2024 MIT Health Science Technology Conference

April 10, 2024 - April 11, 2024

Day 1 | Wednesday April 10, 2024

8:00 AM

Registration and Light Breakfast

9:00 AM

Welcome and Introduction Gayathri Srinivasan Executive Director, MIT Corporate Relations



Gayathri Srinivasan Executive Director MIT Corporate Relations

Dr. Srinivasan is a distinguished scientist who received her PhD in Microbiology from The Ohio State University in 2004, where she contributed to the discovery of the 22nd amino acid, Pyrrolysine (2002). She first came to MIT as an NIH Postdoctoral Fellow in Prof. Tom Rajbhandary's lab, where her research focused on understanding protein synthesis mechanisms in Archaea.

Dr. Srinivasan subsequently moved into the business development and technology licensing space, serving in MIT's Technology Licensing Office, where she helped commercialize technologies in medical devices and alternative energies. She then moved to UMass Medical School's Office of Technology Management in 2009 and to Emory University in Atlanta in 2014 as the Director of Public and Private Partnerships for the Woodruff Health Sciences Center. In 2019, Dr. Srinivasan joined Emory's Office of Corporate Relations as Executive Director, and in 2021, she led the Office of Corporate and Foundation Relations.

Sheryl Greenberg

Program Director, MIT Industrial Liaison Program



Sheryl Greenberg Program Director MIT Industrial Liaison Program

Sheryl Greenberg initiates and promotes the interactions and development of relationships between academic and industrial entities to facilitate the transfer of new ideas and technologies between MIT and companies, and has created numerous successful partnerships. By understanding the business, technology, and commercial problems within a company, and understanding the technologies and expertise of MIT researchers, Greenberg identifies appropriate resources and expertise to foster new technology applications and collaborative opportunities.

Prior to MIT, Greenberg created and directed the Office of Technology Transfer at Brandeis University. In the process of managing intellectual property protection, marketing, and licensing, she has promoted the successful commercialization of technologies as diverse as new chemicals and manufacturing, biotechnology, food compositions, software, and medical devices. She facilitated the founding and funding of new companies, as well as creating a profitable technology transfer program. She also facilitated the patenting, marketing, and licensing of Massachusetts General Hospital technologies. In addition to her cellular, biochemical, and genetic research experience in academic and corporate environments, she has also created intellectual property for medical uses. Greenberg has been an independent intellectual property and business development consultant, is a U.S. Patent Agent, and has previously served the Juvenile Diabetes Research Foundation as Co-Chair of the Islet Research Program Advisory Committee and grant reviewer. She currently also mentors startup companies and facilitates partnering them with large life science and healthcare companies.

Rebekah Miller Program Director, <u>MIT Industrial Liaison Program</u>



Rebekah Miller Program Director MIT Industrial Liaison Program

Rebekah Miller joined the Office of Corporate Relations team as a Program Director in March 2022. Rebekah brings to the OCR expertise in the life sciences and chemical industries as well as in applications including sensors, consumer electronics, semiconductors and renewable energy.

Prior to joining the OCR, Rebekah worked for over a decade at Merck KGaA, most recently as a Global Key Account Manager in the Semiconductor division. Rebekah also served as Head of Business and Technology Development for the Semiconductor Specialty Accounts, during which time she led strategic planning and technology roadmapping.

While at Merck KGaA, Miller established a strong track record in industry-university partnerships, corporate entrepreneurship, and innovation management, with experience in roles spanning Technology Scouting, Alliance Management, and New Business Development. Early in her career, she led early phase R&D projects as a member of the Boston Concept Lab, which focused on technology transfer from academia.

Miller earned her B.A. in Chemistry and Biology from Swarthmore College and her Ph.D. in Chemistry, with a Designated Emphasis in Nanoscale Science and Engineering, from the University of California, Berkeley. She first joined MIT as a postdoctoral associate in the Bioengineering and Material Science Departments.

