2021 BioMAN Summit
Technologies to Expand the Reach of Cell & Gene Therapies

Thursday, December 16, 2021
A Virtual Event
9:00 AM – 4:30 PM [EST]

9:00 – 9:30 AM	**Welcome** **Anthony J. Sinskey** *Professor of Microbiology | Faculty Director* **MIT Department of Biology | MIT Center for Biomedical Innovation** **Introduction** **Stacy L. Springs** *Senior Director of Programs; Executive Director, Biomanufacturing Initiatives* **MIT Center for Biomedical Innovation** **Summit Framing** **Jacqueline Wolfrum** *Co-director, Biomanufacturing@MIT-CBI; Director, BioMAN* **MIT Center for Biomedical Innovation**
9:30 – 10:50 AM	**Keynote Presentations** Moderator: Stacy L. Springs, **CBI**
9:30 – 10:20 AM	**Bruce Levine** *Barbara and Edward Netter Professor in Cancer Gene Therapy, Founding Director of the Clinical Cell and Vaccine Production Facility (CVPF), Department of Pathology and Laboratory Medicine and the Abramson Cancer Center, Perelman School of Medicine* **University of Pennsylvania** **Engineering Genetically Enhanced T Cells for Clinical Applications** Since the 1990's, we have conducted clinical trials of gene modified T cells. Gene editing has created T cells resistant to HIV infection. Chimeric antigen receptor (CAR) T cells targeting CD19 on B cells leukemias and lymphomas have induced durable complete responses in patients who are relapsed or refractory to all other available treatments. New designs for genetically modified T cells include switches and potency enhancements that will be required for targeting solid tumors. In one such approach, multiplex gene editing was accompanied by lentiviral transduction of a T Cell Receptor against the cancer antigen NY-ESO-1. The first use of CRISPR in the US in humans demonstrated that multiplex human genome engineering is safe and feasible. Translation of these technologies from research bench to clinical application requires knowledge of the critical quality attributes of the engineered cell product and acceptable limits. Determining dose, potency, and anticipating pharmacokinetics of a living, dividing drug presents unique challenges. The road forward for wide patient access to engineered cellular therapies depends not only on scientific progress in targeting, gene modification and cellular manipulation methods, but also on meeting automation, engineering, clinical site onboarding, and health policy challenge.

10:20 – 10:50 AM	**Peter Marks** *Director, Center for Biologics Evaluation and Research* **United States Food and Drug Administration** **Advancing the Development of Cell and Gene Therapies** Individualized cell-based therapeutics and gene therapies will become increasingly important to address the variety of molecular defects present in several thousand serious rare diseases. Some of these therapies may be targeted to as many as a few thousand individuals, but others only may be targeted to one or few individuals. Development of these products poses challenges to the scientific community. For example, how do we obtain substantial evidence of effectiveness and adequate evidence of safety for products for rare diseases, particularly diseases where there may be as few as one patient with the disease? How do we ensure manufacturing quality for products intended to treat one or a few patients? These are some of the questions that must be addressed to facilitate development and access to individualized therapeutics. Although notable progress has been made since the passage of the 21st Century Cures Act in the United States, from the regulatory perspective there are still unanswered questions regarding how to best facilitate the development of such individual therapeutics.
10:50 – 11:05 PM	**Refreshment Break**
11:05 AM – 12:35 PM	**SESSION 1: Innovation in Cell and Gene Therapy Products** Moderator: James Leung, **CBI**
11:05 – 11:35 AM	**Karen Miller** *Senior Vice President, Pipeline Research* **AdaptImmune** **Rising to the Challenge of Solid Tumors: The Promise of Autologous and Allogeneic TCR T-cell Therapies** The promise of cell therapy for people living with cancer has been realized with several Chimeric Antigen Receptor (CAR) T-cell therapies approved for a range of hematological tumors. However, the challenges presented by solid tumors – including low and heterogenous expression of tumor specific antigen targets and challenging tumor microenvironment – have been associated with limited efficacy, to date, of CAR T-cell therapies for these types of cancer. During this presentation, Dr, Karen Miller, SVP Pipeline Research at Adaptimmune, will talk about the potential of autologous and allogeneic TCR T-cell therapies in clinical trials to treat patients with multiple solid tumor indications. The Company has recently shared data with its most advanced therapy, afamitresgene autoleucel, showing promising efficacy and durability data in synovial sarcoma, which will be used to file a licensing application, and initial data in five solid tumors with a next-generation therapy that will be investigated in Phase 2 trials for people with esophageal, esophagogastric junction and ovarian cancers.
11:35 AM – 12:05 PM	**Giuseppe Ciaramella** *President & Chief Scientific Officer* **Beam Therapeutics** **Base Editing for the Treatment of Beta-hemoglobinopathies** Base editing is a next-generation, CRISPR-based gene editing technology that makes precise conversion of one nucleobase to another by virtue of a human deaminase enzyme, directly on the gene, without making double-stranded breaks. Using this technology, we are developing

