31st Keck Annual Research Conference: Infectious Diseases: Emerging Threats and Emerging Technologies

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October 22, 2021

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The Keck Center and Gulf Coast Consortia for Quantitative Biomedical Sciences

The Keck Center

The Keck Center, established in 1990 with support from the W. M. Keck Foundation, celebrates its 31st year of supporting predoctoral and postdoctoral trainees and their mentors. From the founding institutions, Baylor College of Medicine and Rice University, the Keck Center grew in its first 10 years to six major public and private institutions in the Houston/Galveston area, including University of Houston, The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, and The University of Texas MD Anderson Cancer Center. The Institute of Biosciences and Technology of Texas A&M Health Science Center joined in 2015. Guiding the formation of this collaboration was the realization that significant advances in the biological sciences, such as the DNA sequencing of the human genome, would be driven by the integration of biology and computer science. The partners realized, however, that most biological scientists were not prepared to capitalize on novel approaches to visualization, analysis and interpretation of experimental data made possible by rapid advances in computing technology. Moreover, most researchers in computer programming and analysis systems did not have adequate knowledge about biology and biological systems. The Keck Center was explicitly designed to bridge this gap between biological and computational sciences by fostering collaborations among scientists through specially designed research and training programs.

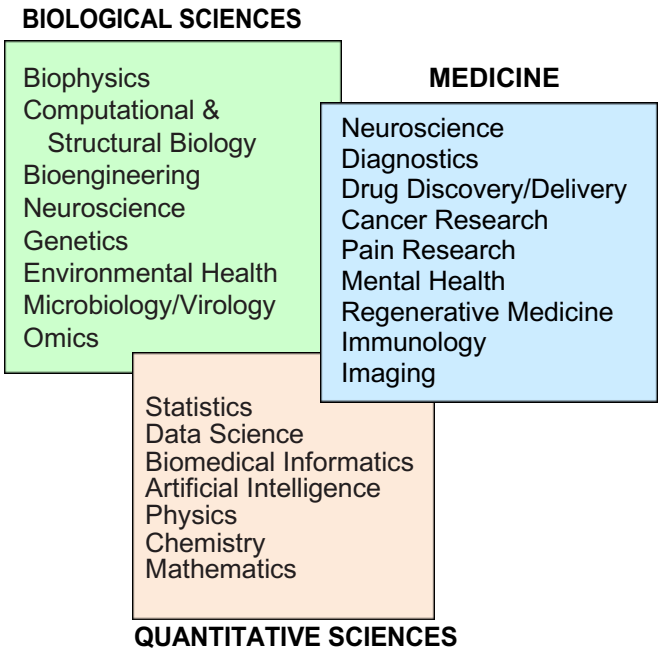
Building on its expertise in interdisciplinary, inter-institutional programs, the Keck Center's focus has evolved to the quantitative biomedical sciences. Participants are drawn from various disciplines such as biophysics, chemistry, bioengineering, neuroscience, computer science, biochemistry, genetics, physics, mathematics, data science, biomedical informatics, environmental health, biology and statistics. Currently, the Keck Center administers training programs in biomedical informatics and data science, molecular biophysics, pharmacological sciences, computational cancer biology, precision environmental health, antimicrobial resistance, cancer therapeutics, and infectious diseases.

Gulf Coast Consortia

In March 2001, the presidents of each of the six founding member institutions of the Keck Center signed an unprecedented agreement establishing the Gulf Coast Consortia (GCC), explicitly designed to coalesce institutional strengths in order to:

1. train new scientists at the intersection of biological sciences with quantitative and physical sciences
2. build cutting-edge research infrastructure and facilities
3. cultivate a supportive atmosphere for the collaboration of basic and translational scientists, researchers, clinicians and students in both biological and non-biological fields
4. apply the resulting knowledge to prevent and treat diseases.

While the Keck Center serves as the training arm of the GCC, the research arm consists of individual, topic-focused research, including translational pain research, antimicrobial resistance, cellular and molecular biophysics, regenerative medicine, drug discovery and development, mental health research, single cell omics, immunology, translational imaging, artificial intelligence in health care, and theoretical and computational neuroscience. These consortia and newly forming clusters provide a supportive environment for the encouragement and development of research that might otherwise be beyond the reach of any one institution. New consortia form when faculty come together around a common interest, establishing a working vision and engaging a broad faculty community to pursue interinstitutional research, present conferences, acquire shared equipment and research cores and/or develop training, research or curriculum grants. https://www.gulfcoastconsortia.org/



