causes severe disease. Interestingly, DENV hijacks autophagy to promote its own replication, yet we still do not understand the underlying mechanisms. Therefore, there is a critical need to quantitatively understand how

DENV influences autophagy. We are using a Tetracycline-inducible expression system to express DENV proteins in various combinations to quantify the corresponding autophagy rates. This work will provide quantitative insight into how DENV proteins can selectively induce and inhibit specific aspects of autophagy throughout the infection.

*DEB Graduate Student

B. Analysis of Eukaryotic Translation Initiation Factor (Eif) Phosphorylation by Mass Spectrometry

Katherine Beglinger*, Armann Andaya, Julie Leary, Christopher Fraser
Department of Molecular and Cellular Biology, University of California, Davis

Photo: Katherine Beglinger
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Chris Fraser

Translation initiation is the rate-limiting step of protein synthesis and is highly regulated by eukaryotic initiation factors (eIFs), which work together to recruit a mRNA to the ribosome and locate the initiation codon. An additional layer of regulation of this pathway is likely influenced by post-translational modifications of initiation factors, specifically phosphorylation. While several global studies have identified extensive numbers of phosphorylation sites on eIF3 and eIF4F, it is still unclear which sites are important in regulating translation. The objective of my research is to identify which phosphorylation sites are key in regulating translation initiation and to determine how phosphorylation regulates the function of translation initiation factors.

We have started to determine which phosphorylation sites on the cap binding complex, eIF4F, are important in regulating translation. To build on our previous work, we have expressed and purified this complex from HeLa cells that have been treated with the kinase inhibitor torin. We are now quantifying site-specific phosphorylation stoichiometries using a novel cerium oxide dephosphorylation and tandem mass tagging method followed by nanoLC-MS/MS. Identified phosphorylation sites that change in response to kinase inhibitors will be characterized using *in vitro* functional assays.

*DEB Graduate Student

C. Developing Host Cell Death Assays As Readouts for Amoebic Trogoytosis

Akhila Bettadapur* and Katherine S. Ralston
Department of Microbiology and Molecular Genetics, University of California, Davis

Photo: Akhila Bettadapur
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Katherine Ralston

Entamoeba histolytica is a microbial eukaryote and causative agent of the diarrheal disease amoebiasis. Pathogenesis is associated with profound damage to human tissues, and treatment options are limited. We discovered that amoebae attack and kill human cells through a cell-nibbling process that we named trogocytosis (*trogo-:* nibble). Trogocytosis is likely to underlie tissue damage during infection and it represents a promising target for therapeutic intervention, although the mechanism is still unknown. Assays in current use to analyze cell killing by amoebae have not been amenable to high-throughput analysis. We developed two complementary high-content assays to measure trogocytosis by quantifying human cell viability. The first assay uses CellTiterGlo, a luminescent readout for cellular ATP levels and a proxy for cell viability. We found that the CellTiterGlo signal is proportional to the quantity of viable cells, and can be used to detect death of human cells after co-incubation with amoebae. Trogocytosis-inhibited amoebae co-incubated with human cells yielded nearly three times higher luminescent values compared to control co-incubation, showing this assay is sensitive to amoebic trogocytosis inhibition. We also established a second assay that is microscopy-based and uses two fluorescent stains to differentiate live and dead human cells. Quantitative image analysis of trogocytosis-inhibited amoebae revealed nearly 20 times fewer dead human cells compared to control amoebae, which indicates this assay effectively captures amoebic trogocytosis inhibition. Further applications of these assays include analyzing the trogocytosis phenotypes of amoebic RNAi knockdown mutants to resolve the molecular mechanism of trogocytosis, as well as performing high-throughput screens of small molecules

in order to identify new trogocytosis inhibitors. These novel assays are tools to improve understanding of amoebiasis pathogenesis, and can be used to develop new candidate therapies.

*DEB Graduate Student

D. Delivery of Biomolecules into Model Membranes Using Nanolipoprotein Particles

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[1]Department of Materials Science and Engineering, University of California, Davis
[2]Department of Radiation Oncology, University of California, Davis Comprehensive Cancer Center
[3]Department of Chemical Engineering, University of California, Davis

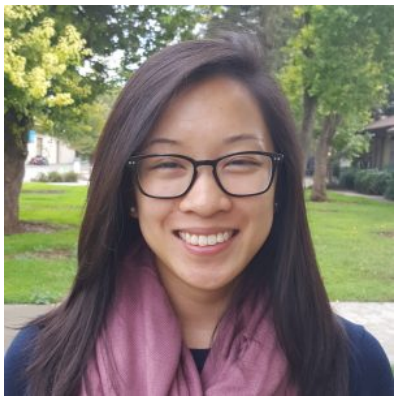

Photo: Amanda Dang
Graduate Group: Materials Science & Engineering
Preceptor: Tonya Kuhl

The goal of this work is to develop a biomimetic, supported lipid bilayer (SLB) platform that will receive integral membrane proteins (MPs) from nanolipoprotein particles (NLPs). Success would enable new opportunities for two-dimensional protein crystallization and studies on protein-protein interactions. A SLB is a lipid membrane that has been reconstituted on a solid support. These systems are advantageous because they are highly modular, easily controlled, and compatible with two-dimensional imaging methods. A NLP is a lipid bilayer disc stabilized by two amphipathic "scaffold" apolipoproteins. Stable in water and amenable to *in vitro* assembly by cell free expression, NLPs are a valuable tool for solubilizing MPs through the formation of MP-NLP complexes. In this study, we applied NLPs as vehicles for delivery of biomolecules into SLBs. We began by investigating the impact of SLB composition on the transport of fluorescently labeled lipids. Lipid transfer from NLPs was enhanced in membranes with a high concentration of defects, and in SLBs composed of nitrilotriacetic acid (NTA)-functionalized lipid mixtures. In the presence Ni^{2+}, NTA was used to specifically bind polyhistidine-tagged NLPs to the SLB surface. Nano-to-micron scale images of rearrangements at the SLB surface upon incubation with NLPs, acquired using Atomic Force Microscopy (AFM), further suggested a defect-mediated interaction between NLPs and SLBs. Preliminary experiments using NLP complexes loaded with receptor tyrosine kinase ErbB2/HER2 showed that protein transfer was also feasible. Ongoing work focuses on determining the orientation and functionality of proteins after delivery into the SLB.

***DEB Graduate Student**

E. How *Entamoeba Histolytica* Goes Vampire: The Hunt for New Genes in the Conserved Process of Trogocytosis

Shea E. Feeney* and Katherine S. Ralston
Department of Microbiology and Molecular Genetics, University of California, Davis

Photo: Shea Feeney
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Katherine Ralston

The eukaryotic pathogen *Entamoeba histolytica* (*histo-*: tissue; *lytic-*: dissolving) causes amoebiasis in humans. The profound tissue damage during infection is likely driven by *E. histolytica's* ability to kill human cells through trogocytosis (*trogo-*: nibble). During trogocytosis, amoebae pinch off and internalize bites of membrane and intracellular contents from human cells, which eventually results in cell death. In contrast, amoebae ingest pre-killed human cells whole *via* phagocytosis. Beyond *E. histolytica,* trogocytosis is part of an underappreciated, emerging theme in eukaryotic biology. While there are some shared features between trogocytosis and phagocytosis, we hypothesize that there are differences. Since *E. histolytica* is capable of both trogocytosis and phagocytosis, it represents an excellent model to dissect the trogocytosis-specific mechanism. Both phagocytosis and trogocytosis are under feed-forward gene regulation in *E. histolytica*. To identify genes differentially involved in trogocytosis versus phagocytosis, *E. histolytica* were fed live or pre-killed human cells, respectively, to induce upregulation of genes involved in these processes. RNA-seq analysis was used to identify genes that changed substantially in comparison to amoebae that had not been fed human cells. We found 621 putative trogocytosis genes to be upregulated compared to phagocytosis and reference transcriptomes. These genes represent a wide distribution of molecular functions and protein classes and include proteins involved in cytoskeletal rearrangement and membrane trafficking. To begin to explore the roles of select genes that were significantly upregulated in ingestion, we are currently generating RNAi knockdown mutants and evaluating their phenotypes. This work should have broad impact since trogocytosis is directly relevant to amoebiasis and also appears to be a fundamental form of eukaryotic cell-cell interaction.

***DEB Graduate Student**

F. Biocompatible Mesoporous Monoliths for Immobilization of Membrane-Bound Proteins

Sukriti Gakhar* and Marjorie L. Longo
Department of Chemical Engineering, University of California, Davis

Photo: Sukriti Gakhar
Graduate Group: Chemical Engineering
Preceptor: Marjorie Longo

Functional soluble proteins are routinely immobilized in sol-gel derived silica for development of novel biomaterials with applications in high throughput devices, biosensing, affinity chromatography and so on. However, since membrane-bound proteins require lipophilic membrane structures to retain their structure and function, their encapsulation in such materials is challenging. In this work, Bacteriorhodopsin, a transmembrane protein from *Halobacterium Salinarum,* was immobilized in sol-gel derived silicon dioxide mesoporous monoliths as its native purple membrane. The amount of alcohol evolved in sol-gel synthesis was minimized to avoid protein denaturation. Absorbance spectrum of the protein has a characteristic peak at 560 nm due to its bound chromophore, is present after encapsulation depicting retention of the protein's tertiary structure. Intrinsic tryptophan fluorescence was used to investigate the microenvironment of the encapsulated protein. A decrease in emission intensity with temperature was observed for the protein in solution and in the silica gel. The protein was more stable at higher temperatures when the concentration of buffer was altered during silica gel synthesis indicating an effect of local pH. Fluorescence anisotropy with change in temperature also showed consistent trends with more unfolding of protein at higher temperatures. Solvent accessibility determined using acrylamide quenching of tryptophan residues indicated similar environment for the tryptophan residues before and after entrapment. This work provides the groundwork for development of biocompatible mesoporous silica for membrane protein encapsulation. In future, Bacteriorhodopsin solubilized in lipid-polymer nanodiscs will be immobilized in silica monoliths and this work would be used for comparative studies to understand the effect of membrane structure on protein stability.