	two therapeutic products, BEAM-101 and BEAM-102, for the treatment of Sickle Cell Disease (SCD). In the case of BEAM-101, we are using the precision of base editing to reproduce point mutations in the promoter of the human gamma 1 and gamma 2 genes that are normally seen in individuals who have a condition known as Hereditary Persistence of Fetal Hemoglobin (HPFH). These individuals retain high levels of expression of the fetal hemoglobin (HbF) in adulthood and, because of this, they are protected from mutations in the beta globin gene that would otherwise cause sickle cell disease. BEAM-101 has been shown to achieve the highest level of HbF reported pre-clinically so far (65%) and is progressing to clinical studies. BEAM-102 directly corrects the single amino acid Valine that causes the cells to sickle under low oxygen conditions. For BEAM-102, we have engineered a novel base editor, where the active site of the deaminase has been inlaid directly within the CAS protein. Using this editor we are able to convert the Valine at position 6 into an Alanine, thus converting the sickling form of hemoglobin (HbS) to a normal variant known as HbG Makassar, which occurs in ~0.1% of the human population, with greater than 80% efficiency.
12:05 – 12:35 PM	**Robert Kotin** *Adjunct Professor, University of Massachusetts Medical School; Co-founder and Interim Chief Scientific Officer, a new Longwood Funds biotech company* **Scalable Production of Recombinant Adeno-associated Virus Vectors** Despite the rapid growth of recombinant adeno-associated virus (rAAV) gene therapy research, access to high-quality rAAV remains the major limitation to the clinical gene therapy pipeline. Due to the cytotoxicity of the Ad helper gene products as well as cytotoxic or cytostatic effects of the AAV Rep proteins, rAAV production is a transient, terminal process. Thus, introducing the essential genetic information into the producer cells remains the major challenge for large-scale rAAV production. The recombinant baculovirus expression vectors (BEVs) and *Spodoptera frugiperda* (Sf9) cells provide an alternative to transient transfection of human embryonic kidney (HEK) 293 cells. The BEVs replicate and are amplified in the same cell that produces rAAV and the subsequent cell-to-cell spread of the BEVs results in essentially quantitative infection of the culture in any volume bioreactor. In the two BEV system, the AAV vector genome is on one BEV and the second BEV provides the Rep and VP ORFs. In the presence of p5 Rep proteins, the AAV vector genome replicates autonomously from baculovirus. Expression of the Rep and capsid proteins are no longer regulated by the native AAV promoters; therefore, optimal AAV gene expression of the Rep and structural proteins involves engineering the coding sequence to achieve stoichiometric expression of Rep 78, Rep 52, VP1, VP2, and VP3. A systematic approach has been developed to increase the likelihood that the capsid composition is near optimal.
12:35 – 1:20 PM	**Lunch**
1:20 – 4:20 PM	**Session 2: Gene Therapy Manufacturing** Moderator: Paul W. Barone, **CBI**
1:20 – 1:50 PM	**David Schaffer** *Hubbard Howe Jr. Distinguished Professor* *Chemical and Biomolecular Engineering, Bioengineering, Molecular and Cell Biology, and the Helen Wills Neuroscience Institute* **University of California, Berkeley** **Directed Evolution of New Adeno-Associated Viral Vectors for Clinical Gene Therapy**

