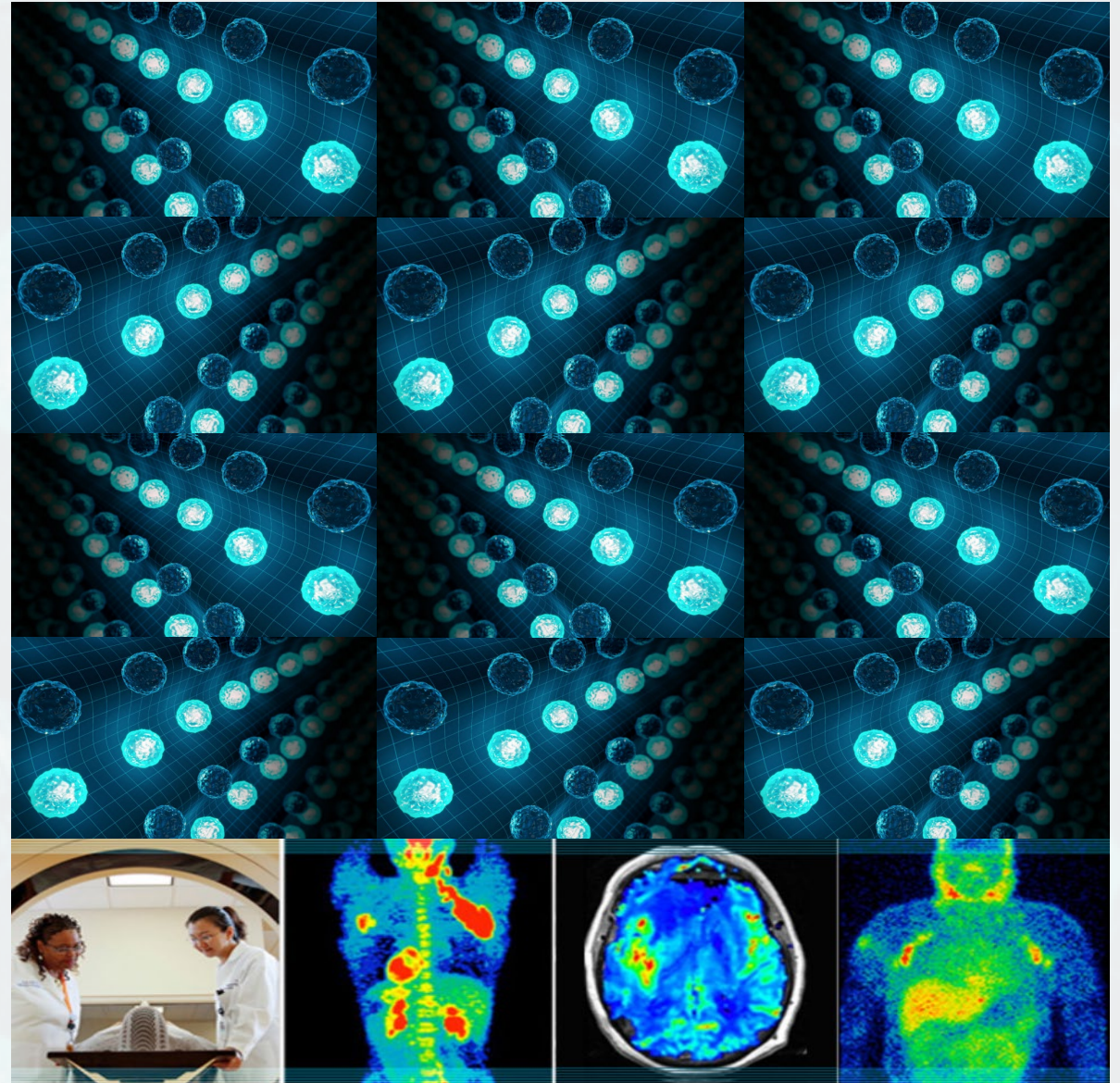




Synthetic Biology for Molecular Imaging in Cancer Workshop

April 22-23, 2024



OVERVIEW

2024 NCI Synthetic Biology for Molecular Imaging in Cancer Workshop

Date: April 22-23, 2024

Location: Virtual attendance via WebEx

Molecular imaging is an integral part of the oncological research, and plays critical roles in cancer detection, diagnosis, treatment, and monitoring. Imaging technology continues to evolve to meet the rising needs in patient care. Despite recent advances in imaging resolution and quality, the complex and dynamic nature of tumor evolution necessitates for improved accuracy and precision in molecular targeted imaging to observe functional changes in a tumor and its microenvironment in real time. A challenge in achieving precision cancer imaging remains to be the development of site-specific and target-oriented delivery of imaging probes and tools. The rapid progress of synthetic biology offers new opportunities for the design of novel imaging agents and platforms to achieve improved selectivity and sensitivity output.

Synthetic biology is a design-driven discipline that centers on engineering biologics with expanded and enhanced properties to perform novel functions through synthesizing of innovative molecules and repurposing naturally existing molecules and structures. It emphasizes precise control with iterative design and refinement to engineer modular and responsive biological elements, with the ability to predict and produce a desired level of output for any given input. Over the last decade, synthetic biology tools and principles have matured tremendously and reached extraordinary levels of sophistication. The field is now beginning to bring new capabilities to molecular diagnostics, expanding the molecular detection palette and creating dynamic sensors to provide near real-time surveillance of pathological conditions.

To facilitate the reach and impact of synthetic biology on molecular cancer imaging, the Cancer Imaging Program (<https://imaging.cancer.gov>) in the NCI plans to convene a two-day virtual workshop (April 22-23, 2024) on Synthetic Biology for Molecular Imaging in Cancer. The workshop will seek input from experts in the scientific community to evaluate the potential of synthetic bioengineering methodologies in advancing molecular cancer imaging for research and clinical application. The overarching goal is to identify new opportunities, delineate the key challenges, and develop strategies to overcome these challenges. We envision this workshop will be a steppingstone to spur discussion and collaboration among scientists to match synthetic bioengineering design principles with agent and tool development in cancer imaging.

AGENDA

DAY 1—Monday April 22, 2024 11:00 am -6:00 pm EST	
11:00 am-11:15 am	Welcoming Remarks and Meeting Overview <ul style="list-style-type: none">Computer checkWelcoming Remarks Janet Eary, M.D., Associate Director, CIP/DCTD/NCIMeeting Overview and Goals; Meeting Logistics Charles Lin, Ph.D., CIP/DCTD/NCI
11:15 am-2:15 pm	Session 1: Applications of Synthetic Biology in Medicine <i>Chair: Joshua Leonard; NIH Moderator: Jerry Li (NCI)</i>
11:15 am-11:45 am	<i>Title:</i> Opportunities and technologies for engineered synthetic sensing and information processing Joshua Leonard (Northwestern University)
11:45 am-12:10 pm	<i>Title:</i> Toward the development of synthetic immunity to cancer Kole Roybal (UC San Francisco)
12:10 pm-12:35 pm	<i>Title:</i> Cell-specific targeted nucleic acid nanomedicine in oncology and beyond Hamideh Parhiz (University of Pennsylvania)
12:35 pm-1:00 pm	<i>Title:</i> Engineering vaccines, cell and gene therapies using synthetic biology Wilson Wong (Boston University)
1:00 pm-1:25 pm	<i>Title:</i> Using genome editing to convert oncogenic mutations to unique protein biomarkers Kevin McHugh (Rice University)
1:25 pm-1:35 pm	Break (10 min)
1:35 pm-2:15 pm	Session 1 Panel Discussion (<i>Chaired by Joshua Leonard, Northwestern U</i>)
2:15 pm-2:45 pm	Break (30 min)

