MIT Industrial Liaison Program Faculty Knowledgebase Report

2022 MIT Health Science Technologies Conference

April 12, 2022 9:00 am - 5:00 pm

8:00 AM - 9:00 AM  Registration with Light Breakfast
Welcome and Introduction
John Roberts
Executive Director (Interim), MIT Corporate Relations

John Roberts has been Executive Director of MIT Corporate Relations (Interim) since February 2022. He obtained his Ph.D. in organic chemistry at MIT and returned to the university after a 20-year career in the pharmaceutical industry, joining the MIT Industrial Liaison Program (ILP) in 2013. Prior to his return, John worked at small, medium, and large companies, holding positions that allowed him to exploit his passions in synthetic chemistry, project leadership, and alliance management while growing his responsibilities for managing others, ultimately as a department head. As a program director at MIT, John built a portfolio of ILP member companies, mostly in the pharmaceutical industry and headquartered in Japan, connecting them to engagement opportunities in the MIT community. Soon after returning to MIT, John began to lead a group of program directors with a combined portfolio of 60-80 global companies. In his current role, John oversees MIT Corporate Relations which houses ILP and MIT Startup Exchange.

Sheryl Greenberg
Program Director, MIT Corporate Relations

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.

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CAR T cell therapies for relapsed/refractory hematologic malignancies induce frequent deep clinical responses in patients who failed all other treatment options. While these results are game changing, the field is only scratching the surface of the potential benefit gene and cell therapies can provide. Future advances include discovery of novel target antigens, extension of CAR T cell clinical benefit to solid tumors, logic gated engineering designs, advances in manufacturing, targeted in situ gene delivery, and off-the-shelf immunologically stealth approaches. The above will be broadly addressed and work from our group developing and translating CAR T cell therapies targeting the novel antigen GPRC5D for myeloma and “OR” gating strategies for hematologic malignancies will be highlighted as examples.

Organoids are tiny, self-organized three-dimensional (3D) tissue cultures derived from stem cells that allow recapitulation of architecture, composition, and physiology of organs. Organoids may be formed by combining individually differentiated cell populations or via the introduction of external cues to human induced pluripotent stem cells (hiPSCs) to mimic stages of human development. However, such approaches may limit intercellular interactions or faithful mimicry of a mature organ’s structure. We employ synthetic gene circuits to genetically engineer human induced pluripotent stem cells (hiPSCs) with transcriptional and post-transcriptional regulatory elements. These networks govern multi-step differentiation of hiPSCs in a cell-specific, semi-automated manner to form 3D liver organoids. Our recent advances in creation and subsequent use of these organoids in toxicology, drug metabolism, and implantation will be presented and discussed.

Self-replicating RNAs termed replicons have begun to be explored as a promising platform technology for vaccines and gene therapy. Upon delivery to host cells, the replicon copies itself and therefore, allows for prolonged and increased transgene expression with a small initial dose. We employ the replicon platform for 1) vaccine development for sustained antigen expression coupled with the intrinsic adjuvanticity of replicons, and 2) cancer immunotherapy to stimulate multiple synergistic pathways of antitumor immunity. In addition, harnessing synthetic biology tools, we are developing next generation replicon platforms that incorporate microRNA-based classifier and small-molecule responsive gene circuits for internal and external regulation of transgene expression, respectively. Our recent advances and directions on gene delivery with replicons will be presented and discussed.
Ariadna Rodenstein
Events Leader
MIT Startup Exchange

Ariadna joined MIT Startup Exchange in a new role as Events Leader in September 2019. She has responsibility for the development and execution of events featuring startups, and for helping to promote collaboration and partnerships between MIT-connected startups and industry. She works closely with the Industrial Liaison Program (ILP), also within Corporate Relations, and with other areas around the MIT innovation ecosystem and beyond. Prior to this, Ariadna worked for over a decade at Credit Suisse Group in New York City and London in a few different roles in event management and later became a Director for client strategy. She has combined her experience in the private sector with work in non-profits as a Consultant and Development Director at the New York Immigration Coalition, Immigrant Defense Project and Americas Society/Council of the Americas. Ariadna also served on the Board of the Riverside Clay Tennis Association in NY for several years. She earned her B.A. in Political Science and Communications from New York University (NYU), also doing coursework at the Instituto Tecnológico y de Estudios Superiores de Monterrey (ITESM) in Mexico City, and her M.A. in Sociology from the City University of New York (CUNY).