Acknowledgements

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National Institute of General Medical Sciences (NIGMS)

Training Interdisciplinary Pharmacology Scientists T32 GM139801

Program Director: Carmen W. Dessauer, PhD, UT Health Science Center at Houston

Houston Area Molecular Biophysics Program T32 GM008280 Program Director: Theodore G Wensel, PhD, Baylor College of Medicine

National Institute of Environmental Health Sciences (NIEHS)

Training in Precision Environmental Health Sciences T32 ES027801

Program Director: Cheryl L. Walker, PhD, Baylor College of Medicine

National Institute of Allergy and Infectious Diseases (NIAID)

Molecular Basis of Infectious Diseases T32 AI055449

Program Director: Theresa M. Koehler, PhD, UT Health Science Center at Houston

Texas Medical Center Training Program in Antimicrobial Resistance T32 AI141349

Program Director: Anthony R. Flores, MD, PhD, UT Health Science Center at Houston

Cancer Prevention and Research Institute of Texas (CPRIT)

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31st Keck Annual Research Conference

Infectious Diseases:
Emerging Threats and Emerging Technologies

Chairs:
Terri Koehler, PhD, Professor and Chair,
Microbiology and Molecular Genetics, McGovern Medical School, UTHealth
and
Sam Shelburne, MD, PhD, Professor,
Infectious Diseases, Infection Control, and Employee Health, M.D. Anderson Cancer Center

October 22, 2021
AGENDA: VIRTUAL CONFERENCE

8:45	Welcome: Keck Center and Conference Overview **Terri Koehler, PhD**, and **Sam Shelburne, MD, PhD**
9:00-10:00	**Peter Kasson, MD, PhD**, Associate Professor, Departments of Molecular Physiology and Biological Physics and of Biomedical Engineering, University of Virginia "Insight into emerging virus infection from single-virus microscopy"
10:00-10:15	**Eva Preisner, PhD**, Microbial Therapeutic Laboratory, Baylor College of Medicine; Training Program in Antimicrobial Resistance; "Characterization of Simplified Microbial Communities that can Inhibit *Clostridioides difficile* Infection"
10:15-10:30	**Pavel Govyadinov, PhD**, Electrical and Computer Engineering/Scalable Tissue Imaging and Modeling Lab, University of Houston; NLM Training Program in Biomedical Informatics and Data Science "Bridging the Gap between Real Macro-Scale Vascular Networks and in vitro Biomimetic Models"
10:30-10:40	Break
10:40-11:40	**Jonathan Livny, PhD,** Senior Research Scientist, Infectious Disease and Microbiome Program, Broad Institute of MIT and Harvard "Developing and leveraging improved RNA-Seq methodologies to explore the cellular functions and interactions that drive infectious disease"
11:40-11:55	**Shelby Simar,** Epidemiology, Human Genetics and Environmental Sciences School of Public Health, UTHealth; Molecular Basis of Infectious Diseases "The Accessory Genome of Vancomycin-Resistant Enterococci and Its Role in Antimicrobial Resistance"
11:55-12:10	**Cuauhtemoc Ulises Gonzalez**, Biochemistry and Cell Biology, UTHealth; Training Interdisciplinary Pharmacology Scientists "Mimicking neuronal synapse cell-cell contacts in HEK cells leads to ligand-induce activity in orphan Delta receptors"
12:10-12:40	Lunch Break
12:40-1:40	**Deborah Hogan, PhD,** Professor of Microbiology and Immunology, Dartmouth Geisel School of Medicine "Evolution in fungal infections-the only constant is change"
1:40-1:55	**Seth Scott**, Molecular Biophysics, UT Medical Branch at Galveston; Houston-Area Molecular Biophysics Program "Hepatitis C Replication is Promoted by Competitive Binding between Host Factors miR-122 and PCBP2"
1:55-2:10	**Nhung Nguyen, PhD**, Center for Transloational Cancer Research, Institute of Biosciences and Technology; Cancer Therapeutics Training Program "Nano-optogenetic engineering of CAR T-cells for precision immunotherapy with enhanced safety"
2:10-2:20	Break

2:20-3:20 **Elissa Hallem, PhD**, Professor of Microbiology, Immunology, & Molecular Genetics, University of California, Los Angeles
"The neural basis of host seeking in skin-penetrating nematodes."