2:45 pm-6:00 pm	Session 2: Synthetic Biology in Molecular Imaging <i>Chair: Mikhail Shapiro; NIH Moderator: Yisong Wang (NCI)</i>
2:45 pm-3:15 pm	<i>Title:</i> Talking to cells: biomolecular ultrasound for deep tissue cellular imaging and biosensing Mikhail Shapiro (Caltech)
3:15 pm-3:40 pm	<i>Title:</i> Accelerating the therapeutic discovery through noninvasive monitoring of the brain Jerzy Szablowski (Rice University)
3:40 pm-4:05 pm	<i>Title:</i> Harnessing synthetic gene circuits to create sensitive reporters and bioresponsive sensors for deep-tissue imaging Arnab Mukherjee (UC Santa Barbara)
4:05 pm-4:30 pm	<i>Title:</i> Engineering synthetic organelles as cellular Imaging and actuating Agents Christopher Contag (Michigan State University)
4:30 pm-4:55 pm	<i>Title:</i> Synthetic G protein-coupled receptors for programmable sensing and control of cell behavior Nicholas Kalogriopoulos (Stanford)
4:55 pm-5:05 pm	Break (10 min)
5:05 pm-5:50 pm	Session 2 Panel Discussion (<i>Chaired by Mikhail Shapiro, Caltech</i>)
5:50 pm-6:00 pm	Day 1 Wrap Up (<i>by Charles Lin</i>)

Workshop organized and managed by

- Mikhail Shapiro (Co-Lead; Caltech)
Charles Lin (Co-Lead; MIB/CIP/DCTD, National Cancer Institute)
Chiayeng Wang (MIB/CIP/DCTD, National Cancer Institute)
Kelly Crotty (CSSI/OD, National Cancer Institute)
Jerry Li (BBCSB/DCB, National Cancer Institute)
Yisong Wang (MIB/CIP/DCTD, National Cancer Institute)
Tatjana Atanasijevic (DAST, National Institute of Biomedical Imaging and Bioengineering)

DAY 2—Tuesday April 23, 2024 11:00 am -6:00 pm EST	
11:00 am-11:05 am	<ul style="list-style-type: none">Computer checkBrief Welcome, Tuesday Recap, and Daily Updates Charles Lin, Ph.D., CIP/DCTD/NCI
11:05 am-2:05 pm	Session 3: Molecular Imaging in Synthetic Biology <i>Chair: Mark Sellmyer; NIH Moderator: Tatjana Atanasijevic (NIBIB)</i>
11:05 am-11:35 am	<i>Title:</i> Imaging and controlling engineered immune cell biology with an orthogonal protein tag Mark Sellmyer (University of Pennsylvania)
11:35 am-12:00 pm	<i>Title:</i> Molecular-genetic imaging of synthetic receptor cancer immunotherapies John Ronald (Western University, Canada)
12:00 pm-12:25 pm	<i>Title:</i> Bioengineering synthetic biomarkers for earlier cancer detection Gabe Kwong (Georgia Institute of Technology)
12:25 pm-12:50 pm	<i>Title:</i> Engineering bacteria as living cancer drug delivery systems Tetsuhiro Harimoto (Harvard University)
12:50 pm-1:15 pm	<i>Title:</i> Synthetic biology for next-generation therapeutics Tim Lu (MIT)
1:15 pm-1:25 pm	Break (10 min)
1:25 pm-2:05 pm	Session 3 Panel Discussion (<i>Chaired by Mark Sellmyer, U Penn</i>)
2:05 pm-2:35 pm	Break (30 min)
2:35 pm-5:35 pm	Session 4: Translational Potential and Clinical Needs: Opportunities and Challenges <i>Chair: Anna Wu; NIH Moderator: Charles Lin (NCI)</i>
2:35 pm-3:05 pm	<i>Title:</i> Engineered antibodies for imaging in oncology and immunology: From preclinical models to patients Anna Wu (City of Hope)
3:05 pm-3:30 pm	<i>Title:</i> Antigen-dependent inducible T-cell reporter system for PET imaging of breast cancer and glioblastoma David Wilson (UC San Francisco)
3:30 pm-3:55 pm	<i>Title:</i> Evolution of reporter tools for molecular imaging: from bench to bed Vladimir Ponomarev (MSKCC)
3:55 pm-4:20 pm	<i>Title:</i> Strategies to augment imaging features by circulating tumor DNA assessment Laura van't Veer (UC San Francisco)
4:20 pm-4:45 pm	<i>Title:</i> Translation of [¹⁸ F]4FN, a redox-tuned radiopharmaceutical for PET imaging of innate immunity activation David Piwnica-Worms (MD Anderson Cancer Center)
4:45 pm-4:55 pm	Break (10 min)
4:55 pm-5:35 pm	Session 4 Panel Discussion (<i>Chaired by Anna Wu, City of Hope</i>)
5:35 pm-5:45 pm	Session 5: NCI Resources and Funding Opportunities Chiayeng Wang and Kelly Crotty
5:45 pm-6:00 pm	Concluding Remarks (<i>Mikhail Shapiro, Caltech</i>)

VIRTUAL MEETING CONNECTION

Join from the meeting link

<https://cbiit.webex.com/cbiit/j.php?MTID=m3bff0c07469c1d0ea9a68001c539ab03>

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Meeting number (access code): 2306 700 8787

Meeting password: fsFJWVQ*374

Tap to join from a mobile device (attendee only)

1-650-479-3207 (US/Canada)



Christopher H Contag, PhD

Engineering synthetic organelles for imaging and cellular control, Michigan State University

contagch@msu.edu

Dr. Contag is the inaugural chair of the Department of Biomedical Engineering and founding Director of the Institute for Quantitative Health Science and Engineering (IQ) at Michigan State University. Dr. Contag joined the faculty of Michigan State University in 2017 as the James and Kathleen Cornelius Chair in the Departments of Biomedical Engineering and Microbiology & Molecular Genetics, with an adjunct appointment in the Center for Bioethics and Social Justice at MSU. Dr. Contag is also Professor emeritus in the Department of Pediatrics at Stanford University. Dr. Contag received his B.S. in Biology from the University of Minnesota, St. Paul in 1982. He received his Ph.D. in Microbiology from the University of Minnesota, Minneapolis in 1988. He did his postdoctoral training at Stanford University from 1990-1994, and then joined Stanford faculty in 1995 where he was professor in the Departments of Pediatrics, Radiology, Bioengineering and Microbiology & Immunology until 2016. Dr. Contag is a pioneer in the field of molecular imaging and is developing imaging approaches aimed at revealing cellular and molecular processes in living subjects, including humans, and advancing therapeutic strategies through imaging. He is a founding member and past president of the Society for Molecular Imaging (SMI, now part of WMIS), and recipient of the Achievement Award from the SMI for his contributions to imaging, and the Britton Chance Award from SPIE for his fundamental contributions to optics. Dr. Contag is a Fellow of the World Molecular Imaging Society (WMIS) and the past President of WMIS. Dr. Contag was a founder of Xenogen Corp. (now part of PerkinElmer) established to commercialize innovative imaging tools for biomedicine. He is also a founder of BioEclipse—a cancer therapy company, PixelGear—a point-of-care pathology company, and EXOForce—a company developing exoskeletons for athletics and military applications.