Natalie Kim

Program Director, MIT Corporate Relations



Natalie Kim

Program Director, MIT Corporate Relations

Dr. Najung "Natalie" Kim is a Program Director at the MIT Industrial Liaison Program. She brings to the Office of Corporate Relations (OCR) expertise in strategic collaboration in life sciences and biotech industries, including cell and gene therapy and Al/ML analytics. Kim comes to OCR from Adjuvant Partners where she has been serving as Senior Consultant, Strategic Partnering, working to connect industry, startups, and academic leaders in the cell and gene therapy sector. Before Adjuvant, Natalie worked at Ajinomoto, where she was Manager of the Research & Innovation Center, facilitating collaborations on preclinical and clinical development of biologics, diagnostics, and cell therapy ancillary products in Asia, Europe, and North America. Prior to Ajinomoto, Kim was a business development manager at Medipost, where she led strategic partnerships in mesenchymal stem cell therapeutics in orthopedic and neurodegenerative applications. Kim also went through her postdoctoral training at the Wake Forest Institute for Regenerative Medicine as a Department of Defense Research Fellow working on translational gene therapy in tissue engineering programs.

Kim earned her B.S. Bioscience and Food Engineering at Handong Global University, her M.S. Medicine at Seoul National University in South Korea, and her Ph.D. Biomedical Engineering at the University of Iowa.

9:15 AM

Machine Learning and the Biomedical Sciences - A Two-Way Street

Caroline Uhler

Machine learning and the biomedical sciences have both experienced revolutions in the 21st century. We will discuss how these two fields are coming together and, in particular, also how today's biomedical questions are motivating new developments in machine learning to help find answers.

9:50 AM

Research using Machine Learning from the Eric and Wendy Schmidt Center at Broad Institute

Wengong Jin Postdoctoral Fellow

Eric and Wendy Schmidt Center at Broad Institute

Modeling antibody-antigen binding is pivotal to drug discovery. Geometric deep learning is a promising paradigm for binding energy prediction, but its accuracy is limited by the size of training data, as high-throughput binding assays are expensive. Herein, we propose an unsupervised binding energy prediction framework named DSMBind, which does not need experimental binding data for training. DSMBind is an energy-based model that estimates the likelihood of a protein complex via SE(3) denoising score matching (DSM). This objective, applied at both backbone and side-chain levels, builds on a novel equivariant rotation prediction network derived from Euler's Rotation Equations. We find that the learned log-likelihood of protein complexes is highly correlated with experimental binding energy across multiple antibody-antigen binding prediction benchmarks. We further demonstrate DSMBind's zero-shot binder design capability through a PD-L1 nanobody design task, where we randomize all three complementarity-determining regions (CDRs) and select the best CDR sequences based on DSMBind score. We experimentally tested the designed nanobodies with ELISA binding assay and successfully discovered a novel PD-L1 binder. In summary, DSMBind offers a versatile framework for binding energy prediction and binder design.

Tavor Baharav Postdoctoral Fellow Eric and Wendy Schmidt Center at Broad Institute

Computational genomics pipelines often rely heavily on alignment of sequencing data to a reference genome; however, this use of a reference genome can bias downstream inference and limit discovery of novel biology. In this talk I will discuss a unifying paradigm for genomic inference, SPLASH, which performs inference directly on raw sequencing data. We demonstrate SPLASH's power for unbiased discovery by identifying viral strain mutations, cell-type-specific isoforms, and Ig and TCR diversity, in addition to tissue-specific transcripts in octopus and geographic and seasonal variation and diatom association in eelgrass.

Jiaqi Zhang

Sequential experimental design to discover interventions that achieve a desired outcome is a key problem in various domains. A predominant example is how to identify optimal genetic perturbations that induce a specific cell state transition. This talk covers our methods for predicting unseen combinatorial perturbational effects and actively selecting the next most-informative experiment for identifying desirable interventions more efficiently.

 10:25 AM
 MIT Professional Education

 Myriam Joseph
 Manager, Business Development and Marketing, MIT Professional Education

10:30 AM Networking Break

10:55 AM

Continuous, Intensified Manufacturing of Gene Delivery Vectors Enabled by High-Throughput Microfluidic Systems Jongyoon Han

Professor of Electrical Engineering, <u>Department of Electrical Engineering & Computer</u> Science (EECS)

Professor of Biological Engineering, Biological Engineering Division



Jongyoon Han

Professor of Electrical Engineering, <u>Department of Electrical Engineering & Computer</u> <u>Science (EECS)</u> Professor of Biological Engineering, <u>Biological Engineering Division</u>