***DEB Graduate Student**

G. Role of Somatostatin in Preserving Beta Cell Function

Jessica L. Huang* and Mark O. Huising
Department of Neurobiology, Physiology and Behavior, University of California, Davis

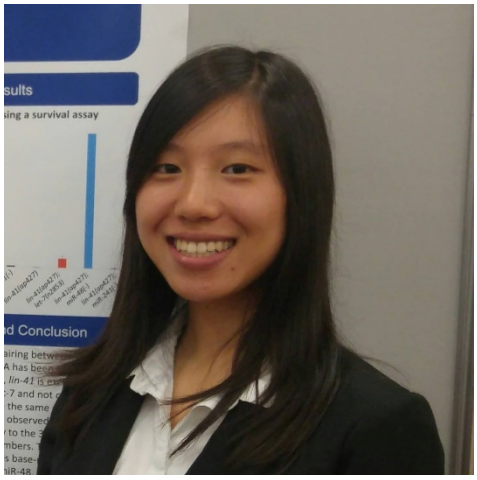

Photo: Jessica Huang
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Mark Huising

Type 2 diabetes affects over 30 million in the U.S. and is characterized by insufficient insulin release, preceded by insulin resistance of peripheral tissues. In healthy individuals, beta cells secrete insulin to lower blood glucose levels. Simultaneously, they secrete the peptide hormone Urocortin 3 (Ucn3), which acts in a paracrine manner to stimulate secretion of somatostatin (Sst) from delta cells. Sst then represses insulin secretion, creating a negative feedback loop that allows for the timely attenuation of beta cell activity. In pre-diabetic individuals, beta cells lose expression of Ucn3, marking the beginning of dedifferentiation. Loss of Ucn3 results in significantly reduced Sst tone within the local environment of the beta cell. The subsequent disinhibition of insulin then allows for increased insulin secretion to combat rising hyperglycemia. However, faced with constant stimulation, beta cells eventually undergo exhaustion, followed by dedifferentiation into a dysfunctional and immature-like state. It has been suggested that "beta cell rest" - providing beta cells with a break from secreting insulin - may allow for recovery of function. Restoration of Sst feedback may enforce beta cell rest, allowing for the beta cells to recover from their dysfunctional state.

*DEB Graduate Student

H. A New Method for Taxonomic Classification Using Minhash and Sequence Bloom Trees

Luiz Irber*, Philip Brooks, Taylor Reiter, C. Titus Brown
Department of Population Health and Reproduction, University of California, Davis

Photo: Luiz Irber
Graduate Group: Computer Science
Preceptor: Titus Brown

We introduce *sourmash gather*, a new method for taxonomic classification using MinHash and Sequence Bloom Trees. We ran the McIntyre benchmark and *gather* has better precision and recall than other tools.

gather uses the same Sequence Bloom Tree index we already use for searching similar datasets in public databases (like RefSeq and GenBank), but a different search strategy: instead of looking for all datasets above a similarity threshold, `gather` does a greedy search for the best match, report it and then remove the match from the query. This process is repeated while there are enough items in the query to find matches above a certain threshold.

gather is a new feature in sourmash 2.0, available on Bioconda and PyPI.

*DEB Graduate Student

I. The Actin Sun-Kash Enhancer Pathway and its Regulation of Nuclear Migration Through Constricted Spaces

Linda Ma* and Daniel Starr
Department of Molecular and Cellular Biology, University of California, Davis

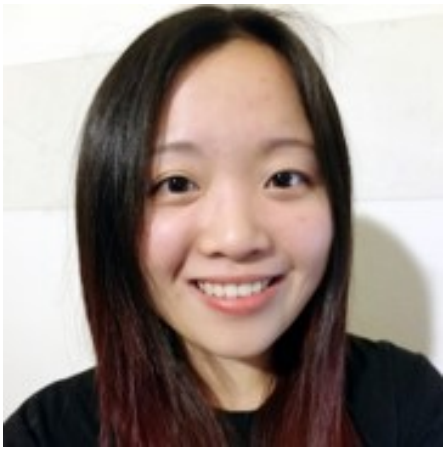

Photo: Linda Ma
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Daniel Starr

Nuclear migration through narrow constrictions is important for development and the maintenance of pro-inflammatory response. While studies have been conducted *in vitro*, they have not been delineated *in vivo*, which would provide a whole system view of the players which mediate nuclear migration. *Caenorhabditis elegans* P-cell nuclear migration through a narrow constriction serve as an *in vivo* model for this process. P-cells migrate from the lateral to the ventral part of the worm to develop into vulva and GABA neuron precursor cells. Failing P-cell nuclear migration, the worm fails to develop a vulva and the adequate number of GABA neurons, leading to the Egl (egg-laying deficient) and Unc (uncoordinated) phenotypes. This process is typically maintained by the SUN-KASH pathway, where SUN proteins (UNC-84) recruit KASH proteins (UNC-83) to the nuclear envelope, which recruit microtubule motors, primarily dynein, that facilitate nuclear migration toward the minus ends of microtubules. When major players (UNC-84 and UNC-83) of the SUN-KASH pathway are knocked out, they produce a temperature-sensitive mutant phenotype, leading to our prediction of a parallel enhancer pathway. We performed a forward genetics *enhancer of the nuclear migration defect of unc-84 (emu)* screen and found three putative actin regulators: CGEF-1, TOCA-1, and FLN-2, indicating that there is an actin SUN-KASH enhancer pathway. We are in the process of GFP-tagging FLN-2 to observe its localization *in vivo*. We propose that nuclear deformation is facilitated by a branched actin network, which is crosslinked by FLN-2.

*DEB Graduate Student

J. A Simplified Bioreactor Process for Recombinant Butyrylcholinesterase Production in Transgenic Rice Cell Suspension Cultures

Kantharakorn Macharoen*[1], Karen McDonald[1,2] and Somen Nandi[1,2]
[1]Department of Chemical Engineering, University of California, Davis
[2]Global HealthShare® Initiative, University of California, Davis

Photo: Kantharakorn Macharoen
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Karen McDonald

Butyrylcholinesterase (BChE), a ~340 kDa tetrameric hydrolase enzyme composed of four identical monomers (~85 kDa), binds tightly to organophosphorus (OP) nerve agents and pesticides, making it a potent bio-scavenger against these compounds. Recombinant butyrylcholinesterase (rBChE) has been expressed in various host systems aiming to replace human BChE purified from outdated blood plasma, an approach which is exceptionally expensive. Among several systems, metabolically regulated transgenic rice cell suspension culture is a potentially cost-effective platform. In this system, production of rBChE is controlled by the rice alpha-amylase promoter which is turned on under sugar starvation conditions. Our group has produced and reported an active and tetrameric form of rBChE produced in transgenic rice cell suspension cultures via a cyclical semicontinuous operation in which media exchanges are performed to provide sugar-rich media for the growth phase and sugar-free media for the production phase. However, further process development is needed to enhance rBChE yield and simplify the process to facilitate scale-up in conventional bioreactors.

In this study, the expression level of cell-associated rBChE was enhanced 2-fold from previous reports using the same cell-line. We found that the maximum active cell-associated rBChE level is around 50 µg rBChE/g fresh weight in a two-stage (growth and induction phases) batch operation and did not change significantly over a range (10% to 40%) of controlled dissolved oxygen (DO) concentration. Interestingly, when DO is uncontrolled with a fixed aeration rate (a constant flowrate of compressed air is sparged to the system) during the production phase, the maximum expression level is also equivalent to above experiments in which DO is controlled using a feedback control system with the composition of the sparging gas as the

manipulated input. We also found that a single stage batch operation with no media exchange (the production of rBChE is triggered simply through sugar depletion due to uptake by the the cells) yields maximum active cell-associated rBChE similar to a two-stage batch operation with a medium exchange. Altogether, these studies demonstrate a simpler and potentially more efficient, economical, and scalable bioreactor process for rBChE production from metabolically regulated transgenic rice cell cultures.

*DEB Graduate Student

K. Characterization of R-Loop Structures in the Human Genome Using SMRF-seq

Maika Malig*, Stella Hartono, Jenna Giafaglione, Lionel Sanz, Frédéric Chédin
Department of Molecular and Cellular Biology, University of California, Davis

Photo: Maika Malig
Graduate Group: Integrative Genetics & Genomics
Preceptor: Frédéric Chédin

R-loops are non-B DNA structures formed during transcription upon reannealing of the nascent RNA to the template DNA, causing the non-template DNA strand to be displaced and single-stranded. These structures are prevalent in mammalian genomes and form over conserved genic hotspots. R-loops are associated with contrasting cellular processes. R-loops plays a key role in controlling gene expression and are involved in Immunogloblulin (Ig) class-switch recombination and efficient transcription termination. However, deregulation of these structures, primarily attributed to their aberrant formation and persistence, have been associated to genomic instability, a phenomenon linked to a growing number of human disorders such as neurodegenerative disorders and cancers.

Most genome-wide R-loop profiling studies have relied on short-read sequencing technology resulting in a population average view of R-loop formation. Here we present a high-throughput, high-resolution R-loop footprinting method, SMRF-seq (single-molecule R-loop footprinting sequencing). This method leverages third generation single-molecule, real-time (SMRT) sequencing coupled to non-denaturing bisulfite treatment. Under non-denaturing conditions, sodium bisulfite leads to the conversion of cytosine to uracil on inherently single-stranded regions such as the patches found on the looped out strand of R-loops. Following PCR amplification and sequencing, long stretches of cytosine (C) to thymine (T) conversions are indicative of the presence of an R-loop. This technique was applied to a variety of R-loop forming hotspots and resulted in the most comprehensive characterization of R-loops at the single-molecule level. Long, contiguous C to T footprints were observed specifically on the

looped out strand but not on the RNA-paired DNA strand, as expected. SMRF-seq confirmed that R-loops form at promoter regions and validates extensive R-loop hotspots over gene bodies and terminal regions. Given that individual footprints often extend past exon/intron boundaries, the data further suggests that R-loops form on pre-mRNA. Examination of R-loop lengths showed median lengths ranging from 250 to 450 bp at most loci, making R-loops the longest non-B DNA structures known to date. At almost all loci, a small fraction of R-loops reached kilobase lengths, with the largest continuous R-loop known to date covering 2.7 kb. The data also revealed that individual R-loops often pile up over larger R-loop-prone regions following non-random and partially overlapping molecular clusters. This data enabled us to annotate at near-base pair resolution, the starts and ends of individual R-loop structures. While no clear sequence motifs could be identified, we observed a weak trend towards G-rich sequences within footprints, which is consistent with previous requirements to form R-loops.

We expect the application of SMRF-seq to enable a big step forward in our understanding of R-loop formation under a variety of conditions, including disease states.

*DEB Graduate Student

L. Optogenetic Regulation of Autophagy in Chinese Hamster Ovary Cells for Increased Production of Therapeutic Proteins

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[2]Department of Microbiology and Molecular Genetics, University of California, Davis

Photo: Shiaki Minami
Graduate Group: Chemical Engineering
Preceptor: Priya Shah

Autophagy is a potential tool to significantly increase the production of therapeutic proteins. As a central process in the cellular energy balance, autophagy is an evolutionarily conserved catabolic process by which proteins, organelles, and lipid matter are degraded to provide cells with amino acids and free fatty acids. Several groups have demonstrated that modulating autophagy rate significantly influences protein production, supporting a model in which autophagy generates the necessary components for protein production. While the effects of various industrially relevant stimuli on autophagy are well documented, precise regulation of autophagy remains a significant challenge. Current methods of physically or chemically modulating autophagy lack precise control over time and specificity to the autophagy pathway. Thus, developing a method for sensitive control of the process is critical for deepening our understanding of autophagy and elucidating the relationship between autophagy and protein production.