ABSTRACT

Engineering Synthetic Organelles as Cellular Imaging and Actuating Agents

Mitochondria originated from previously free-living bacteria that were taken up by other cells, and then over 2 billion years of evolution the bacterial genome was stripped down to the essential genome of the mitochondria in a symbiotic relationship with the host cell. Based on this endosymbiont theory of the origin of eukaryotes, we asked the question, “What if we could we use molecular imaging and molecular biology to engineer bacteria into mitochondrial mimics to control and image cellular functions in vivo?” That is, can these engineered endosymbionts be used as biologically encoded remote control modules that receive signals from outside the body to direct the biology of cells, tissues and organs in living mammals? Decades of advances in molecular imaging and molecular biology have made it possible to ask, “Can we recapitulate in a few years of lab work what took evolution took 2-billion years to do, and then build on this concept to image and treat cancer?” We have engineered synthetic endosymbionts that can be imaged with optical and magnetic signals and engineered them to control cellular programming through expression of mammalian transcription factors under external chemical and magnetothermal control. We have begun to minimize the genomes of these chassis organisms as we work toward minimal genome synthetic organelles for cellular control and imaging.



Tetsuhiro Harimoto, Ph.D.
Postdoctoral Fellow, Harvard University

Tetsuhiro received his Ph.D. in Biomedical Engineering from Columbia University in 2022. His graduate work in Dr. Tal Danino's lab focused on the engineering of living microbes as advanced drug delivery vehicles, with a specific focus on tumor-homing bacteria as cancer therapeutics. Currently, Tetsuhiro is an NCI F99/K00 postdoctoral fellow in the Wyss Institute for Biologically Inspired Engineering at Harvard University. Working with Dr. David Mooney, Tetsuhiro is developing engineered living materials as next-generation drug delivery systems. Tetsuhiro was named as one of STAT's Wunderkinds and recognized in MIT Technology Review's Innovators Under 35 in 2023.

ABSTRACT

Engineering Bacteria as Living Drug Delivery Systems

Engineered living cells as therapeutic agents are transforming modern medicine. An emerging focus is tumor-colonizing bacteria, where systemically delivered bacteria have been demonstrated to selectively grow within solid tumors. This natural tropism to tumors presents a unique opportunity to engineer bacteria as programmable drug delivery vehicles to regions inaccessible with existing chemo- and immuno-therapeutics. In this talk, I will describe our recent efforts to enhance bacterial cancer therapies through synthetic biology. I will focus on strategies to address several key challenges for clinical translation, including bacterial delivery, therapeutic identification, and off-target effects. Our multidisciplinary approach, spanning from gene circuit design to *in vitro* and *in vivo* models, advances bacteria as next-generation drug carriers with potentials for advanced disease imaging within the body.



Nicholas A. Kalogriopoulos, Ph.D.
Postdoctoral Fellow, Stanford University
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Nick obtained a B.S. in Genetics and Molecular Biology from the University of Wisconsin-Madison in 2012. During his predoctoral work, he trained with Dr. Paul Sondel, where he worked on the development and preclinical testing of novel immunotherapeutic agents for the treatment of neuroblastoma. Nick obtained a Ph.D. in Biomedical Science from the University of California San Diego in 2019. During his doctoral studies in the laboratory of Dr. Pradipta Ghosh, he studied a novel protein family of heterotrimeric G protein modulators and their role in normal and oncogenic signal transduction. Nick is currently a postdoctoral fellow in the laboratory of Alice Ting at Stanford University where he is developing novel synthetic receptors for the study and treatment of complex diseases, including cancer. Nick is a recipient of the Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship (F32) from the National Cancer Institute.

ABSTRACT **Synthetic G protein-coupled receptors for programmable sensing and control of cell behavior**

Synthetic receptors that mediate antigen-dependent cell responses are transforming therapeutics, drug discovery, and basic research. However, existing modular synthetic receptor technologies are largely limited to immobilized target antigens, have limited output scope, and lack built-in drug control. To address these limitations, we engineered synthetic G protein-coupled receptors (GPCRs) capable of driving a wide range of native or nonnative cellular processes in response to user-defined antigen, a new class of modular synthetic receptors we have termed Programmable Antigen-gated G protein-coupled Engineered Receptors (PAGERs). We have created PAGERs responsive to more than a dozen biologically and therapeutically important soluble and cell surface antigens. Different PAGER scaffolds permit antigen binding to drive transgene expression, real-time fluorescence, or endogenous G protein activation, enabling control of cytosolic Ca^{2+} , lipid signaling, cAMP, and neuronal activity. Due to its modular design and generalizability, we expect PAGER to have broad utility in discovery and translational science.



Gabriel Kwong, Ph.D.

Associate Professor , Department of Biomedical Engineering Georgia Tech and Emory School of Medicine

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Dr. Kwong is an Associate Professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University. He earned his B.S. from UC Berkeley and his Ph.D. from Caltech both in Bioengineering. His research program is centered at the interface of bioengineering, immunology and medicine. His group pioneers cell therapies and biosensors to address frontier challenges in cancer, transplantation medicine, and infectious diseases. Among his distinctions, Dr. Kwong is a recipient of the NIH Director's New Innovator and Pioneer Awards, and currently leads the \$49.5 million Cancer and Organ Degradome Atlas (CODA) project, a multi-institutional research enterprise supported by ARPA-H to revolutionize multi-cancer early detection. Dr. Kwong co-founded two biotechnology companies, and holds over 35 issued or pending patents.

ABSTRACT

Bioengineering Synthetic Biomarkers for Earlier Cancer Detection

Cancer early detection could increase the number of cancers detected sooner and reduce cancer-related deaths, yet native tumor-shed biomarkers are found at such vanishingly small quantities in biofluids that they offer limited potential to set early-stage tumors apart from healthy tissue. Over the past decade, our work has charted a radical new path forward based on querying tissues, instead of a biological sample, for earlier cancer detection. Our approach deploys bioengineered sensors inside the body to hunt for malignant cells and then use their ubiquitous dysregulation of protease activity to drive the release of a synthetic biomarker to levels that can far exceed those achievable by a native tumor biomarker, allowing earlier cancer detection. This talk will focus on our recent work that applies synthetic biology principles to the design of cell- and gene-free biocircuits for activity-based sensing of tumors inside the body.

BIOS



Joshua N Leonard, Ph.D.
Professor of Chemical and Biological Engineering, Northwestern University

Leonard is Charles Deering McCormick Professor of Teaching Excellence at Northwestern University. Leonard trained in chemical engineering (B.S. from Stanford University, Ph.D. from the University of California Berkeley) and immunology (postdoctoral fellowship at the National Cancer Institute's Experimental Immunology Branch). Leonard's group invents and develops novel technologies enabling next-generation biological therapies. Leonard is an early pioneer in mammalian synthetic biology, and his group develops technologies including synthetic receptors and genetic control systems enabling programmable cell-based therapies for cancer and novel gene therapy platforms including bioengineered nanoscale vesicles. Leonard is a founder of Northwestern's Center for Synthetic Biology. He is actively engaged in the development of national science policy, testifying as an expert witness before the U.S. House of Representatives and serving as a council and board member of the Engineering Biology Research Consortium. He fosters training, entrepreneurship, and industrial impact as director of Northwestern's NIH-funded Biotechnology Training Program (T32) and entrepreneurial activity as a founder and officer of his biotech startup, Syenex.

ABSTRACT

Opportunities and technologies for engineered synthetic sensing and information processing

Engineered biological therapies are a transformative medical frontier. Employing living cells to perform sophisticated and complex tasks within the human body has already revolutionized the treatment of some cancers, and the prospect of extending these capabilities to promote health in myriad ways is now within reach. However, realizing the full potential of this approach requires improved engineering tools, ranging from improved biological technologies to computational and conceptual frameworks to guide their development and deployment. Here, I will present recent advances and prospects for achieving the vision of design-driven engineering of novel mammalian cellular functions through the emerging technical discipline of synthetic biology. I will focus on contemporary challenges and solutions for engineering sensing and information processing towards the applications contemplated in this workshop.