3:20-3:35 **Alyssa Alaniz Emig**, Cancer and Cell Biology, Baylor College of Medicine; Training in Precision Environmental Health Sciences
"The Role of Gene-Environment Interactions in Neural Tube Defect Risk"

3:35-3:50 **Hu Chen, PhD**, MD Anderson Cancer Center; Computational Cancer Biology rainng Program
"DrBioRight, a natural language-oriented and artificial intelligence-driven analytics platform"

3:50-4:50 **Gerald Keusch, MD**; Professor of Medicine, Associate Director, National Emerging Infectious Diseases Laboratory, Boston University
"Emerging technologies to prevent pandemic diseases: Vaccine R&D for COVID-19"

4:50-5:00 Closing

Speaker Abstracts
(in order of appearance)

Insight into Emerging Virus Infection from Single-Virus Microscopy

Peter Kasson, MD, PhD
Associate Professor
Departments of Molecular Physiology and of Biomedical Engineering
University of Virginia

Abstract: Our work seeks to understand the activation and entry mechanisms of emerging enveloped viruses at a molecular level. To accomplish this, we develop technologies ranging from semiphysiological systems, chemically controllable microfluidic devices, and molecular simulations. I will describe results on both influenza and SARS-CoV-2 entry, in particular showing how single-virus studies of viral entry can provide clearer insight into fundamental mechanisms as well as guide opportunities and illuminate challenges for antiviral inhibition.

Bio: Dr. Kasson's lab studies physical mechanism in infectious disease, with interests including infection by influenza, SARS-CoV-2, and other enveloped viruses as well as drug-resistant bacteria. The lab is also interested in the fundamental physics by which viruses infect cells, how the immune system can block infection, and how these materials and processes can be adapted for therapeutic purposes. In addition, the lab develops computational models, new physical tools, and combines the two for insight into viral infection. The goal is to improve diagnosis and therapy. Website.

After receiving his B.S. from Stanford University, Dr. Kasson worked with Axel Brunger, completing his PhD/MD in Stanford's MSTP program. His postdoctoral work was with Vijay Pande at Stanford. He joined the University of Virginia in 2010. Dr. Kasson was one of 29 young researchers to receive the honor of being named a Wallenberg Academy Fellow in 2015.

Characterization of Simplified Microbial Communities that can Inhibit Clostridioides difficile Infection

Eva Preisner, PhD
Postdoctoral Researcher
Department of Virology and Microbiology
Baylor College of Medicine

Abstract: Human fecal microbial transplantations (FMT) restore the homeostasis within the gut environment that resists Clostridioide difficile and are an effective treatment option in recurrent C. difficile infections (CDI). However, safety concerns of FMTs arise due to indications that acute and chronic disease can be transferred and long-term effects on human health remain unknown, in addition, they have yet to be regulated by the Food and Drug Administration (FDA). Due to C. difficile being classified as an urgent threat by the Center for Disease Control and Prevention (CDC), there is an immediate need for an alternative treatment option that is safe and doesn't pose short or long-term adverse outcomes to human health. In this study we identify and characterize multiple defined and simple microbial communities originating from the human intestine that are aimed to prevent CDI and disease recurrence. Four independent simplified human fecal microbial communities consisting of 15-30 members that reduce C. difficile invasion were generated. In a mouse model, those communities were able to significantly reduce the severity of initial CDI and limit susceptibility to disease relapse. To get a better understanding of key organisms that are required to resist the invasion to the pathogen, the communities will be deep sequenced. Individual strains have been isolated from the communities and further studies are aimed to characterize each individual isolate and reconstitute the communities one strain at a time.

Bio: Dr. Eva Preisner conducted her undergraduate studies in Water Sciences at the University of Duisburg-Essen in Germany. After moving to the United States, she linked her passion for the environment with her interest in public health and studied at The Arnold School of Public Health at the University of South Carolina, where she received her MS and Ph. D.

Dr. Preisner joined the Microbial Therapeutic Laboratory under Dr. Britton at Baylor College of Medicine in 2018 as a postdoctoral researcher and has been a trainee in the Training Program for Antimicrobial Resistance since 2020. Her current research interest is developing microbial therapeutics to prevent and treat gastrointestinal diseases as an alternative to antibiotic use.