Paulo Garcia
CEO & Co-founder
Kytopen

Marinna Madrid
Co-founder
Cellino

Gopi Shanker
Chief Scientific Officer
Tevard Biosciences

Fred Parietti
Founder & CEO
Multiply Labs

Floris Engelhardt
CEO
Kano Therapeutics

Udayan Umapathi
Co-founder & CEO
Volta Labs

Daniel Meyer
CEO
CellChorus

Elisabeth Maida
Co-founder & CEO
Fathom Data

12:15 PM - 1:25 PM
Lunch with Startups Exhibit

LiquiGlide: Friction-reducing coating technology to enhance cell/gene delivery performance
Unlocking the Potential of Life Sciences Innovation by Harnessing the Power of Mission-driven Collaborations

Ran Zheng
CEO
Landmark Bio

We have entered the golden age of biology with an unprecedented explosion of discoveries that could lead to life changing therapies and have profound impact on human health. However, the shortage of manufacturing capacity and expertise in recent years has constrained therapeutic translation especially for the life sciences innovators who explore emerging modalities and unique technologies. Manufacturing scalability, reproducibility and the cost of goods remain as major challenges, while the evolving science and regulatory landscape require continuous learning.

In 2021, Harvard and MIT partnered with Cytiva, Fujifilm Diosynth Biotechnologies and Alexandria Real Estate Equities to bring the best of academia, the life sciences industry, and world-class research hospitals together to accelerate life sciences innovation. Landmark Bio was established to break down the barriers in novel therapeutics development and industrialization. We collaborate with academics, startups and drug developers to take groundbreaking discoveries from bench to clinics by providing capacity and expertise in CMC development and manufacturing. Uniquely positioned as pre-platform and technology agnostic, we help design, de-risk, and develop early innovations into future platforms. Our cross-sector partnership offers an unparalleled academic, industry, hospitals and investor network with a magnetic pull to power biomanufacturing innovation. As a mission-driven organization, we embrace risk and opportunities at the bleeding-edge in order to advance emerging technologies, demonstrate therapeutic potential and improve human health.

Label-Free Biophysical Critical Quality Attributes (CQAs) for Cell Therapy Products

Jongyoon Han
Professor of Electrical Engineering and Professor of Biological Engineering

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).

One of the critical challenges in cell therapy is the lack of reliable, specific, and non-destructive quality attributes, which are sorely needed for all aspects of biomanufacturing of these cells, including donor selection, in-process quality monitoring, and release testing. Most biological and biochemical assays are destructive or perturbative, which limits their utility, especially for autologous cell therapy. In this talk, I will showcase some of the emerging ideas of label-free, biophysical critical quality attributes (CQAs) we have been working on, including magnetic, electrical, and mechanical signatures of cells. Once the strong correlation with biochemical cell phenotypes, these will serve an important role to improve the overall production of both allogeneic and autologous cell therapy products.
Many powerful molecular biology tools have their origin in nature, and, often, microbial life. From restriction enzymes to CRISPR-Cas9, microbes utilize a diverse array of systems to get ahead evolutionarily. We are interested in exploring this natural diversity through bioinformatics, biochemical, and molecular work to better understand the fundamental ways in which living organisms sense and respond to their environment and ultimately to harness these systems to improve human health. Building on our demonstration that Cas9 can be repurposed for precision genome editing in mammalian cells, we began looking for novel CRISPR-Cas systems that may have other useful properties. This led to the discovery of several new CRISPR systems, including the CRISPR-Cas13 family that target RNA, rather than DNA. We developed a toolbox for RNA modulation based on Cas13, including methods for precision base editing. We are expanding our biodiscovery efforts to search for new microbial proteins that may be adapted for applications beyond genome and transcriptome modulation, capitalizing on the growing volume of microbial genomic sequences and building on our bioengineering expertise. We are particularly interested in identifying new therapeutic modalities and vehicles for delivering cellular and molecular cargo. We hope that this combination of tools and delivery modes will accelerate basic research into human disease and open up new therapeutic possibilities.
CAR-NK Cell Therapies for Cancer
Jianzhu Chen
Professor of Biology, Koch Institute for Integrative Cancer Research
MIT Department of Biology