To regulate autophagy, we are developing a Chinese Hamster Ovary (CHO) cell line containing an optogenetics-based CRISPR-dCas9 system that controls the expression of a gain-of-function AMP-activated protein kinase (AMPK) mutant. AMPK is a well-known autophagy activator, which is expressed in this system by inducing transcription with 450nm light. Once activated, high expression of constitutively active AMPK mutant will induce autophagy, while removal of light will restore basal conditions. We have performed controlled experiments in CHO cells by using this system to express green fluorescent protein (GFP). Using flow cytometry, we observed a five-fold increase in GFP intensity after cells were illuminated for 24 hours. We are currently optimizing lighting conditions for higher

expression. By adjusting the intensity and pulse frequency of the light, we expect to achieve orthogonal, temporal control over autophagy. This method will be used to regulate autophagy to increase protein production.

*DEB Graduate Student

M. Chemical Modifications of Anti-microRNAs to Enhance Binding Interactions with the MicroRNA-Argonaute2 Complex

Kevin M. Pham*, Scott R. Suter, Shannon S. Lu, and Peter A. Beal
Department of Chemistry, University of California, Davis

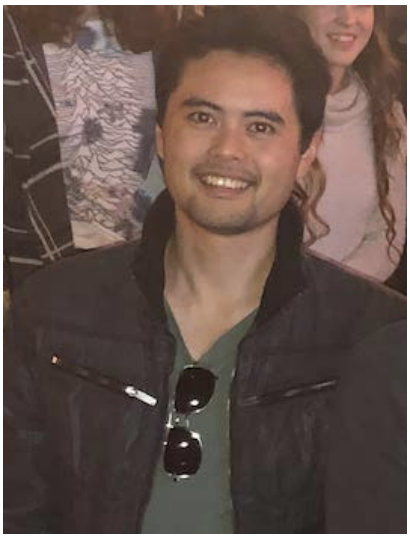

Photo: Kevin Pham
Graduate Group: Chemistry
Preceptor: Peter Beal

MicroRNAs are short noncoding RNA molecules that play an important role in gene regulation through the RNA interference (RNAi) pathway. Deregulated levels of microRNAs are strongly correlated with a variety of diseases, including cancer. One mode of microRNA therapeutics is the use of synthetic antisense oligonucleotides targeting microRNAs, or anti-miRs, to inhibit microRNA function by complementarily hybridizing a microRNA strand. Research towards improving anti-miR potency and binding potential towards a microRNA strand has mainly been focused on chemically modifying the sugar or phosphate backbone. However, there are no current reports of chemically modified anti-miRs that bind to specific sites of Argonaute2 (hAgo2), the catalytically active component of RNAi, when loaded with a microRNA guide strand. We present a structure-guided approach to chemically modify an anti-miR at the t1 position that potentially binds to the t1-Adenosine- (t1A) binding pocket of hAgo2, thus improve potency of microRNA inhibition. We determined the potency of chemically modified anti-miR21 that inhibits upregulated levels of endogenous microRNA-21 (miR-21) in HeLa cells using the dual luciferase assay. A fully 2′-O-methylated (2′-OMe) 15mer anti-miR21 with an alkynyl modification at the t1 nucleotide was determined to have a measurable level of potency when compared to a 2′-OMe 15mer anti-miR21 with t1 as canonical adenosine. The alkynyl modification was used to serve as a substrate for the copper(I)-catalyzed alkyne-azide cycloaddition reaction to generate triazoles containing various functional groups. Using fast rigid exhaustive docking (FRED), nearly 200 triazole modified t1 nucleosides were computationally screened for improved binding capability

into the t1A-binding receptor of hAgo2. 17 triazoles that scored better than adenosine were evaluated in potency using the dual luciferase assay on transfected HeLa cells. Interestingly, furan, methyl furan, and thiophene-modified triazole anti-miR21 showed an upwards of twofold higher potency than t1A anti-miR21. And, astonishingly, a methyl acetate triazole showed an eightfold higher potency than t1A anti-miR21. Future work includes performing serum stability, nuclease resistance, and pulldown assays on the t1-modified anti-miR21 oligonucleotides to evaluate their ability to resist nucleases and/or increase binding into the t1A-binding pocket of hAgo2.

*DEB Student

N. Development of Exosome Mimics for Vascularization in Ischemic Wound Sites

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Photo: Lalithasri Ramasubramanian
Graduate Group: Biomedical Engineering
Preceptor: Aijun Wang

Exosomes derived from endothelial progenitor cells (EPC) have been shown to facilitate vascularization *via* delivery of miRNA-126 but their therapeutic translation has been greatly hindered by the inherent disadvantages in exosome isolation, purification, and standardization. Here, we sought to overcome these shortcomings by engineering a biomimetic synthetic exosome that can recapitulate the pro-angiogenic, targeting, and cell recruiting properties of native EPC-derived exosomes. We propose that exosome mimics (EM) can be synthesized by coating a miRNA-126-loaded poly(lactic-co-glycolic acid) (PLGA) core with an endothelial cell-targeting ligand LXW7-functionalized EPC-membrane shell in order to mimic the miRNA cargo, targeting potential, and physical characteristics of native EPC exosomes. Here, we show a proof-of-concept system in which PLGA cores are made using a nanoprecipitation method and coated with isolated plasma membrane (PM) *via* mechanical extrusion. PLGA nanoparticle cores were successfully synthesized and demonstrated high stability in water, remaining a homogenous and consistent size of ~90 nm over 15 days at 4°C. Molecules were also able to be loaded within the PLGA core using DiI as a proof-of-concept cargo. The PM: PLGA ratio was seen to affect the size and stability of the EMs, with higher PM: PLGA ratios resulting in smaller sizes of ~250 nm and increased stability. Thus far, the proposed system shows potential as an exosome mimic in terms of physical characteristics. Future work will focus on completing and optimizing the EM structure and subsequently assessing angiogenic properties *in vitro* and *in vivo.*

***DEB Graduate Student**

O. Multiple Factors Regulated D-Loops in DNA Repair by Homologous Recombination

Shanaya Shah*, Aurele Piazza, Stella Hortono, William Wright, Frédéric Chédin and Wolf-Dietrich Heyer
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Shanaya Shah
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Wolf-Dietrich Heyer

Homologous recombination is a universal DNA double-strand break repair mechanism that uses an intact copy as a template for repair. Homology search and DNA strand invasion are signature reactions of homologous recombination, whose immediate outcome is formation of a single-end invasion intermediate called Displacement loop (D-loop). Extension of D-loop leads to a commitment to the use of the invaded DNA as a template. Despite its pivotal role in the fidelity of recombination and anti-crossover decisions, D-loop detection in somatic cells has proven extremely challenging. Consequently, apart from meiosis, regulation of D-loop formation/stability has only been inferred from end-point assays.

We developed D-loop Capture (DLC) assay, a sensitive method for detecting both nascent and extended D-loops in real-time in S. cerevisiae. Using the assay, we showed that D-loops maybe dissolved by two independent disruption pathways composed of Srs2 or Sgs1-Top3-Rmi1 and Mph1, which are delineated by Rdh54 (Piazza et al., 2019). To further characterize the disruption pathways and their D-loop substrate specificity, we also established a D-loop Mapping Assay (DMA) *in vitro* using bisulfite sequencing under non-denaturing conditions. We are in process of testing the effect of helicases and Rdh54 on D-loop length, kinetics and stability. We propose that the metastable, dynamic nature of D-loops resulting from these multiple opposing activities enforces homology search fidelity and recombination outcome.

*DEB Graduate Student

P. Characterizing the Encapsulation and Release of Lentivectors and Adeno-Associated Vectors from Degradable Alginate Hydrogels

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Photo: Shahin Shams
Graduate Group: Biomedical Engineering
Preceptor: Eduardo Silva

Gene therapies have been licensed for use by the FDA since 2017. Approved gene therapies utilize lentivectors (LV) or adeno-associated vectors (AAV), and future applications of these vectors will benefit from methods of localizing and controlling their delivery. Degradable alginate hydrogels have shown promise as delivery vehicles for vector payloads. Utilizing two different degradable alginate hydrogel formulations, we compare the ability of alginate hydrogels to encapsulate and deliver LV (diameter > 100nm) and AAV (diameter < 50nm). We hypothesize that physical properties of the viral vector and delivery vehicle impact the release of viral particles. 2% alginate hydrogels of slow degrading formulation (75:25 ratio 1% oxidized LF10/60 and 1% oxidized LF20/40) or fast degrading formulation (80:20 ratio of 5% oxidized LF20/40 and non-oxidized LF10/60) crosslinked with calcium carbonate and gluconic acid delta-lactone were used to encapsulate multiplicity of infection (MOI) = 10 of LV or AAV. Physical properties of both hydrogel formulations initially and over time were determined by rheometry. Viral loaded disks were placed in media, and this media was collected and replaced every 24 hours for 5 days to quantify release by either real time PCR (AAV) or ELISA (LV). The two degradable alginate hydrogel formulations differed significantly in their initial mesh size, thus the release of larger LV particles from alginate hydrogels was dependent on hydrogel degradation, while release of smaller AAV relied on a diffusive mechanism and was independent of the formulation used. We have shown that alginate hydrogels can successfully encapsulate LV and AAV, and that vector release was dependent on different mechanisms. To our knowledge this is the first direct comparison of

LV and AAV release and the first ever study of AAV release from degradable alginate hydrogels. Future studies will focus on tuning the physical properties of alginate hydrogels for the controlled release of AAV.

*DEB Graduate Student

Q. Parallel Analysis of Regulatory Variants in Mouse Brain

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Photo: Linda Su-Feher
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Alexander Nord

Regulatory DNA elements known as enhancers play critical roles in the regulation of gene expression during brain development. Sequence variation in enhancers is hypothesized to contribute to genetic risk for neurological disorders such as epilepsy and schizophrenia. The advancement of massively parallel reporter assays, which can screen thousands of DNA sequences at a time for enhancer activity, has enabled the functional characterization of enhancers in both *in vitro* and *in vivo* models, but few of these assays have been applied to the brain. We adapted an enhancer reporter assay known as STARR-seq for *in vivo* delivery into the mouse brain. We developed a pilot library of genomic candidates containing common non-coding sequence variants, including those associated with epilepsy and schizophrenia, in order to identify whether these variants contribute to altered gene expression in the brain. We also tested a library of ~800 *de novo* sequence variants identified in individuals with autism spectrum disorders. Results from preliminary deliveries of these libraries to the postnatal mouse brain via adeno-associated virus suggest that this method is able to identify sequences capable of acting as enhancers. We validated a schizophrenia-associated regulatory element and show that it drives reporter gene expression in developing mouse brain. By utilizing this approach, we hope to identify how non-coding sequence variation in human populations contributes to brain development and neurological disorders.