Bridging the Gap between Real Macro-Scale Vascular Networks and in vitro Biomimetic Models

Pavel Govyadinov, PhD
Postdoctoral Researcher
Department of Computer Science
University of Houston

Abstract: Artificial tissue synthesis is a novel technology that promises to help thousands of people on the organ donor waiting list. One method of generating synthetic tissue is through bioprinting. These methods print a scaffold consisting of vascular components, which is then seeded with cells to grow synthetic tissue volumes. The challenge lies in synthesizing capillaries, which serve as sites for exchanging small molecules, like oxygen and glucose, between blood cells and surrounding tissue. Compared to arteries and veins, capillaries are much smaller in diameter (5-10 μm), denser, do not form tree-like structures, and exhibit wide variability across organisms, making analysis challenging. We are developing computational models for generating synthetic capillary systems that are statistically similar to vasculature found in real tissue samples, facilitating the design of functional scaffolds. To build these models, we first collect large-volume images of vascular networks composed of several cubic millimeters. We have developed a range of methods to reconstruct, visualize, and characterize these vascular models to produce a wide range of statistical metrics. The resulting metrics are used as input to a mathematical model that generates stochastic capillary networks that attempt to replicate the functionality of the original while applying constraints on complexity that facilitate building synthetic scaffolds.

Bio: Pavel Govyadinov is a post-doctoral researcher at the University of Houston, where he also completed his Ph.D. in Computer Science in 2019. His research is focused on high-performance computing, image analysis, modeling, and data visualization using traditional and VR technologies. His biotechnology research interests focuses on degenerative diseases and brain-related disorders. His current project for the National Library of Medicine's Biomedical Informatics Training Program aims to generate models for producing and validating next generation printed synthetic organs for transplant patients.

Developing and Leveraging Improved RNA-Seq Methodologies to Explore the Cellular Functions and Interactions that Drive Infectious Disease

Jonathan Livny, PhD
Senior Group Leader and Senior Research Scientist
Infectious Disease and Microbiome Program
Broad Institute of MIT and Harvard

Abstract: To survive and proliferate in their human hosts, microbes must rapidly alter their physiology in response to myriad environmental changes and diverse interactions with other microbes and with host cells. Often these physiological responses are mediated by changes in expression of genes that make up complex and inter-connecting transcriptional networks. RNA-Seq has emerged as a uniquely effective tool for mapping transcriptomes and profiling changes in gene expression in both microbes and eukaryotes. In this talk I will highlight some of the key methodological advances made by our group to expand the power of RNA-Seq in infectious disease research and describe several recent and ongoing studies we have undertaken that leverage this technology to study diverse aspects of microbial physiology, evolution, and pathogenesis.

Bio: Dr. Livny's research focuses on understanding how bacteria adapt to changes in their environment by altering the expression of their genes. Much of his work is dedicated to developing more robust and high-throughput methods for generating bacterial cDNA libraries and mining bacterial RNA-Seq data for biologically relevant trends. Website

Dr. Livny has a B.S. in molecular biology from the University of Wisconsin, Madison and earned his Ph.D. in cell and molecular biology at the University of Michigan, Ann Arbor, His postdoctoral research was conducted at Tufts University School of Medicine and Brigham and Women's Hospital/Harvard Medical School. He joined the Broad Institute in 2009.

The Accessory Genome of Vancomycin-Resistant Enterococci and Its Role in Antimicrobial Resistance

Shelby Simar
Predoctoral Researcher
Department of Epidemiology, Human Genetics and Environmental Sciences
University of Texas Health Science Center at Houston

Abstract: Vancomycin-resistant enterococci are important causes of bloodstream infections in severely ill and immunocompromised patients. The plasticity of the enterococcal accessory genome— the genetic material that varies between strains— promotes development of resistance to multiple antibiotics by acquisition of antimicrobial resistance (AMR) determinants through horizontal gene transfer of mobile genetic elements. Evaluating the transmission of AMR determinants among enterococci has previously been challenging due to limitations of existing surveillance and sequencing methodologies, as these approaches generally focus only on a subset of the bacterial genome. Thus, the significant gap in our understanding of the epidemiology and clinical implications of the intricacies of the bacterial genome limits our understanding of the dynamics of infection and prevents the use of robust interventions in clinical settings. The Vancomycin-Resistant Enterococcal Bacteremia Outcomes (VENOUS) study is a prospective study of patients with enterococcal bacteremia being carried out worldwide. VENOUS utilizes cutting-edge sequencing approaches to identify enterococcal genomic elements associated with development of AMR that may impact patient outcomes. Preliminary data has revealed a large amount of genomic heterogeneity in infecting isolates, particularly in E. faecium, where accessory genes comprised nearly half of the total genome. Phylogenetic analysis showed the previously described split between Clades A (hospital-adapted) and B (community-associated), with a variety of Clade B isolates causing bloodstream infections. Furthermore, more than half of E. faecium isolates harbored the vanA gene cluster, and we also identified 15 vancomycin-resistant E. faecium strains that harbored W73C and T120A substitutions in LiaR and LiaS, respectively, that have been associated with daptomycin resistance. These results suggest that accessory genes, including AMR genes, comprise a significant proportion of the enterococcal pan-genome, indicating major genetic plasticity within these organisms that plays a substantial role in expansion of the genomic repertoire in clinical isolates.