Timothy Lu, M.D., Ph.D.
Associate Professor, Massachusetts Institute of Technology
timlu@mit.edu

Timothy Lu is CEO and Co-Founder of Senti Biosciences, a biotechnology company applying synthetic biology to create next-generation cell and gene therapies. Tim graduated with his SB and MEng from MIT, and his MD/PhD from the Harvard-MIT Health Sciences and Technology program. Tim joined the MIT faculty in 2010 leading the Synthetic Biology Group in the Department of Electrical Engineering and Computer Science and the Department of Biological Engineering at MIT. He is a co-founder of multiple biotechnology companies innovating new diagnostic and therapeutic technologies for human health, including Senti Biosciences, Eligo Biosciences, BiomX, Tango Therapeutics, Engine Biosciences, and others.

ABSTRACT **Synthetic Biology for Next-Generation Therapeutics**

Over the last 50 years, exponential increases in our ability to manipulate electrons and engineer electronic systems spawned the information technology revolution. Similarly rapid improvements in technologies for reading and writing DNA are now transforming our capacity to engineer biological systems. Leveraging these technologies, synthetic biology is an emerging discipline for designing biological systems with novel functionalities. This field has opened up new strategies for interrogating and understanding biology, as well as for diagnosing and treating human diseases.

I will discuss the development of Gene Circuit technologies for cell and gene therapies that enable enhanced efficacy and specificity. For example, SENTI-202 incorporates Gene Circuits to maximize cancer killing despite heterogeneity while simultaneously sparing healthy cells using a combination of OR + NOT Logic Gates. SENTI-202 is being developed for the treatment of Acute Myeloid Leukemia (AML) in clinical studies. Our Gene Circuits are also incorporated into gene therapies for more accurate targeting of diseased tissues and cell therapies to treat autoimmune diseases more effectively.



Kevin J. McHugh, Ph.D.
Assistant Professor of Bioengineering, Rice University
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Dr. Kevin McHugh is an Assistant Professor and CPRIT Scholar in Cancer Research in the Department of Bioengineering at Rice University whose work has been featured in journals including Science, Science Translational Materials, Advanced Materials, and PNAS. Dr. McHugh received his B.S. in Biomedical Engineering from Case Western Reserve University in 2009, where he worked with Dr. James M. Anderson to evaluate the biocompatibility of biomaterial devices. Next, he earned his Ph.D. in Biomedical Engineering from Boston University in 2014 where his Ph.D. work focused on developing retinal tissue engineering scaffolds for dry age-related macular degeneration. He then joined Dr. Robert Langer's Laboratory at the Massachusetts Institute of Technology (MIT) as a Ruth L. Kirschstein Postdoctoral Fellow where he developed vaccine delivery systems to improve patient access in low-resource environments. At Rice University, Dr. McHugh's lab is broadly interested in developing translational technologies for cancer, infectious disease, and other chronic conditions, employing cutting-edge techniques in chemistry, microfabrication, and genome editing.

ABSTRACT **Using genome editing to convert oncogenic mutations to unique protein biomarkers**

Aside from developing a highly effective pan-cancer therapeutic capable of treating any stage of the disease, the most effective way to reduce cancer mortality is to identify cancer earlier when treatments are far more successful. Unfortunately, due to the small number of cancer cells and a lack of unique biomarkers, there is an inherent signal-to-noise challenge in detecting burgeoning tumors. Our goal is to create tumor-specific biomarkers by converting oncogenic mutations into either secreted or cell surface proteins using genome-editing tools, which can then be detected with minimal background. Briefly, CRISPR using customized, mutation-specific combinations of Cas9 and guide RNA will be co-administered with a donor plasmid encoding an exogenous protein, leading to selective expression of the protein by cells harboring the oncogene(s) of interest and subsequent detection using a functionalized contrast agent. Ultimately, we envision this technology being used for (1) cancer screening, (2) disease staging, and (3) recurrence detection.



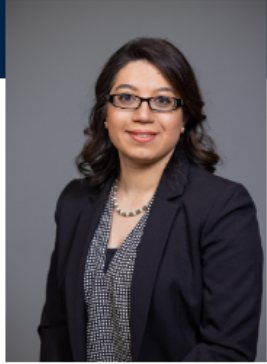
Arnab Mukherjee, Ph.D.
Assistant Professor, University of California Santa Barbara
arnabm@ucsb.edu

Arnab Mukherjee is an Assistant Professor of Chemical Engineering & Biological Engineering at the University of California, Santa Barbara. Prior to arriving at UCSB, Dr. Mukherjee completed a James G. Boswell fellowship in Molecular Engineering at Caltech (working with Prof. Mikhail Shapiro) and obtained his Ph.D. in chemical and biomolecular engineering from the University of Illinois, Urbana-Champaign. The primary focus of the research in Dr. Mukherjee's laboratory is the development of genetic reporters for precise measurements of biological functions, largely using magnetic resonance imaging (MRI). This research program aims to address the need for innovative genetic tools to unravel the functional architecture of complex biological systems, such as the mammalian brain; and advance the clinical development of gene- and cell-based therapies for various cancers and central nervous system disorders. The Mukherjee lab's research is highly interdisciplinary, incorporating concepts from molecular engineering, synthetic biology, chemical biology, and biomedical imaging to create novel genetic technologies.. Research in the Mukherjee group has been consistently supported by the NIH, Army, and foundations and recognized with notable awards, including an Outstanding Young Investigator Award (NIH MIRA), a Discovery Award from the DoD, the NARSAD Young Investigator Award from the Brain & Behavior Research Foundation, and a 2022 Scialog Fellows award in Advanced Bioimaging.

ABSTRACT **Merging synthetic biology with diffusion biophysics to create new genetic tools for deep-tissue imaging**

Synthetic biology, which entails combining genetic parts to generate new biotechnology capabilities, has made significant strides in developing cell-based therapies, gene editing technologies, and designer gene networks. In our laboratory, we utilize this approach to find innovative solutions for persistent challenges in the creation of sensitive and responsive molecular-genetic tools for non-invasive deep-tissue imaging. In this talk, I will briefly summarize three recent advancements stemming from this effort. First, we successfully increased the sensitivity of MRI reporter genes to detect a small number of genetically labeled cells by combining genetic tools to increase cellular water diffusion and paramagnetism. Second, we developed a modular approach for programming genetic circuits for MRI-based biosensing based on the regulation of intracellular protein trafficking in response to biochemical events, such as protease activity and protein interactions. Finally, we created conditionally destabilized MRI reporters to image enzyme activity in prodrug-based cancer gene therapy. These advances have the potential to establish new capabilities for basic research on disease mechanisms and biomedical applications, including the development of cell- and gene-based therapies and noninvasive diagnostics for cancer and neurological diseases.

BIOS



Hamideh Parhiz, PharmD., PhD.
Research Assistant Professor, University of Pennsylvania

Hamideh Parhiz, PharmD, Ph.D. is a Research Assistant Professor in the Perelman School of Medicine at the University of Pennsylvania where she leads the targeted LNP delivery program. Her expertise is developing novel nucleic acid delivery systems including a new generation of targeted LNP-mRNA therapeutics for a variety of non-vaccine applications such as blood gene disorders, cancer, fibrosis, and acute inflammatory conditions. Hamideh's work has resulted in the publication of more than 40 papers including two papers in Science magazine and several patents. Her work in designing an efficient targeted LNP-mRNA platform is now the basis for academic programs as well as industrial product developments in companies such as Capstan Therapeutics.