	Gene therapy –the delivery of genetic material to the cells of a patient for therapeutic benefit– has been increasingly successful in human clinical trials over the past decade, and there are numerous FDA-approved gene therapies. The most successful gene delivery vehicles, or vectors, are based on adeno-associated viruses (AAV); however, vectors based on natural versions of AAV face a number of delivery barriers that limit their efficacy and will thus preclude the extension of these successes to the majority of human diseases. These delivery limitations arise since the parent viruses upon which these vectors are based were not evolved by nature for our convenience to use as human medicines. Unfortunately, due to the highly complex mechanisms of virus-host interactions, there is currently insufficient mechanistic knowledge to enable rational design to be sufficiently successful in creating new vectors. As an alternative, however, we developed the concept of using directed evolution to engineer highly optimized variants of AAV for a broad range of cell and tissue targets. Directed evolution involves the iterative genetic diversification of a biomolecule to create a gene pool and functional selection to isolate variants with optimal properties. Using this approach, we have engineered AAV variants with greatly improved delivery efficiency to multiple organs including the retina; lung, and muscle; targeted delivery to specific cell types; and the capacity to evade immune responses. Our novel AAV variants are currently used in 5 human clinical trials involving delivery to the retina and heart, and two additional clinical trials will be initiated this year. In parallel, the advent of genome editing technologies such as the CRISPR/Cas9 system raises the possibility of using gene delivery not only for gene replacement but for repair or knockout of endogenous genes. We have thus been combining engineered AAVs with CRISPR/Cas9 for a range of applications. The integration of these new technologies –AAV delivery or genome editing machinery– can enable a broad range of basic and therapeutic applications.
1:50 – 2:20 PM	**Richard D. Braatz** *Edwin R. Gilliland Professor of Chemical Engineering* **Massachusetts Institute of Technology** **Tam N. T. Nguyen** *PhD Student, Chemical Engineering* **Massachusetts Institute of Technology** **Rational Design of rAAV Production via Mechanistic Modeling** 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.
2:20 – 2:35 PM	**Refreshment Break**
2:35 – 3:05 PM	**Wade Wang** *Scientist, Technical Operations* **BioMarin** **Overcoming Low Throughout Testing Issues of AAV Using SEC-MALS** Adeno associated virus (AAV) capsids are a leading modality for *in vivo* gene delivery. Complete and precise characterization of capsid particles, including capsid and vector genome concentration, is necessary to safely and efficaciously dose patients. Size exclusion chromatography (SEC) coupled to multiangle light scattering (MALS) offers a straightforward approach to comprehensively characterize AAV capsids, including, but not limited to aggregation profile, size-distribution, capsid content, capsid molar mass, encapsidated DNA molar mass, and total capsid and vector genome titer. Currently, multiple techniques are required to generate this information, with varying accuracy and precision. SEC-MALS can leverage intrinsic physical properties of the capsids and encapsidated DNA to quantify multiple AAV attributes in one 20-min run with minimal sample manipulation, high accuracy, and high precision. As such, SEC-MALS is a powerful tool for product development and process analytics in future gene therapy programs.
3:05 – 3:35 PM	**Scott Manalis** *David H. Koch (1962) Professor of Engineering, Koch Institute for Integrative Cancer Research, Departments of Biological and Mechanical Engineering* **Massachusetts Institute of Technology** **Biophysical Approaches for Process Analytical Technology** Previously we developed a method based on the suspended nanochannel resonator (SNR) that is capable of weighing nanometer sized particles with high precision. Here I will describe how we're using the SNR to quantify the empty:full capsid ratio for a purified Adeno-Associated Virus (AAV) samples in a way that provides a direct readout without the need to calibrate based on serotype. This approach achieves a resolution near 10 zeptograms (corresponding to 1% of the genome holding capacity of the AAV capsid) in a 10-minute sampling window using only a few µL of sample. I will also present recent progress towards using suspended microchannel resonators to provide nondestructive measurements of single-cell biophysical properties (e.g. mass, density and stiffness) with the goal of predicting transfection and vector production yield.
3:35 – 4:20 PM	**Konstantin Konstantinov** *Chief Technology Officer* **Codiak BioSciences** **Industrialization of the GMP Manufacture of Exosome Therapeutics and Opportunities for Further Multifold Process Productivity Increase** Exosome therapeutics are rapidly evolving as a promising new modality in various clinical areas, such as oncology, immuno-oncology, neurology and metabolic diseases, among others. As some of these indications involve large patient populations, the success of exosome therapeutics depends on our ability to manufacture allogenic exosomes at a large scale, with