***DEB Graduate Student**

R. Transient Production of an Anthrax Decoy Fusion Protein in Glycoengineered Plant Cell Suspension Cultures

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Photo: Sara Sukenik
Graduate Group: Biomedical Engineering
Preceptor: Karen McDonald

In a bioterrorist attack or emerging infectious disease outbreak, rapid production of novel protein-based drugs or vaccines would be invaluable. We are developing a transient plant cell culture platform designed for rapid recombinant protein production in emergency situations. Our system uses genetically engineered *Agrobacterium tumefaciens* to deliver the DNA encoding a protein of interest to *Nicotiana benthamiana* plant cells in suspension culture. Different proteins can be produced on this platform simply by co-culturing with a different recombinant *Agrobacterium*. Compared to stable transgenic mammalian cell line development, our process would reduce the initial development time before large-scale protein production can begin since the required *Agrobacterium* constructs can be produced in as little as two weeks. Additionally, because agrobacteria can self-replicate to high densities and transfer the DNA construct directly to plant cells, there are also advantages compared with transient production in mammalian cell culture which requires expensive reagents, purified plasmid DNA, or use of mammalian viral vectors.

As a model protein, we have successfully produced a recombinant anthrax toxin receptor-Fc fusion protein (a fusion between the extracellular domain of the human capillary morphogenesis receptor protein that binds anthrax protective antigen and the Fc domain of human IgG, referred to as CMG2-Fc) by adding *Agrobacterium* to plant cells in suspension culture. Initial process development studies will be discussed, which resulted in expression levels up to 10 μg CMG2-Fc per g plant cell fresh weight after 7 days of co-culture. Although

plants are capable of a wide variety of post-translational modifications, there are slight differences between plant and mammalian glycosylation. To reduce plant-specific glycosylation patterns, β(1,2)-xylosyltransferase and α(1,3)-fucosyltransferase knockdown glycoengineered host *N. benthamiana* cell suspension cultures were generated. CMG2-Fc produced by co-culturing *Agrobacterium* with these glycoengineered *N. benthamiana* cell suspension cultures resulted in a dramatic reduction in plant-specific N-glycans compared to CMG2-Fc produced in wild type *N. benthamiana* plants. In addition to mitigating the risk of an immune response to plant-specific glycans, this proof of concept data demonstrates a method that could be further modified to enhance a product's efficacy and stability by tuning its N-glycan distribution.

***DEB Graduate Student**

S. Effects of ADAR Homodimerization on dsRNA Substrate Specificity

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Photo: Alexander Thuy-Boun
Graduate Group: Chemistry
Preceptor: Peter Beal

Post-transcriptional modification of RNA is an important cellular mechanism that increases the diversity of RNA transcripts. One of the most prevalent post-transcriptional modifications is adenosine deamination, initiated by the enzyme Adenosine Deaminase acting on RNA (ADAR). ADARs are responsible for the deamination of adenosine into the non-canonical base inosine. Because Inosine behaves like guanosine, A to I editing events often lead to transcript diversification, whether it be by changing codon triplets, or by the creation or removal of splice sites. Dysregulation of ADARs have been implicated in numerous human diseases, such as Acardi-Goutieres syndrome, multiple carcinomas, and is known to be vital in maintaining proper neuronal activity.

My research aims to uncover the role of the double stranded RNA binding domains (dsRBDs) in ADAR substrate selectivity. All isoforms of ADAR contain two or three dsRBDs which bind to duplex RNA substrates enhancing its ability to be edited by ADAR. High-resolution structures showing RNA bound both in the active site, and by a dsRBD at the same time, do not currently exist. Using X-ray crystallography in conjunction with in-vitro binding and activity assays, I identified a region involved in forming a protein-protein homodimer. Mutagenesis experiments show that disruption of this interface inhibits enzymatic activity despite not being near the active site. In the future I hope to perform in-vivo studies comparing editing profiles of endogenous RNA substrates when subjected to either wild-type ADAR, or the enzyme mutant with a compromised dimer interface. If dimerization is necessary for a specific ADAR substrate, structure-guided approaches can be taken to design ADAR therapeutics by targeting the dimer interface.

***DEB Graduate Student**

T. Evaluating the Developmental Toxicity of Halogenated Pyrroles in Zebrafish

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Photo: Bianca Yaghoobi
Graduate Group: Pharmacology & Toxicology
Preceptor: Pamela Lein

Halogenated pyrroles, or halopyrroles, are one of the largest classes of halogenated alkaloids. Anthropogenic halopyrroles are increasingly detected in wastewater and drinking water. While they are currently an unregulated class of disinfection by-products, halopyrroles are generating public health concern due to their persistence in the environment, and recent findings indicating that these compounds are cytotoxic and interfere with development in worms. We recently demonstrated that anthropogenic halopyrroles dysregulate calcium dynamics in microsomes isolated from rabbit fast-twitch skeletal muscle by sensitizing ryanodine receptors (RyRs). Because of the importance of calcium signaling in vertebrate development, these observations raise the question of whether halopyrroles interfere with development in vertebrate species. To address this question, teratogenic effects and photomotor response were assessed in developing wild-type (Tropical 5D) zebrafish (*Danio rerio*) exposed to varying concentrations (0.03 μM to 30 μM) of three different halopyrroles: tetrabromopyrrole, 2,3-dibromomaleimide, and 2,3-dibromo-*N*-methylmaleimide. Zebrafish embryos were dechorionated and exposed via static waterborne exposure to halopyrroles beginning at 6 h post-fertilization through 5 days post-fertilization (dpf). Zebrafish were observed daily for gross teratological malformations and mortality. Behavioral tests were conducted at 4 and 5 dpf using the Noldus automated tracking system to assess effects of the compounds on an apical endpoint of developmental neurotoxicity. Tetrabromopyrrole and 2,3-dibromo-*N*-methlmaleimide were embryonically lethal at 1 μM and 30 μM, respectively, while 2,3-dibromomaleimide was not lethal at any concentration tested. Developmental malformations were only observed in fish exposed to tetrabromopyrrole at 0.3 μM to 1 μM. Photomotor response was significantly altered only by 2,3-dibromo-*N*-methylmaleimide, which decreased

swimming during the dark phase in a non-monotonic concentration-response related manner. Given the potential for human exposure to anthropogenic halopyrroles, these observations suggest that further evaluation of the developmental neurotoxicity of this class of compounds in vertebrate species is warranted. Supported by the NIEHS (R01 ES014901, PJL & INP).

***DEB Graduate Student**

U Production of a Plant Alkaloid in a Microbial Host

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Photo: Angela Zhang
Graduate Group: Chemistry
Preceptor: Shota Atsumi

Scopolamine is a tropane alkaloid produced by members of the nightshade plant family with broad clinical applications as a muscarinic antagonist. Extraction of this alkaloid from a plant host is a laborious and costly process, while total chemical synthesis of scopolamine is not viable on an industrial scale. This makes scopolamine an excellent candidate for production via an engineered microbial host. In this project we are exploring a chemoenzymatic synthesis in the microbial host *Escherichia coli* which overcomes the individual difficulties faced in chemical and biological reactions. Our production strategy splits the synthesis of scopolamine into two moieties: a tropane alcohol and an acyl-CoA. The tropane alcohol is biologically produced by feeding in a chemically synthesized precursor and reduction by a heterologous enzyme yielding a 70% conversion efficiency. Similarly, the acyl-CoA is synthesized from glucose assimilation into aromatic amino acid metabolic pathways and by additional reductases and CoA-ligase/transferase. Currently, we are exploring a variety of acyltransferases that can catalyze the esterification of the two moieties into an intermediate ester leading to scopolamine.

***DEB Graduate Student**

V Actin-Based Pathway for Nuclear Migration in P. Cells of C. Elegans

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Department of Molecular and Cell Biology, University of California, Davis

Jamie Ho
Graduate Group: Biochemistry, Molecular, Cellular & Developmental Biology
Preceptor: Daniel Starr

Many developmental events require cells to migrate through constricted spaces, and this process is often limited by the large and rigid nucleus. The mechanisms facilitating nuclear migration through narrow spaces are unclear. Using P. cells in *C. elegans*, we can study nuclear migration *in vivo*. P-cell nuclear migration is facilitated by the linker of the nucleoskeleton and cytoskeleton (LINC) complex, which acts as a bridge, transferring forces generated by the cytoskeleton in the cytoplasm to structures inside the nucleus. Disruption of the LINC complex in P cells leads to a temperature-sensitive nuclear migration defect. At 25°C, less than 50% of P-cell nuclei successfully migrate to a ventral position, but at 15°C, at least 90% of P-cell nuclei successfully migrate suggesting that there is a parallel nuclear migration mechanism pathway in the absence of LINC to move nuclei. Using unbiased forward-genetic screens, our lab previously identified several predicted actin regulators. I hypothesize that there is an actin-based pathway that functions independent of LINC to squeeze P-cell nuclei through constricted space. Using a conditional knockdown approach known as the auxin-inducible degradation system (AID), I propose to knockdown proteins involved in regulating actin branching such as Arx-3, Cap-2, and Cdc-42 during P-cell nuclear migration to determine if nuclear migration is affected.

***DEB Graduate Student**

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(510) 724-3260
www.tethysbio.com/index.html

Tethys Bioscience is dedicated to the discovery, development and commercialization of novel biological markers — biomarkers — that provide a practical tool to address the growing global challenge of chronic metabolic diseases such as diabetes.

By developing new tests that use protein and other bloodborne biomarkers to identify people at high risk for devastating and preventable diseases, we can arm patients and physicians with knowledge they can use to help prevent disease progression. These biomarkers give a snapshot of an individual's current risk, which may be modifiable. Our goal is to provide clinicians with an objective and convenient means to risk-stratify their patients and help them focus appropriate intervention strategies on those most likely to benefit. Our research strategies lead to sets of biomarkers that can be used to quantify the level of an individual's risk.

We approach the market with a unique combination of strengths:

- A research, management and commercialization team with extensive experience in diagnostic innovation
- Alliances with world-class researchers and partners
- A solid financial foundation

The company has become a pioneer in the discovery, development and value creation of novel biological markers for the clinical diagnostics marketplace: ***Biomarkers***. The company believes there is a large unmet need in both the discovery of potentially important biomarkers and the eventual use of them in routine clinical practice for many significant diseases.