ABSTRACT

Cell-specific Targeted Nucleic Acid Nanomedicine in Oncology and beyond

In vivo cellular reprogramming via targeted delivery of RNA-based therapeutics to selective cells could be highly valuable. In this talk, I will describe selective *in vivo* targeting of mRNA therapeutics and interventions to specific cells and cell subtypes such as T cells and hematopoietic stem cells (HSCs) via antibody-modified lipid nanoparticles. I will also discuss the potential applications we explored with this platform technology.



David Piwnica-Worms, M.D., Ph.D,
Professor and Chair, Department of Cancer Systems Imaging, University of Texas MD Anderson Cancer Center
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Dr. Piwnica-Worms has been involved with biochemistry and molecular imaging research for more than 35 years. His research focuses on the development and use of non-invasive imaging technologies to advance the understanding of human health and disease. A pioneer in the field of molecular imaging, Dr. Piwnica-Worms created several innovative genetically-encoded reporter strategies to visually capture and measure biological processes in living animals, model systems and humans at the molecular and cellular level using remote imaging detection methods, such as positron emission tomography (PET), fluorescence, and bioluminescence imaging. These non-invasive imaging strategies can interrogate protein processing, protein-protein interactions, gene expression and flux through metabolic pathways in real-time in cells, live animals, and are increasingly useful in understanding signal transduction and pathobiology of disease to facilitate development of effective therapies. Most recently, his

lab has focused on targeting innate immunity in cancer and inflammation.

Dr. Piwnica-Worms received his M.D./Ph.D. degrees from Duke University, and completed residency training in Radiology at the Brigham and Women's Hospital. Before joining MD Anderson 10 years ago, he was a faculty member at Washington University Medical School in St. Louis for nearly 20 years as director of the Molecular Imaging Center and the BRIGHT Institute (Bridging Research with Imaging, Genomics and High-throughput Technologies). He is a founding Fellow of the Society for Molecular Imaging, an elected Fellow of the American Association for the Advancement of Science, and an elected Member of the National Academy of Medicine.

ABSTRACT

Translation of [¹⁸F]4FN, a redox-tuned radiopharmaceutical for PET imaging of innate immunity activation

High-redox-potential reactive oxygen species and reactive nitrogen species (ROS/RNS), generated by NADPH oxidase-2 (NOX2), myeloperoxidase (MPO) and related enzymes, are key effector molecules of innate immunity. High-redox-potential radicals are difficult to distinguish by imaging from less potent ROS/RNS functioning as background biological signaling molecules (NO, H₂O₂). Here we present 4-[¹⁸F]fluoro-1-naphthol ([¹⁸F]4FN), a redox-tuned radiopharmaceutical that selectively binds proteins and cells when oxidized by human MPO and related peroxidases of activated innate immunity. First-in-human studies have been performed and [¹⁸F]4FN has demonstrated high quality PET images with favorable excretion profiles, safe dosimetry, and high SNRs foci demonstrated in a survey of inflammatory lesions in biomedicine and cancer.



Vladimir Ponomarev, MD, PhD
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Vladimir Ponomarev MD, PhD is an Associate Attending within the Department of Radiology at Memorial Sloan Kettering Cancer Center, who focuses on the development of new multimodal imaging approaches for specific applications, such as sequential in vivo imaging studies in cancer biology, cancer immunotherapy, and radiation sciences. His lab interests include developing widely applicable methods for in vivo, noninvasive imaging of molecular-biological processes in cancer-specific cell therapies and monitoring their efficacy using multimodality molecular imaging approaches, including optical, magnetic resonance, and nuclear techniques. Supported by the NIH, he has developed a significant individual research program focusing on theranostic applications of genetically targeted T-lymphocytes in cancer patients.

ABSTRACT Evolution of reporter tools for molecular imaging: from bench to bed

The pre-clinical and translational applications of noninvasive in vivo reporter gene imaging include (i) quantitative monitoring of the gene therapy vector and transduction efficacy in clinical protocols by imaging the location, extent, and duration of transgene expression; (ii) monitoring cell trafficking, targeting, replication, and activation in adoptive T cell and stem/progenitor cell therapies; and (iii) assessments of endogenous molecular events using different inducible reporter gene imaging systems. While pre-clinical use of regional and whole-body imaging heavily relies on xenogeneic optical reporters, the clinical application of reporter tools will expand over the next several years, with an emphasis on the development and use of non- and low-immunogenic reporter systems.



John A. Ronald, Ph.D.

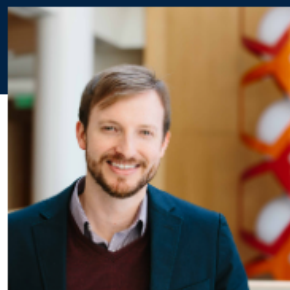
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Dr. John Ronald is the Co-Director of the Imaging Laboratories at the Robarts Research Institute at Western University and an Associate Professor in Medical Biophysics. He completed his doctoral studies at Western and a postdoctoral fellowship at Stanford University. His lab combines advances in molecular and synthetic biology with multimodal imaging to build new tools for early detection and treatment of cancer, as well as non-invasive monitoring of cellular therapies. Recent advances have included monitoring of lentiviral-engineered and CRISPR-edited chimeric antigen receptor T (CAR-T) and NK (CAR-NK) cells and visualizing antigen-specific immune-cancer cell communication with molecular magnetic resonance imaging.

ABSTRACT **Molecular-Genetic Imaging of Synthetic Receptor Cancer Immunotherapies**

Cellular immunotherapies have revolutionized blood cancer treatment by employing synthetic receptors to target cancer antigens. Now, these therapies are showing promise for solid tumors, although patient response varies widely and on-target, off-tumor effects can be severe. Molecular-genetic imaging, a non-invasive method using reporter genes, offers crucial insights into cell fate post-transfer. In this presentation, I'll discuss our efforts in creating advanced imaging tools to monitor synthetic immunotherapies. Specifically, I'll showcase our research on tracking CRISPR-edited chimeric antigen receptor T (CAR-T) cells using positron emission tomography (PET) in ovarian cancer. Additionally, I'll delve into our exploration of synthetic Notch (synNotch) systems for visualizing T and NK cell interactions with cancer cells, employing bioluminescence imaging and magnetic resonance imaging (MRI).



Kole Roybal, Ph.D.

Associate Professor and Director, UCSF and the Parker Institute for Cancer Immunotherapy

Dr. Roybal is the Director of the UCSF Parker Institute for Cancer Immunotherapy and an Associate Professor in the Department of Microbiology and Immunology. His lab has focused on the development of advanced engineered receptor systems (e.g. synNotch, SNIPRs, and CARs) that allow for the precise detection of tumors and the customization of the therapeutic response specifically at the site of disease. His mission is to engineer and distribute a comprehensive toolkit of clinically optimized molecular parts including new receptors and therapeutic signaling circuits that can be deployed in a broad range of cell-based therapeutics for diseases such as cancer and autoimmunity.

He was awarded the Sartorius and Science Magazine Prize for Regenerative Medicine and Cell Therapy in 2017, the NIH New Innovator Award in 2018, and the Cancer Research Institute STAR Award in 2022. He has also founded next-generation cell therapy companies based on his body of work including Cell Design Labs (now a Gilead company), Arsenal Bio, Dispatch Therapeutics, and Moonlight Bio.

ABSTRACT **Toward the Development of Synthetic Immunity to Cancer**

Cell therapies are transforming how we treat cancers and other diseases. I will discuss 1) new receptor designs that allow cells to sense a broad range of disease-related cues and designer ligands and induce custom gene programs and 2) new strategies to enhance therapeutic T cell function with evolutionarily selected mutations found in T cell malignancies.