	high purity and quality, acceptable CoG, and under GMP conditions. Due to the complexity and natural heterogeneity of exosomes, the development of such an advanced production technology is not a trivial task. This presentation will discuss our ability to develop GMP processes to manufacture precisely engineered engEx exosomes from Codiak's pipeline. With two lead programs in clinical trials in cancer patients, and an IND approved for a third program in immuno-oncology this year, we have significantly scaled our GMP production capacity. Our large-scale process uses either 2,000L fed-batch or, more recently, 500L high-density perfusion bioreactors culturing HEK cells at high density in chemically defined media. The bioreactor harvest is processed through a sequence of purification steps yielding exosomes of high potency and purity, and with consistent quality attributes. Opportunities for a further multifold increase of process productivity and reduction of CoG through implementation of integrated continuous biomanufacturing technology will be outlined. This presentation will also review the applicability of the above technology to the manufacture of other ATMPs.
4:20 – 4:30 PM	**Closing Remarks** **Stacy L. Springs** *Senior Director of Programs; Executive Director, Biomanufacturing Initiatives* **MIT Center for Biomedical Innovation**

MIT CBI
Center for Biomedical Innovation

BioMAN
BioMANufacturing Consortium

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9:00 – 9:10 AM	**Welcome Remarks**
9:00 – 9:10 AM	**Stacy L. Springs** *Senior Director of Programs; Executive Director, Biomanufacturing Initiatives* **MIT Center for Biomedical Innovation**
9:10 – 9:20 AM	**Kenneth L. Turner** *President and Chief Executive Officer* **Massachusetts Life Sciences Center** **Cell and Gene Therapy Manufacturing in the Commonwealth** The Massachusetts Life Sciences Center is an economic development and investment agency dedicated to supporting the growth and development of the life sciences in Massachusetts, home to the most verdant and productive life sciences ecosystem in the world. Through public-private funding initiatives, the MLSC supports innovation, research & development, commercialization, and manufacturing activities in the fields of biopharma, medical device, diagnostics, and digital health. Since its creation in 2007, the MLSC has strategically deployed over $700 million in Massachusetts, through a combination of grants, loans, capital infrastructure investments, tax incentives, and workforce programs. These investments have created thousands of jobs, and propelled the development of new therapies, devices, and scientific advancements that are improving patient health and well-being in Massachusetts and beyond.
9:20 – 10:20 AM	**Session 2: Gene Therapy Manufacturing (continued)** Moderator: Stacy L. Springs, **CBI**
9:20 – 9:50 AM	**Claire Davies** *Head of Bioanalytics, US, UK, Amsterdam* **Sanofi** **Automation: Powering the Next Generation of Therapeutics**
9:50 – 10:20 AM	**Cullen Buie** *Co-Founder & Chief Technology Officer* **Kytopen** **Electro-Mechanical Transfection for Scalable Cell Engineering**