Bio: Shelby Simar obtained her B.S. in Microbiology from Louisiana State University in 2015 and her MPH in Epidemiology from UTHealth School of Public Health-Houston in 2019. She is currently a third-year PhD student in the Department of Epidemiology, Human Genetics and Environmental Sciences at the UTHealth School of Public Health. Under the mentorship of Drs. Blake Hanson and Cesar Arias, Shelby's work focuses on characterizing the molecular epidemiology and population structure of multidrug-resistant enterococci and investigating the role of the accessory genome in outcomes of patients with enterococcal bacteremia through the use of short- and long-read whole genome sequencing methodologies.

Mimicking Neuronal Synapse Cell-Cell Contacts in HEK Cells Leads to Ligand-Induce Activity in Orphan Delta Receptors

Cuauhtemoc Ulises Gonzalez
Predoctoral Researcher
Department of Biochemistry and Cell Biology
University of Texas Health Science Center at Houston

Abstract: Ionotropic glutamate delta receptors are neuronal membrane receptors that have been implicated in multiple motor and neurocognitive functions such as ataxia, autism, schizophrenia, and retarded speech. Delta receptors belong to the family of ligand-activated ionotropic glutamate receptors. However, unlike its family members, Delta receptors have not been shown to evoke ligand-induced currents and have been thought to be primarily structural elements. Delta receptors are localized in the postsynaptic membrane and have been found to make junction with the presynaptic membrane through interactions with soluble extracellular protein, cerebellin (Cbln), which in turn binds to presynaptic membrane protein, Neurexin1β. Interruption of this interaction leads to a decrease in synaptic long-term depression which is thought to be due to the loss of structural integrity. We show that Delta receptors can be activated by glycine and D-serine and that this opening of ion channel is stabilized through cell-to-cell interactions with Cbln and NRXN1β. Furthermore, we have established that this is due to Neurexin1β and Cbln acting as biological cross-linkers by holding the extracellular domains together, thus allowing for efficient transfer of the ligand-binding conformational changes towards the transmembrane segments and inducing channel opening. This was further verified using chemical linkers at the amino-terminal domain. Together, these findings conclude Delta receptors have a role as ligand-induced channels in neurons and presents opportunities in developing drugs that can modulate this activity directly.

Bio: Cuauhtemoc Ulises Gonzalez is a third-year PhD student in Biochemistry and Cell Biology at the University of Texas Health Science Center at Houston. He graduated from Middle Tennessee State University with a BS in Biochemistry. He then completed an MS degree in Applied Cognition and Neuroscience at the University of Texas at Dallas. He is currently training under the mentorship of Dr. Vasanthi Jayaraman. His project focuses on the modulatory effects of Neurexins and C1q family members on the ionotropic glutamate receptors, which will ultimately lead to the identification of novel targets in the central nervous system.

Evolution in Fungal Infections – The Only Constant is Change

Deborah Hogan, PhD
Professor
Department of Microbiology and Immunology
Geisel School of Medicine at Dartmouth

Abstract: Candida spp. comprise a group of fungal pathogens that can cause a range of superficial and invasive infections. Our work currently focuses on less well-studied members of the Candida clade including Candida auris, a multidrug resistant pathogen that has repeatedly caused hospital associated outbreaks with high mortality around the world, and its close relative, Candida lusitaniae. Both species are associated with the increased rates of development of drug resistance. Using unique collections of antifungal naïve C. lusitaniae isolates obtained from chronic fungal infections in subjects with cystic fibrosis, collected over time, we learned about selective pressures in chronic infections and new relationships between drug resistance and resistance to in vivo stresses such as those imposed by reactive metabolites associated with infection such as methylglyoxal. Recently, we have found that similar pathways exist in C. auris. We will discuss how our data indicate the need for new ways to evaluate fungal infections for treatment decision making, tradeoffs and synergies in drug resistance and stress resistance, and how genomics analysis of strains within a species and advance our understanding of fungal biology and host-microbe interactions.