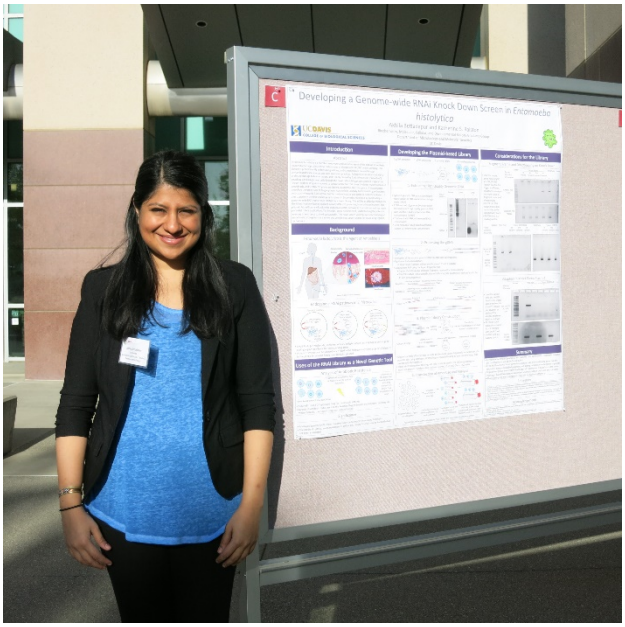
Tethys Bioscience has built expertise, created significant intellectual property, and is executing its business plan around three key areas: ***Biomarker Discovery, Clinical Validation and ValueCreation***. Tethys is focused upon introducing products that yield significant savings to the health care system and improve the quality of life for patients.

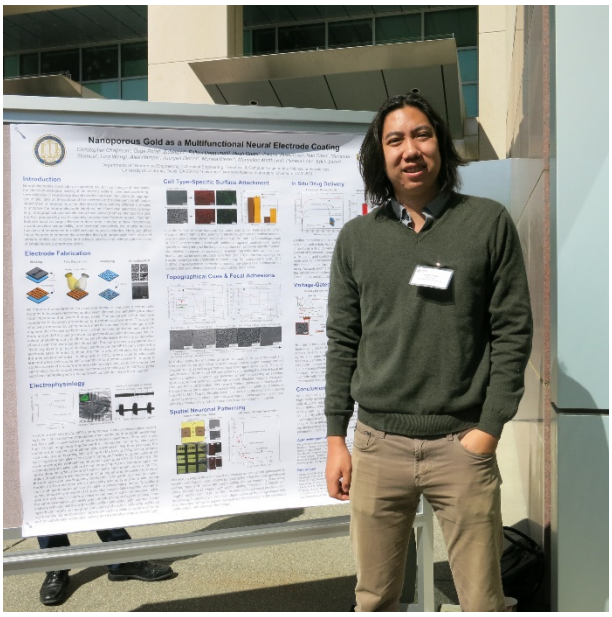
- Biomarker discovery efforts are focused on applying advanced research tools to identify important biomarkers associated with diseases that affect many people and are very costly to health care systems throughout the world today.

- Clinical validation involves a complex process that results in defining a set of new biomarkers and the application of the resulting test to enhance current clinical practice.
- Value creation encompasses the use of sophisticated health economic analyses to define appropriate performance criteria for new biomarkers and the execution of market development strategies to drive the adoption of new biomarkers in clinical practice.

UCDAVIS
Biotechnology Program

Participants





Retreat Participants

Graduate Students/Post-docs	
Rigoberto Arenas	DEB, Chemistry
Nitin Sai Beesabathuni	DEB, Chemical Engineering
Katie Beglinger	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Akhila Bettadapur	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Takeyah Campbell	DEB, Biomedical Engineering
Nkechinyere Chidi-Ogbolu	DEB, Biomedical Engineering
Amanda Dang	DEB, Materials Science and Engineering
Shea Feeney	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Sukriti Gakhar	DEB, Chemical Engineering
Anirudh Gaur	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Noah Goshi	DEB, Biomedical Engineering
Naomi Hamada	DEB, Chemical Engineering
Carly Hennessey	DEB, Molecular, Cellular and Integrative Physiology
Jamie Ho	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Jessica Huang	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Kuei-Pin Huang	DEB, Molecular, Cellular and Integrative Physiology
Luiz Irber	DEB, Computer Science
Hwoi Chan Kwon	DEB, Biophysics
Sharon Lee	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Dan Lewis	DEB, Genetics
Yulong Liu	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Linda Ma	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Korn Macharoen	DEB, Chemical Engineering
Maika Malig	DEB, Integrative Genetics and Genomics
Morgan Matson	DEB, Chemistry
Matt McNulty	DEB, Chemical Engineering
Shiaki Minami	DEB, Chemical Engineering
Rachel Olson	DEB, Integrative Genetics and Genomics
Kevin Pham	DEB, Chemistry

Anita Rajamani	DEB, Biomedical Engineering
Lalithasri Ramasubramanian	DEB, Biomedical Engineering
Shanaya Shah	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Shahin Shams	DEB, Biomedical Engineering
Linda Su-Feher	DEB, Biochemistry, Molecular, Cellular and Developmental Biology
Sara Sukenik	DEB, Biomedical Engineering
Alexander Thuy-Boun	DEB, Chemistry
Tina Truong	DEB, Immunology
Lei Wei	DEB, Microbiology
Jackie Whitehead	DEB, Biomedical Engineering
Alonna Wright	DEB, Microbiology
Yongao (Mary) Xiong	DEB, Chemical Engineering
Bianca Yaghoobi	DEB, Pharmacology and Toxicology
Angela Zhang	DEB, Chemistry
UC Davis Faculty	
Alan Bennett	DEB, Plant Sciences
Chao Chen	DEB, Pharmacology
Joanna Chiu	DEB, Entomology and Nematology
Annaliese Franz	DEB, Chemistry
Somen Nandi	DEB, Chemical Engineering
Anthony Passerini	DEB, Biomedical Engineering
Erkin Seker	DEB, Electrical and Computer Engineering
Eduardo Silva	DEB, Biomedical Engineering
Cheemeng Tan	DEB, Biomedical Engineering
Mariel Vazquez	DEB, Mathematics, Microbiology and Molecular Genetics
Industry	
Alberto Iandolino,PhD	Bayer Crop Science
Tom Turpen, PhD	SensIT
Guests	
Nancy Bulger	Executive Director Research Programs, Office of Research
Renata de Almeida Barbosa Assis, PhD	Vising Scholar, Abhaya Dandekar Lab
Judith A. Kjelstrom, PhD	Director Emerita, Biotechnology Program
Prasant Mohapatra, PhD	Vice Chancellor for Research, Office of Research
Yusuke Nakamura	Res Assoc, Biomedical Engineering, Cheemeng Tan Lab

Paulo A. Zaini, PhD	Asst Proj Scientist, Plant Sciences, Abhaya Dandekar Lab
Biotechnology Program	
Jacki Balderama	Biotechnology Program, Event Manager
Michelle Guerra	Biotechnology Program, Program Associate
Marianne Hunter	Biotechnology Program, Assistant Director Administration
Denneal Jamison-McClung	Biotechnology Program, Interim Director

UCDAVIS
Biotechnology Program

The Mission of the Biotechnology Program:

The Biotechnology Program was created in 1986 to assist in the organization of university activities related to biotechnology and to coordinate such activities with other efforts on the Davis campus. It is a central facility of the Office of Research. The Program's missions include:

- Promoting and coordinating the development of biotechnology and biotechnology - related research on the campus;
- Assisting with development of new and improved facilities for biotechnology research;
- Promoting research interactions between faculty and private industry and public agencies;
- Recommending and implementing curriculum development and training in biotechnology;
- Serving as an information and education resource on biotechnology for the campus and the public.

The Program serves as the **Administrative Home** for educational programs:

- Designated Emphasis in Biotechnology (**DEB**) graduate program
  - o http://deb.ucdavis.edu
- Advanced Degree Program (**ADP**) for corporate employees
  - o A PhD program for the working professional
- **BioTech SYSTEM** – K-14 educational consortium

Biotechnology Program Office:
Dr. Denneal Jamison-McClung – Interim Director
Marianne Hunter – Assistant Director, Administration
Jacki Balderama – Event Manager
Kelly Meade – Financial Analyst
Office location: 0301 Life Sciences
Telephone: (530) 752-3260 (main line) FAX: (530) 752-4125
Email: biotechprogram@ucdavis.edu
Website: biotech.ucdavis.edu

Designated Emphasis in Biotechnology Program (DEB)

Goals and Mission of the DEB

The Designated Emphasis in Biotechnology (DEB) is an inter-graduate group program that allows Ph.D. students to receive and be credited for training in the area of biotechnology. The DEB provides a nurturing interactive environment to promote integration of multiple disciplinary approaches to the conduct of research and to promote learning in biotechnology. The mission is to prepare well-educated students to approach problems with creativity and flexibility. The program will provide tools for the students to be leaders, visionaries, entrepreneurs, researchers and teachers in the broad area of biomolecular technology.

DEB Mission:

- To provide well-coordinated, cross-disciplinary training of graduate students in critical areas of biomolecular technology research.
- To promote interdisciplinary research environments that integrate basic biological science, engineering and computational disciplines.
- To allow cross-disciplinary training and trainee experience in a biotechnology company or cross-college laboratory.

Students come from a wide array of disciplines: Participating graduate programs currently include **29 programs**: Agricultural & Environmental Chemistry; Animal Biology; Applied Science Engineering; Biochemistry, Molecular, Cellular & Developmental Biology; Biological Systems Engineering; Biomedical Engineering; Biophysics; Chemistry; Chemical Engineering; Civil & Environmental Engineering; Comparative Pathology; Computer Science, Electrical & Computer Engineering; Entomology; Food Science Technology; Genetics; Immunology; Materials Science & Engineering; Mechanical & Aeronautical Engineering; Microbiology; Molecular, Cellular and Integrative Physiology; Neurosciences; Nutritional Biology; Pharmacology and Toxicology; Plant Biology; Plant Pathology; Soils & Biogeochemistry; and Statistics. The DEB program supplements a student's Ph.D. curriculum and those completing the program will obtain an official designation on their diploma & transcript indicating a qualification in biotechnology. Example: **Doctoral Degree in Microbiology with a Designated Emphasis in Biotechnology**

Brief History:

The DEB was formally established in 1997 as an outgrowth of the first NIH Training Grant in Biotechnology (funded in the early 1990s). The DEB became the formal training program for the current NIH Training Grant in Biomolecular Technology (1-T32-GM08799: July 1, 2002-June 30, 2017). The DEB provides a very effective multidisciplinary biotechnology concentration, which includes exposure to bioethics, business and legal aspects of biotechnology as well as a 3-6 month internship in a biotechnology company or research laboratory in another college or national laboratory. As of 2012, the DEB has 29 affiliated graduate groups or departmentally based graduate programs. The number of students in the Designated Emphasis in Biotechnology has increased dramatically over the last several years with many being first year students. We have graduated 303 students with a DEB notation on their diplomas as of 2016.

Program Administration:

The administrative home for the DEB is the UC Davis Biotechnology Program. Dr. Denneal Jamison-McClung serves as the DEB Program Coordinator for the DEB, in addition to directing the Biotechnology Program. She works closely with the DEB chair, Abhaya Dandekar (Department of Plant Sciences) and the rest of the executive committee: Shota Atsumi (Chemistry) and David Rocke (Applied Science/Biostatistics) to oversee the day-to-day activities of the graduate program.