Dr. Jongyoon Han is currently a professor in the Department of Electrical Engineering and Computer Science and the Department of Biological Engineering, Massachusetts Institute of Technology. He received B.S.(1992) and M.S.(1994) degree in physics from Seoul National University, Seoul, Korea, and Ph.D. degree in applied physics from Cornell University in 2001. He was a research scientist in Sandia National Laboratories (Livermore, CA), until he joined the MIT faculty in 2002. He received NSF CAREER award (2003) and Analytical Chemistry Young Innovator Award (ACS, 2009). His research is mainly focused on applying micro/nanofabrication techniques to a very diverse set of fields and industries, including biosensing, desalination / water purification, biomanufacturing, dentistry, and neuroscience. He is currently the lead PI for MIT's participation for NIIMBL (The National Institute for Innovation in Manufacturing Biopharmaceuticals).

With the explosive growth in cell and gene therapy during the last decade, manufacturing of high quality gene delivery vectors (AAVs and Lentiviruses) now poses a critical bottleneck for the industry. In this presentation, I will introduce a continuous, intensified HEK293 bioprocessing platforms enabled by high-throughput microfluidic systems. Membrane-free vector harvesting by high-throughput inertial microfluidic system could be used to achieve intensified perfusion culture of host cells, and generated vectors are harvested continuously in order to minimize the loss and degradation. We believe that intensification of upstream vector bioprocessing would lead to a significant increase in productivity and reduction in reagents as well as GMP space needs, eventually resulting in reduction in the cost of gene and cell therapies of the future.

11:30 AM

MIT Startup Exchange Lightning Talks Ariadna Rodenstein Program Manager, MIT Startup Exchange



Ariadna Rodenstein Program Manager MIT Startup Exchange

Ariadna Rodenstein is a Program Manager at MIT Startup Exchange. She joined MIT Corporate Relations as an Events Leader in September 2019 and is responsible for designing and executing startup events, including content development, coaching and hosting, and logistics. Ms. Rodenstein works closely with the Industrial Liaison Program (ILP) in promoting collaboration and partnerships between MIT-connected startups and industry, as well as with other areas around the MIT innovation ecosystem and beyond.

Prior to working for MIT Corporate Relations, she worked for over a decade at Credit Suisse Group in New York and London, in a few different roles in event management and as Director of Client Strategy. Ms. Rodenstein has combined her experience in the private sector with work at non-profits as a Consultant and Development Director at New York Immigration Coalition, Immigrant Defense Project, and Americas Society/Council of the Americas. She also served as an Officer on the Board of Directors of the Riverside Clay Tennis Association in New York for several years. Additionally, she earned her B.A. in Political Science and Communications from New York University, with coursework at the Instituto Tecnológico y de Estudios Superiores de Monterrey in Mexico City, and her M.A. in Sociology from the City University of New York.

Hieu Le Mau Director of Operations Zeta Surgical

Bettina Hein Founder and CEO juli Health

Sean Matsuoka Co-Founder & COO General Prognostics

James Flanigon CEO Honeycomb Biotechnologies

Uyanga Tsedev Co-Founder and Chief Scientific Officer Gensaic

Helena de Puig Guixe CEO Externa Bio

Konstantinos Tsioris Co-Founder & President OneCyte Biotechnologies

James Ryan Chief Revenue Officer Epicore Biosystems

Carlos Castro-Gonzalez Co-Founder & CEO Leuko Labs

Sadegh Riazi Co-Founder & CEO Pyte 12:25 PM

MIT Hacking Medicine

Zahra Kanji Director MIT Hacking Medicine

12:30 PM

Lunch with Startup Exhibit

1:30 PM

Engineering Vaccine Delivery Ana Jaklenec Principal Research Scientist and Principal Investigator, David H. Koch Institute for



Principal Research Scientist and Principal Investigator David H. Koch Institute for Integrative Cancer Research

Dr. Ana Jaklenec, a principal research scientist and principal investigator at the David H. Koch Institute for Integrative Cancer Research at MIT, is a leader in the fields of bioengineering and materials science, focused on controlled delivery and stability?of therapeutics for global health. She has over 15 years of experience and is an inventor of several drug delivery technologies that have the potential to enable equitable access to medical care globally. The Jaklenec lab at the Koch Institute is developing new manufacturing techniques for the design of materials at the nano- and micro-scale for self-boosting vaccines, 3D printed on-demand microneedles, heat stable polymer-based carriers for oral delivery of micronutrients and probiotics, and long-term drug delivery systems for cancer immunotherapy. She has published over 100 manuscripts, patents, and patent applications and has founded three companies, Particles for Humanity, VitaKey, and OmniPulse Biosciences.