Bio: The Hogan Lab focuses on how inter- and intra-species interactions involving fungi affect the outcomes of disease. Their work on microbial interactions have revealed the potent effects of metabolic changes in response to the availability of oxygen, metals and different carbon sources on the outcome of microbe-microbe and microbe-host interactions and differences in how different strains within a species and even isolates within a population are in terms of their interactions. Website

Dr. Hogan has B.S. degree in biology with an ecology focus, and a PhD in microbiology from Michigan State University with a year working at Parke-Davis Pharmaceuticals in proteomics. Her post-doctoral training was at Harvard Medical School. She was co-director of the Marine Biological Labs (MBL) in Woods Hole that focuses on molecular mycology and directs a T32 on Host-Microbe Interactions.

Hepatitis C Replication is Promoted by Competitive Binding between Host Factors miR-122 and PCBP2

Seth Scott
Predoctoral Researcher
Department of Molecular Biophysics
University of Texas Medical Branch at Galveston

Abstract: Hepatitis C virus (HCV) is a human pathogen that causes a persistent infection in the liver that requires precise control over viral replication to be maintained. Successful HCV replication is promoted by many host factors; of importance to this study is microRNA-122 (miR-122) and Poly-C Binding Protein-2 (PCBP2). The HCV 5' untranslated region (UTR) of the genome contains two miR-122 binding sites near the first stem-loop (SLI) in the 5' UTR and a PCBP2 binding region that overlaps the second miR-122 binding site. The mechanisms by which these host factors promote viral replication is still unclear. Binding experiments, using isothermal calorimetry (ITC) and fluorescence anisotropy, were conducted by titrating either miR-122 or PCBP2 into the first 45 nucleotides of HCV's 5' UTR (5'-HCV45). Both factors showed nanomolar affinity binding for the HCV RNA and direct competition was observed for the overlapping binding site. As a possible mechanism we looked at the interactions between the HCV polymerase, NS5B, and the 5'-HCV45. We found that and NS5B binds the 5'-HCV45:miR-122 complex with a 5 fold higher affinity than the free 5'-HCV45. To visualize the interaction between 5' HCV RNA and miR-122, cryo-electron microscopy is being used to solve the structure of the first miR-122 binding site. Comparison of the cryo-EM structure with the predicted model will help in identifying the mechanism by which miR-122 promotes HCV replication.

Bio: Seth Scott is a PhD candidate in the Molecular Biophysics Education Track at the University of Texas Medical Branch at Galveston. He graduated from Montana State University in Bozeman with a B.S. in Bioengineering and a B.S. in Earth Science. Afterwards he worked at the National Institute of Allergy and Infectious Diseases' Rocky Mountain Laboratory in Hamilton, Montana developing vaccine candidates for Crimean Congo hemorrhagic fever virus and Lassa virus. He is currently training under Dr. Kyung Choi using structural biology and biophysics to better understand the replication of Flaviviridae viruses, focusing on the Hepatitis C virus.

Nano-Optogenetic Engineering of CAR T-cells for Precision Immunotherapy with Enhanced Safety

Nhung Nguyen, PhD
Postdoctoral Researcher
Center for Translational Cancer Research
Institute of Biosciences and Technology, Texas A&M University

Abstract: Chimeric antigen receptor (CAR) T cell-based immunotherapy approved by FDA shows promising curative potential in patients with CD19-positive hematological immunotherapy. CAR T-cell therapy, nevertheless, lacks precise control over the location and duration of the anti-tumor immune response, and therefore, is fraught with devastating side effects in some patients. Herein, we present the design of light-switchable CAR (designated “LiCAR”) T-cells that enable photo-tunable activation of therapeutic T cells to induce CD19-positive tumor cell killing both in vitro and in vivo. When coupled with imaging-guided, surgically removable upconversion nanoplates (UCNPs) that have enhanced near infrared (NIR)-to-blue upconversion luminescence as miniature deep tissue transducers, LiCAR T-cells enable precise spatiotemporal control over T cell-mediated anti-tumor therapeutic activity with greatly mitigated side effects. This remotely controllable nano-optogenetic device will not only provide a unique tool for interrogating CAR-mediated anti-tumor immunity, but also set the stage for developing smart immunotherapy to deliver personalized anti-cancer therapy.

Bio: Dr. Nhung Nguyen is a Postdoc Research Associate at the Institute of Biosciences and Technology, Texas A&M University. She received her Bachelor of Science in Medical Biotechnology from Vietnam National University. She then joined Institute of Stem Cell Research and Application-Vietnam National University as a teaching and research assistant. She obtained her Master of Sciences from Department of Biological Science, University of Arkansas and PhD degrees in Medical Sciences from Texas A&M University. Dr. Nguyen’s work is centered on on calcium signaling, transcriptional reprogramming, synthetic immuno-engineering, and cancer therapeutics.