Course Work:

The DEB has a required core curriculum for students regardless of whether their graduate major is in biological science, engineering, statistics, etc. A key feature of the DEB is its requirement for a research internship at a cooperating biotechnology company or a cross-college site. When the students complete their Ph.D. requirements as well as the DEB requirements, their diploma notes not only their graduate major, but also that they have completed the DEB (e.g., "Ph.D. in Chemical Engineering with a Designated Emphasis in Biotechnology").

We have created a website for the Designated Emphasis in Biotechnology (deb.ucdavis.edu/) to advertise the program.

1. Course Requirements:

a. **DEB 263** (2 units): Biotechnology Fundamentals and Application (winter quarter, alternate odd numbered years)

An interdisciplinary course which includes: introduction to modern recombinant DNA technology; rate processes of biological systems, optimization of bioreactor performance; practical issues in biotechnology; and some specific case studies of the development of biotechnology products and processes. Grading: Letter grade; two one-hour exams, one research paper (team project) on a selected topic relevant to biotechnology, and regular reading assignments.

b. **DEB 282** (variable): Biotechnology Internship (may be done any quarter)

The internship will expose qualified graduate students to research activities in a biotechnology company, to company culture, to legal and business aspects of industry, and to another career option. A minimum of 3 months internship at a local biotechnology company or cross college or national

laboratory (i.e. Lawrence Berkeley Laboratory, Lawrence Livermore National Laboratory, etc.). S/U grading; research performance (student report) will be evaluated by the professor in charge and in consultation with the company trainer.

c. **DEB/ECH 294** (1 unit): Current Progress in Biotechnology (fall, winter and spring quarters). Three quarters of seminar are required for the DEB Program.

This course is an interdisciplinary seminar, featuring speakers from industry as well as academia. The students will have an opportunity to discuss the seminar topic with the lecturers, to learn about biotechnology research activities at companies and to network with speaker. Grading: S/U grading, attendance is required, and a summary report on the seminars is required at the end of the quarter.

d. **MIC 292** (1 unit): From Discovery to Product - An Introduction to Biotechnology at the Industrial Level. (winter quarter; even numbered years). MIC 292 is an approved **seminar elective** for the DEB program (may substitute for one quarter of DEB/ECH 294).

This course is designed to provide a unique opportunity to gain insight into basic and applied biotechnology at the industrial level. Lectures are presented by senior scientists from Novozymes Biotech, Inc. in Davis California (www.novozymes.com). A tour of the industrial facilities will be arranged. Grading: S/U grading, attendance is required, and a summary report on the seminars is required at the end of the quarter.

e. **GGG 296** (2 units): Scientific Professionalism and Integrity (fall quarter) or approved bioethics course.

The course will allow the student to become familiar with their roles and responsibilities as a professional scientist and/or instructor. While some standards of acceptable scientific behavior will be presented in class, most of the time will be spent discussing various "gray zone" scenarios, in which proper conduct is unclear. Grading: S/U grading; active class participation in class discussions is required. **This course is currently highly recommended, but will be required, pending approval.**

2. **Qualifying Exam Requirements**:

The Ph.D. qualifying exam should demonstrate appropriate knowledge with the area of biotechnology. At least one faculty member of the designated emphasis shall participate in the qualifying examination.

3. **Thesis Requirements**:

The dissertation committee shall include at least one faculty member of the designated emphasis. The major professor must be a participating DEB member.

4. **Additional Requirements**:

Regular attendance at the annual Biotechnology Training retreat and at the informal Pizza Chalk Talk Seminars (talks by students and faculty on current research) is expected.

DEB Program Students as of March 2019

NAME	GRADUATE GROUP/PROGRAM
Betsy Alford	Plant Pathology
Chidera Alim	Molecular, Cellular and Integrative Physiology
Riley Allen	Biomedical Engineering
Dexter Antonio	Chemical Engineering
Benjamin Arbaugh	Biological Systems Engineering
Rigoberto Arenas	Chemistry
Eric Arreola	Biochemistry, Molecular, Cellular & Developmental Biology
Sima Asadi	Chemical Engineering
Krithi Bala	Integrative Genetics & Genomics
DJ Darwin Bandoy	Integrative Pathobiology
Jed Bassein	Immunology
Nitin Sai Beesabathuni	Chemical Engineering
Katherine Beglinger	Biochemistry, Molecular, Cellular & Developmental Biology
Cody Bekkering	Plant Biology
Zachary Bendiks	Microbiology
Anastasia Berg	Biochemistry, Molecular, Cellular & Developmental Biology
Akhila Bettadapur	Biochemistry, Molecular, Cellular & Developmental Biology
Amirhossain Bolandparvaz	Biomedical Engineering
Stephen Bolus	Plant Pathology
Hannah Brinkman	Chemistry
Glory Bui	Microbiology
Tawni Bull (Middleton)	Horticulture and Agronomy
Jonas Calsbeek	Pharmacology and Toxicology
Takeyah Campbell	Biomedical Engineering
Austin Carroll	Chemistry
Alena Casella	Biomedical Engineering
Nkechinyere Chidi-Ogbolu	Biomedical Engineering
Angel Cobo	Chemistry
Nicole Coggins	Molecular, Cellular & Integrative Physiology
Savannah Conlon	Chemistry
Morgan Connolly	Microbiology
Luis Eduardo Contreras Llano	Biochemistry, Molecular, Cellular & Developmental Biolog
Elli Cryan	Plant Biology
Amanda Dang	Materials Science and Engineering
Rachel Danielson	Soils & Biogeochemistry
Destiny Davis	Plant Biology
Marcus Deloney	Biomedical Engineering

Pamela Denish	Biophysics
Claire Depew	Immunology
Nithin Dhananjayan	Biophysics
Erin Doherty	Chemistry
Cintia Helena Duarte Sagawa	Plant Biology
Ameen Eetemadi	Computer Science
Shiva Emami	Food Science
Shea Feeney	Biochemistry, Molecular, Cellular & Developmental Biology
Michael Fong	Biomedical engineering
Sukriti Gakhar	Chemical Engineering
Javier Garcia	Biochemistry, Molecular, Cellular & Developmental Biology
Anirudh Gaur	Biochemistry, Molecular, Cellular & Developmental Biology
Donald Gibson	Integrative Genetics & Genomics
Deepshika Gilbile	Chemical Engineering
Dayn Godinez	Pharmacology & Toxicology
Jake Gonzales	Chemistry
Eduardo Gonzalez	Pharmacology & Toxicology
Noah Goshi	Biomedical Engineering
Mona Gouran	Plant Biology
Charles Graddy	Microbiology
Herra Grajo	Chemistry
Brittany Greenwood (nee-Blankenship)	Microbiology
Benjamin Groth	Microbiology
Angelica Guercio	Integrative Genetics and Genomics
Amanda Guevara	Molecular, Cellular and Integrative Physiology
Orangel Gutierrez	Integrative Genetics & Genomics
Naomi Hamada	Chemical Engineering
Cameron Hatch	Plant Biology
Dustin Heeney	Microbiology
Britta Heiss	Microbiology
Carly Hennessey	Molecular, Cellular and Integrative Physiology
Shawn Higdon	Plant Biology
Alex Hitomi	Biological Systems Engineering
Jamie Ho	Biochemistry, Molecular, Cellular & Developmental Biology
Kayla Horton (Sparks)	Pharmacology and Toxicology
Allison Hsia	Biomedical Engineering
Michelle Hu	Pharmacology and Toxicology
Jessica Huang	Biochemistry, Molecular, Cellular & Developmental Biology
Kuei-Pin Huang	Molecular, Cellular and Integrative Physiology
Alexandria Igwe	Microbiology
Luiz Carlos Irber Jr	Computer Science
Casey Jacobsen	Chemistry

Daisy Johnson	Microbiology
Lisa Johnson (nee Cohen)	Molecular, Cellular and Integrative Physiology
Shannon Joslin	Integrative Genetics & Genomics
Agya Karki	Chemistry
Prema Karunanithi	Biochemistry, Molecular, Cellular & Developmental Biology
Ryan Kawakita	Biological Systems Engineering
Cindy Khuu	Biochemistry, Molecular, Cellular and Developmental Biology
Hyunsoo Gloria Kim (nee Jin)	Microbiology
Sophie Kiss	Pharmacology & Toxicology
Hwoi Chan Kwon	Biophysics
Vu Lam	Entomology
Mirko Ledda	Integrative Genetics and Genomics
Sharon Lee	Biochemistry, Molecular, Cellular & Developmental Biology
Kyle Lewald	Integrative Genetics and Genomics
Daniel Lewis	Integrative Genetics & Genomics
Johnathon Li	Animal Biology
Riyao Li	Chemistry
Jonathan Lin	Microbiology
Yulong Liu	Biochemistry, Molecular, Cellular & Developmental Biology
Zhongrui Liu	Chemical Engineering
Rachel Lombardi	Food Science
Simon (goes by Jesse) Lopez	Integrative Genetics & Genomics
Elizabeth Lotsof	Chemistry
Mikaela Louie	Biochemistry, Molecular, Cellular & Developmental Biology
Yixing Lu	Food Science
Shan Lu	Molecular, Cellular & Integrative Physiology
Linda Ma	Biochemistry, Molecular, Cellular & Developmental Biology
Kantharakorn Macharoen	Chemical Engineering
Chandrima Majumdar	Chemistry
Maika Malig	Integrative Genetics and Genomics
Kasey Markel	Plant Biology
Lauren Matelski	Immunology
Morgan Matson	Chemistry
Lucas McKinnon	Plant Biology
Matthew McNulty	Chemical Engineering
Nathan Meier	Plant Biology
Beatriz Merchel Piovesan Pereira	Microbiology
David Merriam	Microbiology
Shiaki Minami	Chemical Engineering
Jessica Mizzi	Microbiology
Leanna Monteleone	Chemistry