Mark A Sellmyer, M.D., Ph.D.

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Dr. Mark A. Sellmyer is an Assistant Professor in the Radiology Department with a secondary appointment in the Department of Biochemistry & Biophysics at the University of Pennsylvania (UPenn) Perelman School of Medicine. He received his B.S. in Chemistry from M.I.T. in 2004 (research with Dr. Joe Jacobson) and his MD/PhD in Chemical and Systems Biology (Drs. Tom Wandless and Chris Contag) from the Stanford Medical Scientist Training Program in 2012. His residency was in Diagnostic

Radiology at UPenn in the T32 research track residency and his fellowship was in Nuclear Medicine. He clinical mentor was Dr. David Mankoff and post-doc research mentor was Dr. Robert H. Mach. Since 2018, he has been an attending physician in the Nuclear Medicine Imaging and Therapy Division at UPenn in the tenure track. His lab works on chemical tool development for basic biologic research as well as translational imaging, including nuclear imaging strategies for gene and cell therapies, oncologic imaging, and infectious diseases. Recently his group developed the eDHFR/trimethoprim positron emission tomography (PET) reporter gene and radiopharmaceutical probe pair. In addition to imaging, they have further developed proteolysis targeted chimeric small molecules (PROTACs) based on the potential uses of eDHFR as a genetic tag. Technologies from his lab have been licensed commercially and recent radiopharmaceutical probes from his lab have been applied in human patients. He is a recipient of the NIH Director's DP5 award, the Burrough's Wellcome Fund Career Award for Medical Scientists, and R01 support from the NIH. He is the Co-Director of the Center for Translational Chemical Biology (CTCB) at UPenn and is on the executive committees for the Department of Radiology's Small Animal Imaging Facility and PET Center.

ABSTRACT

Imaging and Controlling Engineered Immune Cell Biology with an Orthogonal Protein Tag

The Sellmyer Lab works at the interface of nuclear molecular imaging, chemical biology, and cancer biology. We are especially interested in using synthetic chemistry to create molecules such as radiotracers that can measure biomarkers for clinical cancer imaging and show that imaging can provide critical information to investigators developing new cellular immunotherapies. Recent examples from our lab include, **1)** The repurposing of *E. coli* dihydrofolate reductase (eDHFR) as a positron emission tomography (PET) imaging reporter gene and **2)** a compact genetic tag for controlling therapeutic protein delivery using custom proteolysis targeting chimeric small molecules (PROTACs). In the context of non-native proteins, like eDHFR, being used in potential human patients, we are paying close attention to issues of immunogenicity which will be discussed and carry important considerations for the synthetic biology field advancing in translational directions.



Mikhail G. Shapiro, Ph.D.
Max Delbrück Professor, Caltech

Mikhail Shapiro is the Max Delbrück Professor of Chemical Engineering and Medical Engineering, an HHMI Investigator, and Director of the Center for Molecular and Cellular Medicine at Caltech. The Shapiro laboratory develops biomolecular technologies allowing cells to be imaged and controlled inside the body using noninvasive methods such as ultrasound. These technologies enable the study of biological function *in vivo* and the development of cell-based and gene-based diagnostic and therapeutic agents. Mikhail received his PhD in Biological Engineering from MIT and his BSc in Neuroscience from Brown. He conducted post-doctoral research at the University of Chicago and the University of California, Berkeley, where he was a Miller Fellow. Mikhail's awards include the NIH Pioneer Award, the Packard Fellowship, the Pew Scholarship, the Vilcek Prize for Creative Promise, the

Sontag Foundation Distinguished Scientist Award, the Mark Foundation Emerging Leader Award, the Camille Dreyfus Teacher-Scholar Award, the Carl Hellmuth Hertz Ultrasonics Award and the Roger Tsien Award for Excellence in Chemical Biology. More information about the Shapiro Lab can be found online at shapirolab.caltech.edu.

ABSTRACT **Talking to cells: biomolecular ultrasound for deep tissue cellular imaging and biosensing**

The study of biological function in intact organisms and the development of targeted cellular therapeutics necessitate methods to image and control cellular function *in vivo*. Technologies such as fluorescent proteins and optogenetics serve this purpose in small, translucent specimens, but are limited by the poor penetration of light into deeper tissues. In contrast, most non-invasive techniques such as ultrasound and magnetic resonance imaging – while based on energy forms that penetrate tissue effectively – are not effectively coupled to cellular function. Our work attempts to bridge this gap by engineering biomolecules with the appropriate physical properties to interact with magnetic fields and sound waves. In this talk, I will describe our recent development of biomolecular reporters and actuators for ultrasound. The reporters are based on gas vesicles – a unique class of gas-filled protein nanostructures from buoyant photosynthetic microbes. These proteins produce nonlinear scattering of sound waves, enabling their detection with ultrasound. I will describe our recent progress in understanding the biophysical and acoustic properties of these biomolecules, engineering their mechanics and targeting at the genetic level, developing methods to enhance their detection *in vivo*, expressing them heterologously as reporter genes, and turning them into dynamic sensors of intracellular and extracellular molecular signals.



Jerzy O Szablowski, PhD

Accelerating the therapeutic discovery through noninvasive monitoring of the brain, Rice University

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Jerzy Szablowski is an Assistant Professor of Bioengineering and a core member of Neuroengineering Initiative at Rice University where he leads the Laboratory for Noninvasive Neuroengineering. He received his B.Sc. in Biological Engineering from MIT in 2009. Throughout the studies he worked on engineering protein contrast agents for MRI in collaboration with Alan Jasanoff's, Robert Langer, Frances Arnold's research groups, and on developing light activated receptors in Ed Boyden's synthetic neurobiology group. He received his Ph.D. in Bioengineering at Caltech, while working with Peter Dervan in 2015 on programmable therapeutics for modulating gene expression in animal models of cancer. During postdoctoral fellowship in Shapiro Laboratory at Caltech, he developed Acoustically Targeted Chemogenetics (ATAC) the first method enabling noninvasive neuromodulation with simultaneous spatial, cell-type, molecular, and temporal precision. In his laboratory he aims to accelerate discovery of drugs for brain disorders through reengineering the existing therapy development pipelines. To achieve this, he uses molecular technologies for noninvasive control, monitoring, and therapy of the brain. He is a recipient of a number of awards, including the Packard Fellowship for Science and Engineering, DARPA Young Faculty Award (YFA), NIH NIBIB Trailblazer, NARSAD Young Investigator, NIH Director's New Innovator award (DP2), and others.

ABSTRACT

Accelerating the therapeutic discovery through noninvasive monitoring of the brain

Finding new drug targets is problematic and requires lengthy preclinical research. Unfortunately, many of the drug targets are often identified in animal models and do not fully translate to human disease. At the same time, options for investigating the molecular basis of brain disease in humans are limited – with brain biopsy being reserved for few selected cases, and few other options available. In consequence, new therapeutics for brain disorders have among the highest costs of development, lowest clinical trial success rates, and longest development times. To improve drug development process, our lab pioneers new tools to monitor and control specific brain regions with applications in any regionally-defined disease, including neuropsychiatric disorders and brain cancer. Through our work we develop noninvasive therapeutic platforms that can target specific brain regions and treat multiple different disorders. In parallel, we develop noninvasive tools that allow for monitoring molecular information within the brain in living animals and humans, thus providing the ability to better understand the mechanisms underlying disease. We call our approach of noninvasive interfacing with the brain on the molecular level noninvasive neuro engineering.