The Neural Basis of Host Seeking in Skin-Penetrating Nematodes

Elissa Hallem, PhD
Professor
Department of Microbiology, Immunology and Molecular Genetics
University of California, Los Angeles

Abstract: Gastrointestinal parasitic nematodes infect over a billion people worldwide and are a major cause of neglected tropical disease. Many of these parasites have an infective third-larval stage that actively searches for hosts using host-emitted sensory cues, and then infects by penetrating through host skin. We are interested in understanding the host-seeking behaviors of infective larvae, as well as the molecular, cellular, and circuit mechanisms that drive host seeking. We use the human-parasitic threadworm Strongyloides stercoralis for these studies because S. stercoralis is unique among parasitic nematodes in its amenability to genetic manipulation. We have shown that S. stercoralis infective larvae are robustly attracted to a diverse array of human emitted odorants and mammalian body temperature. In this talk, I will focus primarily on our investigations into heat-seeking behavior. Using CRISPR/Cas9 mutagenesis, we identified a cGMP pathway that is required for heat seeking in S. stercoralis. We then identified the primary thermosensory neurons in S. stercoralis, and found that they use a novel temperature-encoding strategy to precisely detect temperatures ranging from ambient to host body heat. We also identified three S. stercoralis thermoreceptor proteins that act in the primary thermosensory neurons, one of which senses temperatures ranging from ambient to host body heat and two of which are tuned specifically to temperatures near host body heat. Our results pinpoint the parasite-specific neural adaptations that enable parasitic nematodes to target humans, and may facilitate the development of novel infection control strategies.

Bio: Dr. Hallem is a neurobiologist whose research focuses on the sensory behaviors of parasitic and free-living nematodes, and lies at the interface of neurobiology and parasitology. The goals of her lab are to understand how human-parasitic worms use sensory cues to locate hosts to infect, how sensory circuits of parasitic animals differ from those of free-living animals to enable parasitic behaviors, and how sensory microcircuits generate flexible outputs. Website

In 2012, Dr. Hallem received a highly prestigious MacArthur “Genius” Fellowship for her work in understanding how parasitic worms use odor detection to find and invade human hosts. She has an undergraduate degree in biology and chemistry from Williams College and received at PhD focusing on neurobiology from Yale in 2006. After completing a postdoctoral fellowship at CalTech in 2010, she joined UCLA. Dr. Hallem also serves as vice chair of Graduate Studies in the Department of Microbiology, Immunology, and Molecular Genetics.

The Role of Gene-Environment Interactions in Neural Tube Defect Risk

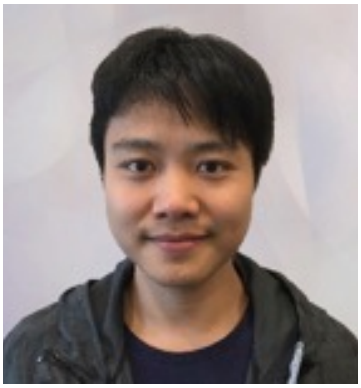
Alyssa Emig
Predoctoral Researcher
Department of Cancer and Cell Biology
Baylor College of Medicine

Abstract: Congenital malformations, including those of the central nervous system (CNS), are among the most common causes of childhood death and loss of pregnancy worldwide. During early embryonic development, the precursor to the CNS – the neuroectoderm - is shaped into a hollow neural tube that will give rise to the brain and spinal cord. This shaping is driven by highly conserved morphogenetic cell movements that extend the head-to-tail axis and ensures proper closure of the developing neural tube. Disruptions in these cell movements by environmental and/or genetic factors results in improper morphogenesis and consequently, neural tube defects (NTDs), conditions characterized by the improper/failed closure of the neural tube. Mutations in developmental signaling pathways such as Planar Cell Polarity and Nodal are known to disrupt neural tube development; however, genetics alone are insufficient to explain the etiology of most NTDs. Exposure to environmental toxicants in utero are correlated with increased NTD risk, but how these factors interact with known risk genes remains poorly understood.

Zebrafish with mutations in Nodal signaling components exhibit open neural tubes with a wide range of phenotypic severity, providing an experimentally and genetically tractable model of NTDs. Using this model, our lab is working to identify modifier genes and environmental exposures that interact with Nodal signaling during early neuroectoderm development to confer enhanced risk of NTDs.