Charles Mordaunt	Biochemistry, Molecular, Cellular & Developmental Biology
Oscar Munoz	Pharmacology & Toxicology
Katherine Murphy	Plant Biology
Kaitlin Murray	Molecular, Cellular and Integrative Physiology
Livingstone Nganga	Plant Biology
Alan Nguyen	Immunology
Jared Nigg	Microbiology
Jennifer Nill	Chemical Engineering
Glyn Noguchi	Biochemistry, Molecular, Cellular & Developmental Biology
Saghi Nojoomi	Molecular, Cellular and Integrative Physiology
Ryan North	Biomedical Engineering
Sarah Odell	Plant Biology
Rachel Olson	Integrative Genetics & Genomics
Noah Pacifici	Biomedical Engineering
SeHee Park	Chemistry
Beau Parry	Microbiology
Sichong Peng	Integrative Genetics & Genomics
Hannah Petrek	Biochemistry, Molecular, Cellular & Developmental Biology
Kevin Pham	Chemistry
Marc Pollack	Microbiology
Anita Rajamani	Biomedical Engineering
Mythili Ramachandran	Pharmacology and Toxicology
Lalithasri Ramasubramanian	Biomedical Engineering
Jamie Randol	Integrative Genetics and Genomics
Niknaz Riazati	Molecular, Cellular and Integrative Physiology
Guy Robinson	Plant Biology
Zachary Rollins	Chemical Engineering
Gabrielle Rossidivito	Plant Biology
Peter Sariano	Biomedical Engineering
Jordan Sayre	Microbiology
Rebecka Sepela	Biochemistry, Molecular, Cellular & Developmental Biology
Shanaya Shah	Biochemistry, Molecular, Cellular & Developmental Biology
Shahin Shams	Biomedical Engineering
Kyle Shankle	Plant Biology
Masuda Sharifi	Biochemistry, Molecular, Cellular & Developmental Biology
Claire Shaw	Animal Biology
Noah Siegel	Immunology
David Silberstein	Chemical Engineering
Rosalie Sinclair	Plant Biology
Daniel Steele	Plant Biology
Eric Stevens	Microbiology
Robert Stewart	Biochemistry, Molecular, Cellular & Developmental Biology
Robert Stolz	Integrative Genetics & Genomics

Linda Su-Feher	Biochemistry, Molecular, Cellular & Developmental Biology
Sara Sukenik	Biomedical Engineering
Rasheed Sule	Biochemistry, Molecular, Cellular & Developmental Biology
Rene Suleiman	Microbiology
Alireza (Ali) Tafazzol	Biomedical Engineering
Srinivas Tapa	Biomedical Engineering
Victoria Thai	Biomedical Engineering
Alexander Thuy-Boun	Chemistry
Tanner Treece	Chemistry
Tina Truong	Medical Microbiology and Immunology
Robert Van Ostrand	Chemistry
Kacey VanderVorst	Biochemistry and Molecular Medicine
Sana Vaziri	Computer Science
Gregory Walker	Microbiology
Marilyn Wang	Immunology
Yaxin Wang	Plant Biology
Lei Wei	Microbiology
Anita Wen	Pharmacology and Toxicology
Taylor Westmont	Immunology
Jacklyn Whitehead	Biomedical Engineering
Alonna Wright	Microbiology
Sydney Wyatt	Integrative Genetics and Genomics
Yongao (Mary) Xiong	Chemical Engineering
Ariga Bianca Yaghoobi	Pharmacology & Toxicology
Phoebe Yam	Integrative Genetics & Genomics
Xiaoxiao Yang	Chemistry
Kevin Yates	Chemical Engineering
Britt Yazel	Neurosciences
Cody Watson Yothers	Chemistry
Kelly Zacanti	Animal Biology
Marwa Zafarullah	Integrative Genetics and Genomics
Yue (Tiffany) Zhang	Chemistry
Angela Zhang	Chemistry
Yihui Zhu	Integrative Genetics and Genomics
Danielle Zumpano	Molecular, Cellular and Integrative Physiology

DEB Faculty Trainers as of March 2019

Venkatesh Akella	Electrical and Computer Engineering
John Albeck	Molecular and Cellular Biology
Rajeevan Amirtharajah	Electrical and Computer Enginering
Paul Ashwood	Medical Microbiology and Immunology, School of Medicine
Shota Atsumi	Chemistry
Matthew Augustine	Chemistry
Sharon Aviran	Biomedical Engineering
Keith Baar	Neurobiology, Physiology and Behavior, Physiology and Membrane Biology, School of Medicine
Alan Balch	Chemistry
Enoch Baldwin	Molecular and Cellular Biology Chemistry
Daniela Barile	Food Science and Technology
Nicole Baumgarth	Center for Comparative Medicine, Pathology, Microbiology and Immunology, School of Veterinary Medicine
Andreas Baumler	Medical Microbiology and Immunology, School of Medicine
Peter Beal	Chemistry
Laurel Beckett	Public Health Sciences
Craig Benham	Mathematics, Biomedical Engineering
Alan Bennett	Plant Sciences, College of Agricultural and Environmental Sciences
Trish Berger	Animal Science
Don Bers	Pharmacology, School of Medicine
Charles L. Bevins	Medical Microbiology and Immunology, School of Medicine
David Block	Viticulture and Enology, Chemical Engineering
Eduardo Blumwald	Plant Sciences, College of Agricultural and Environmental Sciences
Laura Borodinsky	Physiology and Membrane Biology, School of Medicine, Institute for Pediatric Regenerative Medicine
Alexander (Sandy) Borowsky	Pathology and Laboratory Medicine
Julie Bossuyt	Pharmacology, School of Medicine
Richard Bostock	Plant Pathology

Kent Bradford	Plant Sciences, College of Agricultural and Environmental Sciences
Siobhan Brady	Plant Biology, Genome Center
Anne Britt	Plant Biology
Titus Brown	Genome Center, Population Health and Reproduction, School of Veterinary Medicine, Coastal and Marine Sciences Institute
Sean Burgess	Molecular and Cellular Biology
Judy Callis	Molecular and Cellular Biology
Kermit Carraway	Biochemistry and Molecular Medicine, School of Medicine
Luis Carvajal-Carmona	Biochemistry and Molecular Medicine, School of Medicine, Genome Center
Clare Casteel	Plant Pathology
Frederic Chedin	Molecular and Cellular Biology, Genome Center
Xi Chen	Chemistry
Tsung-Yu Chen	Neurology, School of Medicine, Center for Neuroscience
Xinbin Chen	Surgical and Radiological Sciences, School of Veterinary Medicine, Internal Medicine, School of Medicine
Hongwu Chen	Biochemistry and Molecular Medicine, School of Medicine
Chao-Yin Chen	Pharmacology, School of Medicine
Holland Cheng	Molecular and Cellular Biology
Simon Cherry	Biomedical Engineering
Nipavan Chiamvimonvat	Internal Medicine (Cardiology), School of Medicine
Joanna Chiu	Entomology and and Nematology, College of Agricultural and Environmental Sciences
Blaine Christiansen	Orthopaedic Surgery
Gitta Coaker	Plant Pathology, College of Agricultural and Environmental Sciences
Luca Comai	Genome Center, Plant Biology
Douglas Cook	Plant Pathology, College of Agricultural and Environmental Sciences
Gino Cortopassi	Molecular Biosciences, School of Veterinary Medicine
Stephen Cramer	Chemistry
Abhaya Dandekar	Plant Sciences, College of Agricultural and Environmental Sciences
Satya Dandekar	Medical Microbiology and Immunology, School of Medicine
Sheila David	Chemistry
Cristina Davis	Mechanical and Aeronautical Engineering
Scott Dawson	Microbiology and Molecular Genetics

Wenbin Deng	Biochemistry and Molecular Medicine, School of Medicine
Megan Dennis	Biochemistry and Molecular Medicine, School of Medicine, Genome Center, MIND Institute
Elva Diaz	Pharmacology, School of Medicine
Savithramma Dinesh-Kamur	Plant Biology Plant Biology, Genome Center Genome Center
Zhi Ding	Electrical and Computer Engineering
Georgia Drakakaki	Plant Sciences, College of Agricultural and Environmental Sciences
Jason Eiserich	Internal Medicine (Nephrology), School of Medicine, Physiology and Membrane Biology, School of Medicine
Nael El-Farra	Chemical Engineering
JoAnne Engebrecht	Molecular and Cellular Biology
Marc Facciotti	Biomedical Engineering
Bryce Falk	Plant Pathology
Roland Faller	Chemical Engineering
Zhiliang (Julia) Fan	Biological and Agricultural Engineering
Oliver Fiehn	Genome Center, Molecular and Cellular Biology
Vladimir Filkov	Computer Science
Carrie Finno	Population Health & Reproduction
Andrew Fisher	Molecular and Cellular Biology, Chemistry
Paul Fitzgerald	Cell Biology and Human Anatomy, School of Medicine
Annaliese Franz	Chemistry
Christopher Fraser	Molecular and Cellular Biology
David Furlow	Neurobiology, Physiology, and Behavior
Melanie Gareau	Anatomy, Physiology and Cell Biology, School of Veterinary Medicine
Angie Gelli	Pharmacology, School of Medicine
Damian Genetos	Anatomy, Physiology and Cell Biology, School of Veterinary Medicine
Steven George	Biomedical Engineering
Paul Gepts	Plant Sciences, College of Agricultural and Environmental Sciences
J. Bruce German	Food Science and Technology
Jacquelyn Gervay-Hague	Chemistry
Soheil Ghiasi	Electrical and Computer Engineering
Paramita Ghosh	Biochemistry and Molecular Medicine, School of Medicine, Department of Urology, School of Medicine
Mark Goldman	Neurobiology, Physiology and Behavior, Center for Neuroscience
Aldrin Gomes	Neurobiology,Physiology & Behavior and Physiology & Membrane Biology, School of Medicine

Tom Gradziel	Plant Sciences, College of Agricultural and Environmental Sciences
Eleonora Grandi	Pharmacology, School of Medicine
Jeffrey Gregg	Pathology and Laboratory Medicine
Ting Guo	Chemistry
Paul Hagerman	Biochemistry and Molecular Medicine, School of Medicine
Fawaz Haj	Nutrition
Bruce Hammock	Comprehensive Cancer Center
Stacey Harmer	Plant Biology
Dennis Hartigan-O'Connor	Medical Microbiology and Immunology, School of Medicine
Dominik Haudenschild	Orthopaedic Surgery, School of Medicine,
Volkmar Heinrich	Biomedical Engineering
Johannes Hell	Pharmacology, School of Medicine
Paul Henderson	Hematology/Oncology, Internal Medicine
Matthias Hess	Animal Science
Wolf-Dietrich Heyer	Microbiology and Molecular Genetics
Fereydoun Hormozdiari	Genome Center, MIND Institute, Biochemistry and Molecular Medicine, School of Medicine
David Horsley	Mechanical and Aerospace Engineering
You-Lo Hsieh	Textiles and Clothing
Mark Huising	Physiology and Membrane Biology, School of Medicine, Neurobiology, Physiology and Behavior
Neil Hunter	Microbiology and Molecular Genetics, Cell Biology and Human Anatomy, School of Medicine
M. Saif Islam	Electrical and Computer Engineering
Roslyn-Rivkah Isseroff	Dermatology
Tina Jeoh	Biological and Agricultural Engineering
Wilsaan Joiner	Neurobiology, Physiology and Behavior & Dept. of Neurology, School of Med
Thomas Jue	Biochemistry and Molecular Medicine, School of Medicine
Linda Katehi	Electrical & Computer Engineering
Carl Keen	Nutrition
Darshan Kelley	Nutrition, USDA ARS Western Human Nutrition Research Center
Rick Kiehl	Electrical and Computer Engineering
Dan Kliebenstein	Plant Sciences, College of Agricultural and Environmental Sciences, Center for Population Biology, Genome Center
Paul Knoepfler	Cell Biology and Human Anatomy, School of Medicine, Genome Center