Engineering translatable technologies to help global populations, and especially in developing countries has been met with various challenges related to infrastructure, patient access, and cold chain. I will present how polymers can be leveraged with engineering design to develop solutions for global health. For example, the development of the SEAL (StampEd Assembly of polymer Layers) technology that allows controlled pulsatile release of biologics days to months after injection, for single-injection self-boosting vaccines and cancer immunotherapy will be discussed. Additionally, the design of a microneedle vaccine printer that enables decentralized manufacturing of thermostable COVID-19 mRNA vaccine will be presented.

An Injectable Hydrogel Particle Platform Enabling High Concentration Delivery of Biologics Patrick S. Doyle Robert T. Haslam (1911) Professor Singapore Research Professor, MIT Chemical Engineering

Patrick S. Doyle Robert T. Haslam (1911) Professor Singapore Research Professor MIT Chemical Engineering

Patrick Doyle, a Chemical Engineering Professor at MIT, is renowned for his extensive research interests encompassing fundamental studies of single DNA molecules, nanoemulsions, nanofluidic/microfluidic devices, and innovative technologies for detecting DNA, miRNA, and proteins. Within his research group, a significant thrust involves leveraging microfluidics and soft matter concepts for pharmaceutical formulations. Another key focus is the development of barcoded technologies for sensitive miRNA detection, with impactful applications in cancer research and anti-counterfeiting measures.

Beyond his academic pursuits, Patrick Doyle has left an indelible mark as the co-founder of startup companies Firefly Bioworks (acquired by Abcam in 2015) and Motif Micro (acquired by YPB Systems in 2018). His engagement with numerous companies extends to roles as a consultant, Scientific Advisory Board (SAB) advisor, and participation in sponsored research within his lab. Adding to his diverse portfolio, Patrick serves as the Graduate Officer in the Chemical Engineering Department at MIT.

Specializing in micro- and nano-fluidics, multiplexed sensing, DNA biophysics, nanoemulsions, colloids, rheology, Brownian dynamics simulations, and particle engineering in Pharma, Patrick Doyle continues to be a visionary leader and innovator in the field.

View full bio

The fast pace of breakthroughs in cancer immunotherapy, combined with the new paradigm of moving toward high-concentration dosages, is generating new challenges in the formulation of biologics, especially monoclonal antibodies (mAbs). Subcutaneous administration is a desired route for mAbs. However, formulating mAbs for small injection volumes at high concentrations with suitable stability and injectability is a significant challenge. Here, I will present a platform technology that combines the stability of solid forms of antibodies (crystalline or amorphous) with the injectability and tunability of soft hydrogel particles. I will discuss application of this approach to formulate anti-PD-1 antibody pembrolizumab and human immunoglobulin G. *In vitro* and *in vivo*performance of the formulations will be discussed.

2:40 PM

Microfluidic Flow Dynamics for Health: Bridging Experimental and Computational Approaches for Precision Medicine Qin (Maggie) Qi James R. Mares '24 Career Development Chair Assistant Professor, <u>MIT Chemical</u>



Qin (Maggie) Qi James R. Mares '24 Career Development Chair Assistant Professor MIT Chemical Engineering

Dr. Qin (Maggie) Qi is the James R. Mares '24 Career Development Chair Assistant Professor in Chemical Engineering at the Massachusetts Institute of Technology. Her research applies fluid mechanics and transport principles to engineer soft materials for medical applications. She received her Ph.D. in chemical engineering with Prof. Eric Shaqfeh at Stanford University in 2018, where she won the T.S. Lo Fellowship and Stanford Graduate Fellowship. There, she also collaborated with the Royal College of Surgeons and BD Biosciences to develop a diagnostic device for various bleeding disorders. She then conducted postdoctoral research with Prof. Samir Mitragotri at the Wyss Institute of Biologically Inspired Engineering at Harvard University, where she developed a subcutaneous-tissue-on-a-chip model for pharmacokinetic testing (licensed to Sanofi). She was elected to the inaugural class of MIT Rising Stars in Chemical Engineering. She recently received the FY23 MIT research support committee award and was named a Science Influencer Mentor sponsored by the FDA.