Laura J van 't Veer, Ph.D.

Strategies to augment imaging features by circulating tumor DNA assessment, University California San Francisco

Dr. Laura van 't Veer, PhD, is a world-renowned molecular biologist whose research focuses on precision medicine to advance patient management. She is co-leader of the Breast Oncology Program at the University of California San Francisco, USA. She co-founded in 2003 the biotech company Agendia (Amsterdam, The Netherlands and Irvine, CA USA), a spin-off of the Netherlands Cancer Institute. From 1991-2010 she was employed at the Netherlands Cancer Institute-Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, where she instigated the Department of Molecular Pathology (1993), the Hereditary Cancer Clinic (1994), and was Division Leader Diagnostic Oncology (2007-2010). As co-inventor of MammaPrint, FDA 510K cleared since 2008, she has made a seminal impact on “rightsizing” the treatment of breast cancer, especially to indicate that a large proportion of patients can consider foregoing chemotherapy when the tumor is MammaPrint low risk. Dr. van 't Veer is currently in the US co-PI of the multicenter adaptive clinical trial I-SPY2 overseeing FDA-IDE ‘Response-Predictive-Subtyping’ companion diagnostics. This neo-adjuvant trial also explores ctDNA assessment as an early surrogate endpoint to monitor treatment response. Further, she leads the molecular risk assessment of the 55,000 women WISDOM study (Women Informed to Screen Dependent on Measures of Risk). She has over 330 peer-reviewed scientific articles and is a co-inventor of 10 patents. Dr. van 't Veer received many awards, among which the prestigious European Union Women Innovator Award, 2nd prize in 2014, the 2015 European Patent Office Inventor Award, is a 2020 PMWC Luminary Award recipient, and a 2020 Giants of Cancer Care awardee.

ABSTRACT **Strategies to augment imaging features by circulating tumor DNA assessment**

Neo-adjuvant chemotherapy treatment of breast cancer patients allows to identify responders based on tumor shrinkage or preferably absence after 6 months of therapy at the time of surgery. Imaging by serial MRI is a non-invasive method to assess response during the 6 months of treatment, and complemented by serial blood draws to measure circulating tumor DNA is a powerful way to early on determine which patients are likely to respond or not. For the latter group this provides the option to switch to other treatments early on.



David M. Wilson, M.D., Ph.D.
Antigen-dependent inducible T-cell reporter system for PET imaging of cancer., University of California San Francisco
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Dr. Wilson is a Professor in the Department of Radiology and Biomedical Imaging at University of California, San Francisco (UCSF) and is faculty in the UCSF Chemistry and Chemical Biology (CCB) graduate program. His M.D. and Ph.D. were from Columbia University, where he trained under Professor Ronald Breslow, a pioneer in biomimetic chemistry. Dr. Wilson is an attending clinical neuroradiologist, and Associate Director of the UCSF T32 program. He is also the Director of the Chemistry, Probes and Molecular Therapy (CPMT) specialized resource group (SRG) reporting directly to the Chair. Dr. Wilson's lab has exploited bacteria-specific metabolism for developing numerous bacteria-targeted techniques using PET, hyperpolarized ¹³C spectroscopy, and deuterium metabolic imaging. Imaging agents developed by his group include [¹¹C]D-methionine, [¹¹C]D-alanine, [¹¹C]PABA, [¹⁸F]N-acetylmuramic acid, several [¹⁸F]-labeled disaccharides generated via chemoenzymatic radiosyntheses including [2-¹⁸F]maltose, and [2-¹³C] hyperpolarized pyruvate/ 2H-enriched sugar alcohols for MRI. He has also worked in analyte sensing, including reactive oxygen species, formaldehyde, and the acidic tumoral microenvironment. Recently he has worked with Dr. Roybal and Shin to develop an inducible reporter system for therapeutic T-cell imaging based on the synthetic intramembrane proteolysis receptor (SNIPR).

ABSTRACT

Antigen-dependent inducible T-cell reporter system for PET imaging of breast cancer and glioblastoma

For the past several decades, chimeric antigen receptor T cell (CAR T) therapies have shown promise in the treatment of cancers. These treatments would greatly benefit from companion imaging biomarkers to follow the trafficking of T cells in vivo. Using synthetic biology, we engineered T cells with a chimeric receptor SyNthetic Intramembrane Proteolysis Receptor (SNIPR) that induces overexpression of an exogenous reporter gene cassette upon recognition of specific tumor markers. We then applied a SNIPR-based positron emission tomography (PET) reporter system to two cancer-relevant antigens, human epidermal growth factor receptor 2 (HER2) and epidermal growth factor receptor variant III (EGFRvIII), commonly expressed in breast and glial tumors respectively. Antigen-specific reporter induction of the SNIPR-PET T cells was confirmed in vitro using GFP fluorescence, luciferase luminescence, and the HSV-TK PET reporter with [¹⁸F]FHBG. T cells associated with their target antigens were successfully imaged using PET in dual xenograft HER2+/HER2- and EGFRvIII+/EGFRvIII- animal models, with > 10-fold higher [¹⁸F]FHBG signals seen in antigen-expressing tumors versus the corresponding controls. The main innovation described is therefore PET detection of T cells via specific antigen-induced signals, in contrast to reporter systems relying on constitutive gene expression.

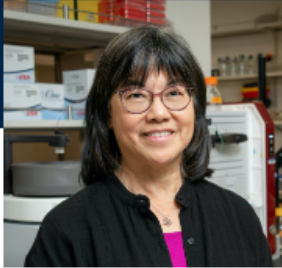


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Dr. Wilson Wong is an Associate Professor of Biomedical Engineering and an Allen Distinguished Investigator at Boston University. He is an expert in immune cell engineering and synthetic biology for therapeutic applications. Dr. Wong's research has been published in numerous high-impact journals, including Nature, Nature Biotechnology, Cell, and Cancer Cell. Dr. Wong has been recognized with multiple academic career awards, including the NIH New Innovator Award, the ACS Synthetic Biology Young Investigator Award, the NSF CAREER Award, and the Allen Distinguished Investigator Award. He has co-founded three companies, with one in the clinical stage. Dr. Wong has a BS in Chemical Engineering from the University of California, Berkeley, and a PhD in Chemical and Biomolecular Engineering from the University of California, Los Angeles. Dr. Wong completed his postdoctoral studies in the laboratory of Professor Wendell Lim at the University of California, San Francisco.

ABSTRACT Engineering Vaccines, Cell and Gene Therapies using Synthetic Biology

In this seminar, I will share with you some of the work that my trainees and colleagues have done on using synthetic biology in various areas, such as foundational circuit engineering, cellular immunotherapy, and vaccines. I will discuss our work on improving the specificity and safety of CAR T cell therapy against cancer using synthetic biology and biomaterials. I will also share our recent discovery on engineering self-amplifying RNA with reduced innate immune response and improved protein expression, leading to a highly potent COVID-19 vaccine as demonstrated in a lethal live virus challenge in mice.