Anne Knowlton	Internal Medicine (Cardiology), School of Medicine, Pharmacology, School of Medicine
Patrice Koehl	Computer Science, Genome Center
Ian Korf	Molecular and Cellular Biology, Genome Center
Dietmar Kueltz	Animal Science
Tonya Kuhl	Chemical Engineering
Hsing-Jien Kung	Biological Chemistry and Molecular Medicine, School of Medicine
Anna La Torre	Cell Biology and Human Anatomy, School of Medicine
J. Clark Lagarias	Molecular and Cellular Biology
Kit Lam	Biochemistry and Molecular Medicine, School of Medicine
Donald Land	Chemistry
Delmar Larsen	Chemistry
Janine LaSalle	Medical Microbiology and Immunology, School of Medicine, Genome Center, MIND Institute
Jerold Last	Internal Medicine, Pulmonary and Critical Care, School of Medicine
Kent Leach	Biomedical Engineering
Carlito Lebrilla	Chemistry
Pamela Lein	Molecular Biosciences, Veterinary Medicine
Harris Lewin	Genome Center, Evolution and Ecology
Jamal Lewis	Biomedical Engineering
Su-Ju Lin	Microbiology and Molecular Genetics
Bo Liu	Plant Biology
Gang-yu Liu	Chemistry
Marjorie Longo	Chemical Engineering
Angelique Louie	Biomedical Engineering
Paul Luciw	Pathology and Laboratory Medicine, Center for Comparative Medicine
Neville C Luhmann, Jr.	Electrical and Computer Engineering
Elizabeth Maga	Animal Science
Maria Marco	Food Science and Technology
Laura Marcu	Biomedical Engineering
Verónica Martínez Cerdeño	Pathology and Laboratory Medicine, School of Medicine
Karen McDonald	Chemical Engineering
Richard J. McKenney	Molecular and Cellular Biology
Frank McNally	Molecular and Cellular Biology
John McPherson	Biochemistry and Molecular Medicine, School of Medicine

Stephen McSorley	Anatomy, Physiology & Cell Biology, Center for Comparative Medicine
Juan Medrano	Animal Science, College of Agricultural and Environmental Sciences
Maeli Melotto	Plant Sciences
Richard Michelmore	Genome Center, Molecular and Cellular Biology, Medical Microbiology and Immunology, School of Medicine, Plant Sciences, College of Agricultural and Environmental Sciences
Michael Mienaltowski	Animal Science
Lee Miller	Neurobiology, Physiology and Behavior, Center for Mind and Brain
Lisa Miller	Anatomy, Physiology and Cell Biology, School of Veterinary Medicine
David Mills	Food Science and Technology
Maria Mudryj	Medical Microbiology and Immunology, School of Medicine
William J. Murphy	Dermatology, Internal Medicine (Hematology/Oncology)
James Murray	Animal Science, College of Agricultural and Environmental Sciences
Florence Negre-Zakharov	Plant Sciences, College of Agricultural and Environmental Sciences
Douglas Nelson	Microbiology and Molecular Genetics, Coastal and Marine Sciences Institute
John Newman	Nutrition, USDA ARS Western Human Nutrition Research Center
Nitin Nitin	Biological and Agricultural Engineering
Stephen Noctor	Psychiatry and Behavioral Sciences, School of Medicine
Jan Nolta	Cell Biology and Human Anatomy, School of Medicine
Alex Nord	Neurobiology, Physiology and Behavior, Center for Neuroscience, Genome Center, Psychiatry and Behavioral Sciences, School of Medicine
Jodi Nunnari	Molecular and Cellular Biology
Anita Oberbauer	Animal Science
Martha O'Donnell	Physiology and Membrane Biology, School of Medicine
Tingrui Pan	Biomedical Engineering
Alyssa Panitch	Biomedical Engineering
Rebecca Parales	Microbiology and Molecular Genetics
Atul Parikh	Biomedical Engineering
Anthony Passerini	Biomedical Engineering
Isaac Pessah	Molecular Biosciences, School of Veterinary Medicine
Ronald Phillips	Chemical Engineering

Kent Pinkerton	Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, Pediatrics, School of Medicine
David Pleasure	Neurology and Pediatrics, School of Medicine
Robert Powell	Chemical Engineering
Martin Privalsky	Microbiology and Molecular Genetics
Jinyi Qi	Biomedical Engineering
Gerald Quon	Molecular and Cellular Biology, Genome Center, Comprehensive Cancer Center
Katherine Ralston	Microbiology and Molecular Genetics
Katherine Rauen	Pediatrics
Helen Raybould	Anatomy, Physiology and Cell Biology, School of Veterinary Medicine
Alexander Revzin	Biomedical Engineering
Crystal Ripplinger	Pharmacology
Subhash Risbud	Materials Science and Engineering
William Ristenpart	Chemical Engineering
David Rocke	Biomedical Engineering
Jorge Rodrigues	Land, Air and Water Resources
Ray Rodriguez	Molecular and Cellular Biology
Pamela Ronald	Plant Pathology, College of Agricultural and Environmental Sciences, Genome Center
Alan Rose	Molecular and Cellular Biology
Lesilee Rose	Molecular and Cellular Biology
Pablo Ross	Animal Science
Jeffrey Ross-Ibarra	Plant Sciences, College of Agricultural and Environmental Sciences
John Rutledge	Cardiology/Cardiovascular Medicine, Internal Medicine
Jon Sack	Physiology and Membrane Biology, School of Medicine, Anesthesiology and Pain Medicine, School of Medicine
Earl Sawai	Pathology, Microbiology and Immunology, School of Veterinary Medicine
Kate Scow	Land, Air and Water Resources
David Segal	Genome Center, Biochemistry and Molecular Medicine, School of Medicine, UC Davis MIND Institute, Pharmacology
Erkin Şeker	Electrical and Computer Engineering
Barbara Shacklett	Medical Microbiology and Immunology, School of Medicine
Priya Shah	Microbiology and Molecular Genetics, Chemical Engineering, College of Engineering
Frank Sharp	Neurology, School of Medicine, UC Davis MIND Institute

Justin Siegel	Biochemistry and Molecular Medicine, School of Medicine, Genome Center, Chemistry
Eduardo Silva	Biomedical Engineering
Christopher Simmons	Food Science and Technology
Sergi Simó	Cell Biology and Human Anatomy, School of Medicine
Scott Simon	Biomedical Engineering
Neelima Sinha	Plant Biology
David Slaughter	Biological and Agricultural Engineering
Carolyn Slupsky	Nutrition
Athena Soulika	Dermatology
Daniel Starr	Molecular and Cellular Biology
Francene Steinberg	Nutrition
Ioannis Steriopoulos	Plant Pathology
Pieter Stroeve	Chemical Engineering
Alexei Stuchebrukhov	Chemistry
Dawn Y. Sumner	Earth and Planetary Sciences
Gang Sun	Textiles and Clothing
Ilias Tagkopoulos	Computer Science
Cheemeng Tan	Biomedical Engineering
Dean Tantillo	Chemistry
Alice Tarantal	Pediatrics, School of Medicine, Cell Biology and Human Anatomy, School of Medicine, California National Primate Research Center
Flora Tassone	Biochemistry and Molecular Medicine, School of Medicine
Steven Theg	Plant Biology
Li Tian	Plant Sciences, College of Agricultural and Environmental Sciences
Michael Toney	Chemistry
Jose Torres	Medical Microbiology and Immunology
Renee Tsolis	Medical Microbiology and Immunology, School of Medicine
Richard Tucker	Cell Biology and Human Anatomy, School of Medicine
Judy Van de Water	UC Davis Center for Children's Environmental Health, Internal Medicine, School of Medicine
Alison Van Eenennaam	Animal Science
Marta Van Loan	Nutrition
Jean VanderGheynst	Biological and Agricultural Engineering
Rachel Lee Vannette	Entomology and Nematology
Mariel Vazquez	Microbiology and Molecular Genetics
John Voss	Biochemistry and Molecular Medicine, School of Medicine

Bart Weimer	Population Health & Reproduction, Veterinary Medicine
Robert H. Weiss	Internal Medicine (Nephrology), School of Medicine
Valerie Williamson	Entomology and Nematology
David Wilson	Molecular and Cellular Biology
Matthew J. Wood	Environmental Toxicology
Reen Wu	Internal Medicine, Pulmonary and Critical Care
Stefan Wuertz	Civil and Environmental Engineering
Heike Wulff	Pharmacology, School of Medicine
Kevin Xiang	Pharmacology, School of Medicine
Lifeng Xu	Microbiology and Molecular Genetics
Soichiro Yamada	Biomedical Engineering
John Yoder	Plant Sciences, College of Agricultural and Environmental Sciences
Glenn Young	Food Science and Technology
Aiming Yu	Biochemistry and Molecular Medicine, School of Medicine
Philipp Zerbe	Plant Biology
Ruihong Zhang	Biological and Agricultural Engineering

The Value of Internships

Over the last 20 years (even before the formal DEB program was established), we have placed pre-doctoral students in a variety of biotechnology companies for their industrial research experience. They include:

Advanced Micro Devices (AMD)
Agilent Technologies
AgraQuest (a Bayer company)
Alza
Amgen
Amyris
Antibodies, Inc.
Aqua Bounty
Bayer
Berlex Biosciences
BioMarin Pharmaceuticals, Inc.
Carollo
Celera AgGen
Cytokinetics
DuPont
Exelixis
Expression Systems
Genencor
Genentech
Hoffmann Eitle
ICOS
Igenica
Institut Charles Sadron
Marone Bio Innovations
Maxygen
Novartis (formerly Chiron)
Novozymes
Nunhems
OncoMed
Scios
Somagenics
Syntex

Recovery Sciences
Roche Biosciences
Sutro Biopharma
State Water Control Resources Board
Tethys Bioscience, Inc.
Unilever
Ventria Biosciences
and others

Industry Partners gain many things from internships:

- Access to highly talented creative researchers
- Opportunity to gain inside track on future employees
- Through students, further collaboration with scientists on campus
- Participate in the annual retreat to meet UC scientists students, potential interns, other company scientists
- Potential to use UC facilities through the collaboration
- Opportunity to participate in weekly campus seminars

Students gain much from internships:

- Ability to work in a highly creative non-academic environment
- Opportunity to participate in focused team approach to defined research goals
- Ability to use equipment and facilities not available on campus
- Discover the type of environment, which suits future career goals
- Participate in industry seminars
- Enhanced curriculum vitae: reference letters and new skills
- Access to potential employment opportunities

Currently, there are ~220 students enrolled, so we need more Academic-Industry Partnerships.