Microscopic flows in a biological environment play a remarkable role in regulating human health, from disease causes to driving forces behind diagnostics and therapeutics. Its influence on other living organisms also has far-reaching impact in energy and environment. Such flow-induced dynamic effects, however, are often overlooked in engineering designs due to limitations in existing research toolsets. As a result, conventional biological and medical research face various challenges in accuracy, cost and translational success. In this talk, I will present our group's work on applying fluid mechanics principles to design biomaterials, cell therapies and pharmacological models. We develop both experimental (in vitro) and computational tools mimicking a dynamic biological flow environment. The combination of these new tools enables us to reduce the use of animal models and shorten the preclinical research timeline while achieving tailor-made design outcomes towards precision medicine.

3:15 PM

Networking Break

Owen Leddy

T cell recognition of Mycobacterium tuberculosis (Mtb)-specific peptides presented on major histocompatibility complex class I and II (MHC-I/II) contributes to immunity to tuberculosis (TB), but the principles that govern the presentation of Mtb antigens on MHCs are incompletely understood. We hypothesized that addressing this knowledge gap would accelerate TB vaccine development for use in diverse human populations. We utilized mass spectrometry (MS) analysis to identify the repertoire of peptides presented on MHCs by Mtbinfected primary human phagocytes. We revealed that substrates of Mtb's type VII secretion systems (T7SS) are overrepresented among Mtb-derived peptides presented on MHC-I. Quantitative, targeted MS showed that Mtb's ESX-1 secretion system is required for the presentation of Mtb antigens on MHC-I. This system is notably absent in attenuated mycobacterial strains currently used for immunization against TB. We next established a biochemical workflow for the identification of antigens presented on MHC-II. These studies revealed Mtb protein antigens that could be presented on MHC-II by human phagocytes expressing a range of MHC-II alleles. We leveraged these discoveries to develop a workflow to evaluate new vaccine candidates for their capacity to generate peptide-MHC complexes in human antigen-presenting cells that are identical to those generated during Mtb infection, a potentially critical pre-clinical screening step. Our study identifies Mtb antigens presented on MHCs that could serve as targets for TB vaccines and reveals potential explanations for the limited efficacy of existing TB vaccines in human populations.

4:20 PM

Tissue-Specific Control of T Cell Responses

Harikesh Wong Assistant Professor of Biology, MIT Department of Biology Core Member Ragon Institute of Mass General, MIT, and Harvard

T cells are pivotal in mounting protective responses against pathogens and tumors, yet their activity entails a critical balance to avoid detrimental host tissue damage. This trade-off necessitates mechanisms that continually adjust the magnitude of T-cell responses, both in time and space. In physiological tissue environments, such control involves coordinated communication among multiple cell types, resulting in intercellular regulatory circuits. While this concept has become increasingly appreciated, in most instances, it fails to account for a critical variable: not all tissues are the same. Indeed, tissues differ markedly in their functions, selection pressures, and capacities for regeneration, implying that the trade-offs between effective host defense and the risk of collateral damage may be tissue-specific. We hypothesized that T cell regulatory circuits are uniquely adapted to the specific demands and characteristics of each tissue type, leading to variable immune responses across the body. To explore this concept, we employed high-resolution multiplexed imaging and computational approaches to examine the baseline variations in regulatory circuits across different tissues, such as barrier sites, endocrine organs, and reproductive organs. Our preliminary data has revealed distinct patterns of T cell regulation that correlate with tissuespecific attributes, suggesting a nuanced framework of immune control that is finely adjusted to the local tissue context. These findings challenge the one-size-fits-all view of immune regulation and open new avenues for understanding how tissue-specific immune responses contribute to health and disease.

4:55 PM

An Emerging Era: Conformable Ultrasound Electronics

Canan Dagdeviren Associate Professor of Media Arts and Sciences LG Career Development Professor of Media Arts and Sciences <u>MIT Media Lab</u>

Conformable electronics are regarded as the next generation of personal healthcare monitoring and remote diagnosis devices. In recent years, piezoelectric-based conformable ultrasound electronics (cUSE) have been intensively studied due to their unique capabilities, including nonradiative monitoring, soft tissue imaging, deep signal decoding, wireless power transfer, portability, and compatibility. In this talk, recent advancements in wearable ultrasound technologies will be presented with applications spanning from early breast detection to transdermal drug delivery.