Jianzhu Chen is Professor of Biology at Koch Institute for Integrative Cancer Research and Department of Biology at Massachusetts Institute of Technology (MIT). Dr. Chen received a Ph.D. degree from Stanford University. He was a postdoctoral fellow and then an instructor at Harvard Medical School before he joined the faculty at MIT. Dr. Chen’s research seeks fundamental understanding of the immune system as well as its application in disease intervention. Over the years, Dr. Chen has made significant contributions to a broad area of research in immunology, cancer research, infectious diseases, and animal models of human diseases. His research on lymphocyte homeostasis and immunological memory challenged the prevailing paradigm at the time and revealed unexpected effect of lymphopenia-induced proliferation on memory T cell development. Dr. Chen pioneered innovative research in development of novel mouse models through genetic manipulations and cell complementation and in development of novel anti-microbial, including surface coatings that inactivate microbes on contact, universal anti-influenza siRNAs, and polymer-attached antivirals that minimize drug resistance of influenza viruses. Recently, Dr. Chen’s research activity has focused on development of tumor-specific CAR-NK cells and re-programming macrophages for disease intervention, including cancer, metabolic diseases and infectious diseases.

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Natural Killer (NK) cells and CD8+ cytotoxic T cells are two types of immune cells that can kill target cells through similar cytotoxic mechanisms. With the remarkable success of chimeric antigen receptor-engineered T (CAR-T) cells for treating hematological malignancies, there is a rapidly growing interest in developing CAR-engineered NK (CAR-NK) cells for cancer therapy. Compared to CAR-T cells, CAR-NK cells could offer some significant advantages, including (1) better safety, such as a lack of or minimal cytokine release syndrome and neurotoxicity in autologous setting and graft-versus-host disease in allogeneic setting, (2) multiple mechanisms for activating cytotoxic activity, and (3) high feasibility for “off-the-shelf” manufacturing. We are developing the next generation of CAR-NK cells by combining tumor-specific CAR, additional armors, and cytokine-induced memory-like (CIML) NK cells, with a goal to achieve better tumor-specific targeting, enhanced proliferation and persistence in vivo, resistance to the suppressive tumor microenvironment, and ultimately an effective and durable anti-tumor response in patients.
Recombinant adeno-associated virus (rAAV) is one of the most commonly used platforms for in vivo gene therapy treatments. The reduced toxicity, robust and long-term transgene expression, and ability to transduce both dividing and non-dividing cells as well as target a wide range of tissues have made rAAV the most widely used viral vector. However, the standard method of producing rAAV via transient transfection of mammalian cells, specifically human embryonic kidney 293 (HEK293) cells, typically has low yield and generates a high portion of empty particles, laying extra burden on downstream processing.

To elucidate the mechanisms of rAAV synthesis in HEK293 suspension-adapted cells, we have developed a mechanistic model based on the published understanding of the underlying biology and existing data. Quantitative analysis suggests the misaligned dynamics of capsid and viral DNA production result in the high ratio of empty particles. Through a model-based strategy, we explored a novel transfection method using low-dose multiple transfections in HEK293 cell culture that successfully increased the ratio of full to empty capsids in the viral harvest without compromising the viral titer. Molecular analysis through a next-generation rAAV production model attributed the improvements to changes in the kinetics of viral protein expression and DNA replication. Here, we demonstrate that the use of multiple transfection times is a practical method for increasing the genome titer and improving the percentage of full capsids for rAAV production. Our results also demonstrated the capability to manipulate product composition from an operational standpoint.
Michael Birnbaum
Associate Professor of Biological Engineering
MIT Department of Biological Engineering

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Michael obtained an A.B. in Chemical and Physical Biology at Harvard University in 2008. He then moved to Stanford University, where he completed his Ph.D. in Immunology in 2014. At Stanford, he worked in Professor K. Christopher Garcia’s laboratory, studying the molecular mechanisms of T cell receptor recognition, cross-reactivity, and activation. He then conducted postdoctoral research in Professor Carla Shatz’s laboratory, studying novel roles for immune receptors expressed by neurons in neural development and neurodegenerative disease. Michael joined the Department of Biological Engineering in 2016 as an Assistant Professor.

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Cell and gene immunotherapies are revolutionizing how we treat disease, with multiple FDA-approved therapies that have transformed cancer treatments. However, advances in gene delivery, manufacturing, and therapeutic cargoes are still required to increase the impact and scope of these promising approaches. The Birnbaum laboratory is working to develop approaches that improve the specificity of cellular engineering, and the potency of cells once engineered.

4:50 PM - 6:00 PM
Closing Remarks and Networking Reception