Bio: Alyssa completed her B.S. in Biochemistry at Baylor University and is now a third year Ph.D. candidate in the Cancer and Cell Biology graduate program at Baylor College of Medicine. Her research interests include using zebrafish in vivo and ex vivo models to understand neural tube morphogenesis during early embryonic development. Her goal is to characterize the role of the Nodal signaling pathway in morphogenesis and elucidate gene-environment interactions leading to neural tube defects. Alyssa's research is co-advised by mentors Dr. Margot Williams and Dr. Richard Finnell.

DrBioRight, a Natural Language-oriented and Artificial Intelligence-driven Analytics Platform



Hu Chen, PhD
Postdoctoral Researcher
Department of Bioinformatics and Computational Biology
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Abstract: High-throughput molecular profiling technologies have generated a tremendous amount of data and revolutionized biomedical research. The data surge presents a major challenge for researchers, especially those with little bioinformatics expertise, to obtain meaningful insights. Despite impressive progress in the development of user-friendly tools, packages, and platforms for easy data exploration, users still spend considerable time identifying appropriate tools and learning how to use them. In general, bioinformatics analysis is time-consuming and suffers from a lack of transparency and consistency. We hypothesize that most of the commonly used standard analyses of omics data can be conducted effectively by natural languages. So we have developed DrBioRight, a first natural language-oriented and artificial intelligence (AI)-driven analytics platform that allows users to explore and analyze omics data intuitively and efficiently. DrBioRight employs a simple online chat interface and interacts with users through human languages directly. We are improving the AI core ability of DrBioRight to make it smarter and more powerful.

Bio: Dr. Hu Chen is a postdoctoral fellow in the Department of Bioinformatics and Computational Biology at the University of Texas MD Anderson Cancer Center. He obtained his Ph.D. from Baylor College of Medicine in 2020. His Ph.D. thesis focused on the multi-omics analysis of cancer genomes, with a special focus on esophageal squamous cell carcinoma. He is now working with Dr. Han Liang and Dr. George Calin, through the support of the Computational Cancer Biology Training Program. His current work aims to develop a natural language-oriented analytics platform that the broad research community can use to perform bioinformatics analysis in an intuitive, efficient, transparent, and collaborative way.

Emerging Technologies to Prevent Pandemic Diseases: Vaccine R&D for COVID-19

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Abstract: The West Africa Ebola pandemic of 2014-2015 and the pandemic of COVID-19 have forever changed the course of research and development of medical countermeasures for pandemic diseases and the timeline for delivering effective drugs, vaccines, and diagnostics. Many lessons learned have been applied more rapidly than ever before, and many lessons have remained unaddressed. The issue is not can we do better, but because we must do better what are the barriers and how do we move beyond them. It is clear that preparatory research is a starting point. We must be able to better assess and predict future threats, invest in research to understand the biology of such pathogens with pandemic potential, identify targets for interventions and diagnostics, and develop platform technologies that are rapidly adaptable to the specific microbial threats that emerge. Greater efficiency in the way the multiple steps in product development are solved and aligned with more nimble regulatory mechanisms in a manner that does not sacrifice safety is essential. Planning for clinical research and clinical trials must also antedate the next pandemic, be functional and ready to target any new outbreak and address the added challenges of an uncontrolled emergency with high transmission, substantial morbidity and mortality, and limited ability to control the outbreak in its early stages. Finally, because ongoing transmission of these diseases anywhere represents a threat to populations everywhere, achieving equity of access to countermeasures across the world that are affordable and accessible is essential, including investments in greater future R&D equity among high-, middle-, and low-income countries. These challenges will be discussed using vaccines as an example in the context of emerging technologies in basic and translational research, product development, and successfully implementing vaccine delivery programs.

Bio: Dr. Keusch is an internationally recognized basic and clinical researcher in infectious diseases. His research has ranged from the molecular pathogenesis of tropical infectious diseases to field research in nutrition, immunology, host susceptibility, and the treatment of tropical infectious diseases and HIV/AIDS. Website.

Among the many awards he has received are the Consortium of Universities for Global Health: Lifetime Achievement Award in 2013, and all three of the major awards from the Infectious Diseases Society of America -- the Squibb, Finland, and Bristol awards for research and training excellence. Dr, Keusch received his B.A. from Columbia College and his M.D. from Harvard Medical School and is board certified in Internal Medicine and Infectious Diseases.