5:30 PM

Networking Reception

Day 2 | Thursday April 11, 2024

9:00 AM

Welcome and Introduction

9:15 AM

Translating Spatial RNA Atlas to Tissue Function and Dysfunction Xiao Wang Assistant Professor, MIT Department of Chemistry Core Member, Broad Institute



Assistant Professor, MIT Department of Chemistry Core Member Broad Institute

Xiao Wang is a core institute member of the Broad Institute of MIT and Harvard and an assistant professor in the Department of Chemistry at MIT. She started her lab in 2019 to develop and apply new chemical, biophysical, and genomic tools to better understand tissue function and dysfunction at the molecular level. Xiao conducted postdoctoral research at Stanford University with Prof. Karl Deisseroth. She received her B.S. in Chemistry and Molecular Engineering from Peking University in 2010 and her Ph.D. in Chemistry from the University of Chicago in 2015, mentored by Prof. Chuan He.

Spatially charting molecular cell types at single-cell resolution across the entire threedimensional (3D) volume of the brain is critical to illustrating the molecular basis of the tissue anatomy and functions. Recent development of spatial transcriptomic methods has enabled scalable profiling of transcriptome-defined spatial cell atlas. Yet, there is still a big gap between spatial cell atlas and tissue function. In this presentation, I will introduce a few experimental and computational advances in the mapping of RNA life cycle in our lab that further enable multi-modality deep profiling of cell types and states in situ, bridging singlecell molecular profiles with single-cell functional status in intact biological tissues and accelerating gene-to-function discoveries in development and diseases.

9:50 AM

3D Genome Structure and Function in Health and Disease

Anders Sejr Hansen Underwood-Prescott Career Development Professor MIT Department of Biological Engineering

Proper regulation of gene expression is essential for cell function, and dysregulation of gene expression is a primary cause of disease. The primary units of gene control in humans are enhancers. Enhancers can be located far away from the genes they control on the linear genome, raising the question of how the cell ensures that the right enhancer contacts and activates the right gene. We will present new super-resolution live-cell imaging and 3D genomics methods we have developed to begin to answer this question, what we have learned from these studies, and how we are beginning to use these technologies to translate findings from human genetics into a better understanding of how 3D genome misfolding causes disease.

10:25 AM

Networking Break

10:55 AM	Exploiting Carbohydrate Recognition in Health and Disease
	Laura L. Kiessling Novartis Professor of Chemistry <u>MIT Department of Chemistry</u>
	Blueprints for agents regulating immune responses (vaccines or tolerizing agents) are needed. The design principles have been elusive because many immune system receptors can transmit signals that lead to either immunity or tolerance; therefore, a molecular understanding is needed. Our group is interested in how cell surface glycans of foreign cells (pathogens, cancer cells) influence immune responses and how such information can be co-opted to combat disease. To this end, we are generating small molecules and polymers as chemical probes to elucidate the different combinations of signals that give rise to tolerance or immunity. To this end, we found that glycan conjugates can give rise to potent signals that result in anti-cancer immunity. This seminar will discuss the relevant design features of these conjugates and the mechanisms underlying their activity against tumors.
11:30 AM	Protein Design with Generative AI
	Jason Yim Ph.D. Candidate, (PI: Tommi Jaakkola) <u>MIT Computer Science and Artificial Intelligence Laboratory (CSAIL)</u>
	Deep learning has enabled considerable progress in protein structure prediction and design. In particular, the same technology underlying ChatGPT and DALL-E is rapidly being integrated into the workflows for de novo protein design. I will describe our work on this recent progress, RoseTTAFold Diffusion (RFdiffusion), that has enabled a generative AI framework for a wide range of protein design challenges. At the same time, generative AI is far surpassing the capabilities of traditional methods. These challenges span designing binder, enzymes, and peptides that have therapeutic applications. I will discuss the innovations, challenges, and future outlook of how generative AI will enable advancements in protein design.
12:05 PM	Adjournment with Boxed Lunch