Anna M. Wu, Ph.D.
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Anna M. Wu, Ph.D, is Professor and Chair, Department of Immunology and Theranostics at the Beckman Research Institute of City of Hope and the Fouad Kandeel Chair in Diabetes and Metabolism Research, Arthur Riggs Diabetes and Metabolism Research Institute. She serves as Co-Director, Center for Theranostic Studies at the City of Hope. She previously served as Professor and Vice Chair, Department of Molecular and Medical Pharmacology, Geffen School of Medicine at UCLA, where she was also Director, Cancer Molecular Imaging Program, Jonsson Comprehensive Cancer Center and Co-Associate Director, Crump Institute for Molecular Imaging. She is a past Chair of the California Breast Cancer Research Council, Fellow and Past President of the World Molecular Imaging Society, and Fellow of the Society of Nuclear Medicine and Molecular Imaging. Dr. Wu's research interests include engineered antibodies and proteins for targeting, imaging, and therapeutic applications in cancer and immunology, including the use of SPECT, PET, optical and multimodality and theranostic approaches. She is the Co-Founder of ImaginAb, Inc., which develops and commercializes radiolabeled antibodies for clinical use. Dr. Wu received her A.B. degree in Biochemical Sciences from Harvard University, and a Ph.D. from Yale University in Molecular Biophysics and Biochemistry. Postdoctoral studies were conducted at Yale University and at the University of California, San Francisco.

ABSTRACT

Engineered antibodies for imaging in oncology and immunology: From preclinical models to patients

Antibodies offer unmatched diversity and specificity as recognition molecules, and the success of antibody therapeutics highlights their utility in hitting their targets *in vivo*. Labeling antibodies with positron-emitting radionuclides has led to broad applications of immunoPET, allowing non-invasive, whole-body imaging based on cell surface phenotypes. However, native antibodies are less than ideal as vectors for imaging, exhibiting long circulating half-lives resulting in unwanted background activity. Protein engineering can be employed to design optimal antibody-based imaging agents, providing control over many characteristics including pharmacokinetics, organ of clearance, removal of unwanted effector functions, reduction of immunogenicity, and provision of site-specific conjugation/radiolabeling. We have developed engineered antibody fragments (e.g. minibodies, cys-diabodies) optimized for immunoPET detection of tumor-associated antigens and more recently expanded the approach to detection of key immune cell subsets (such as CD8+ cytotoxic T lymphocytes). Importantly, the use of humanized/human antibodies has enabled translation and clinical applications in oncology, immuno-oncology and other disease areas.



Tatjana Atanasijevic Ph.D.
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Dr. Tatjana Atanasijevic was trained as a physicochemist with broad-based interdisciplinary training, over 15 years or experience in the field of biomedical imaging applied to neuroscience. She is a program director at the National Institute of Biomedical Imaging and Bioengineering, managing portfolios in the areas of Molecular Probes and Imaging Agents, and Nuclear Medicine. The Molecular Probes and Imaging Agents program supports development and biomedical application of molecular probes and imaging agents across all imaging modalities for the visualization, characterization and quantification of normal biological and pathophysiological processes and anatomy in living organisms at the molecular, cellular and organ levels. The Nuclear Medicine program supports the research and development of technologies and techniques that create images using gamma-ray (SPECT) or positron (PET) emissions from radioactive biological agents that are injected, inhaled, or ingested into the body.



Kelly Crotty, Ph.D.

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Dr. Kelly Crotty works in the Center for Strategic Scientific Initiatives (CSSI) within the Office of the Director at the National Cancer Institute (NCI). Kelly applies her research background to develop and evaluate cancer research programs and initiatives, identify and reduce barriers to progress, and communicate research outputs with the goal of advancing cancer research and reducing the burden of cancer on those whose lives are affected by it. She directs the Innovative Molecular Analysis Technologies (IMAT) program, manages collaborative projects for the Informatics Technology for Cancer Research (ITCR) program, and coordinates the CONsortium of METabolomics Studies (COMETS) program. Kelly joined the National Cancer Institute in 2019 as an NCI Communications Fellow. Prior to joining NCI, Kelly was a graduate student at the University of California – San Francisco (UCSF) in Dr. Peter Walter's lab. She used protein and RNA biochemical methods to investigate the Unfolded Protein Response across yeast species. In addition to her dissertation work, she organized an intramural seminar series at UCSF and volunteered with organizations supporting women and minorities in science.



Jerry Li, M.D., Ph.D.

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Dr. Jerry Li manages grants focusing on bioinformatics, deep learning, protein structure modeling, synthetic biology, genomics, and computational biology, at the Division of Cancer Biology, NCI. Along with his DCB responsibilities, Dr. Li is also a member of the Cancer Moonshot Implementation Team, the [NIH Scientific Data Council](#) - Sustainability Subcommittee, and the trans-Agency Animal Genomics Working Group. Dr. Li is also involved with DCB cooperative agreement, NIH Common Fund, and Cancer Moonshot programs. Prior to his work in DCB, Dr. Li was a program director for National Institute of General Medical Sciences (NIGMS) where he managed the Structural Genomics Program. Dr. Li joined DCB for the “opportunity to leverage his experience in genomics and systems biology to contribute to the overall mission against cancer.”



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Dr. Charles Lin is a program director in the Molecular Imaging Branch of the Cancer Imaging Program, Division of Cancer Treatment and Diagnosis at the National Cancer Institute (NCI). Dr. Lin received a Ph.D. in Cell and Molecular Biology. He was a senior investigator in the Center for Cancer Research of the NCI for more than a decade. Dr. Lin joined the NCI after over a decade of service as a tenured professor of Radiation Oncology, Cancer Biology and Cell & Developmental Biology in the Vanderbilt University Medical Center. He was a member of the Vanderbilt-Ingram Cancer Center. Dr. Lin's research focused on the roles of angiogenesis, inflammation and the tumor microenvironment in tumor growth and progression. Dr. Lin has a broad spectrum of expertise in Cancer Biology, Molecular and Cell Biology, Genetics, Cell Signaling and Cancer Imaging Science.



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Dr. Chiayeng Wang is the Chief of Molecular Imaging Branch of the Cancer Imaging Program, Division of Cancer Treatment and Diagnosis at the National Cancer Institute (NCI). She received her Ph.D. in Medical Biochemistry from the University of Calgary followed by a post-doctoral fellowship in Molecular and Cell Biology at the Dana Farber Cancer Institute/Harvard Medical School. Dr. Wang joined National Institutes of Health (NIH) after more than two decades with the University of Illinois-Chicago (UIC) where she was a tenured professor with the Center for Molecular Biology of Oral Diseases, the Oral Biology Department, and the Biochemistry and Molecular Genetics. Her research explored the roles of growth factor signaling network in early mammalian embryogenesis and chromosomal translocations in pediatric cancer pathogenesis. Prior to coming to NCI, Dr. Wang served as a Scientific Review officer in the Surgical Sciences, Biomedical Imaging, and Biomedical (SBIB) Integrated Review Group at the Center for Scientific Review (2014-2017) and a Program Director of the Head and Neck Cancer Biology program at the National Institute of Dental and Craniofacial Research (2017-2020). Dr. Wang has a wide-ranging basic, translational, and clinical research experience in Biochemistry, Developmental Biology, Molecular and Cell Biology, Cancer Biology, Genetics, Cell Signaling, and Applied Imaging Science.



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Dr. Yisong Wang is a program director at the Molecular Imaging Branch in the Division of Cancer Therapeutics and Diagnosis at NCI. He completed his Ph.D. in the molecular biology of lymphocytes and cancer development at Karolinska Institute, Sweden. Dr. Wang started his own laboratory as a PI in 2002 in the Systems Genetics Section, Biosciences Division, Oak Ridge National Laboratory. He joined the Center for Cancer Research at NCI in 2009, and then moved to Georgetown University, serving as an associate professor. Prior to becoming a program director at NCI, he was a program director at NCCIH. Dr. Wang has a broad spectrum of basic and translational cancer research experience, including the molecular mechanistic investigation of cell cycle checkpoint proteins, immune regulatory proteins, microtubule regulatory proteins and phosphatases, as well as the genomics, proteomics, and receptor tyrosine kinase inhibitor therapeutics of lung cancer and thymic epithelial tumors.