	Kytopen is a spin-out of MIT developing proprietary platforms for non-viral delivery of payloads for *ex vivo* cell therapy discovery and manufacturing. The scalable solution leverages electro-mechanical energy to make transfection easier, faster, and more cost-effective than the state-of-the art solutions**.** Kytopen has integrated their platforms with automated liquid handling systems for processing small volumes and also has developed a large volume platform for therapeutic manufacturing applications. This non-viral solution will accelerate the time-to-market of next-generation cell and gene therapies by enabling discovery of therapeutic targets and direct transfer to a scaled manufacturing solution, reducing cell therapy manufacturing complexity and cost. Kytopen recently closed a $32M Series A financing and is actively exploring strategic partnership opportunities. In this talk, we intend to provide a general overview of the non-viral transfection platforms we are developing for *ex vivo* cell therapy discovery and manufacturing for clinically relevant cell types such as T cells, NK cells, and hematapoietic stem cells.
10:20 – 10:40 AM	**Refreshment Break**
10:40 AM – 2:50 PM	**Session 3: Cell Therapy Manufacturing** Moderator: Jacqueline Wolfrum, **CBI**
10:40 – 11:10 AM	**Ran Zheng** *Chief Executive Officer* **Landmark Bio** **Breaking New Ground: Building the Future of Biological Innovation and Manufacturing Today** We all know that innovation is happening faster now than ever before. Phase I and Phase II assets have transitioned 50 percent faster since 2018 than between 2013 and 2018, according to a McKinsey study earlier this year. Investors are following suit, and the amount of money and number of deals involving the biotech sector has continued to grow, even throughout these tumultuous economic times. However, with progress comes challenge. We are still seeing too many bottlenecks in the development of new modalities-from the availability of biological ingredients to scaling of techniques to the execution of clinical trials. In 2021, Harvard and MIT partnered with Fujifilm Diosynth Biotechnologies, Cytiva, and Alexandria Real Estate Equities to bring the best of academia, the life sciences industry, and world-class research hospitals together to accelerate the development and production of novel cell and gene therapies and mRNA products. The result: Landmark Bio, a collective endeavor that seeks to forge a pathway for life sciences innovators to translate leading-edge research into life-changing therapies. Join Landmark Bio CEO Ran Zheng to learn more about this new endeavor, what makes it different, and key takeaways for developing ATMP capabilities for today and tomorrow.
11:10 – 11:40 AM	**Amey Bandekar** *Associate Director, Biologics Drug Product Development & Manufacturing* **Sanofi** **Challenges and Considerations for Lipid Nanoparticle Formulation Development** Lipid Nano Particle (LNP) technology is currently one of the most promising and emerging technologies for delivery of nucleic acid therapeutics. The recent approvals of COVID-19 vaccines have demonstrated the feasibility, manufacturability and clinical safety of lipid based nano carriers. The choice of each lipid component (namely, Ionizable lipid. Helper lipid,

	Cholesterol and Pegylated lipid) that comprises a LNP is critical in determining the in-vivo behavior and efficacy of nucleic acid delivery. In addition, these parameters can be modulated to maneuver and change the biodistribution of LNPs depending on the organ of interest. Further specificity especially for organs that lack endogenous targeting, cellular uptake can be further improved by use of targeting ligands. Hence selecting the right LNP composition based upon the target of interest and gene to be delivered becomes extremely critical. With all the challenges associated it is important to understand the intracellular behavior of LNPs. Here an equimolar mixture of fluorescently labeled nucleic acid and a GFP producing nucleic acid was encapsulated inside the LNP that was manufactured using a microfluidic platform to examine cellular uptake, endosomal release, and intracellular trafficking. This technique and platform allow for comparison of intracellular trafficking and nuclear uptake with different LNP formulations and ionizable lipids employed, enabling improved screening prior to in vivo studies.
11:40 AM – 12:10 PM	**Rajeev Ram** *Professor, Department of Electrical Engineering & Computer Science* **Massachusetts Institute of Technology** **Michael Birnbaum** *Associate Professor, Department of Biological Engineering* **Massachusetts Institute of Technology** **Understanding Cell Therapy Critical Process Parameters and Critical Quality Attributes with a Continuous Perfusion Microbioreactor** With five chimeric antigen receptor (CAR) T cell immunotherapy products currently approved by the FDA for the treatment of hematological cancers, there are increasing efforts to develop novel and better manufacturing technologies and processes for cell therapies to improve efficacy, reduce variability, and reduce cost. To address this possibility, we demonstrate CAR-T manufacturing using the Erbi Breez closed sterile single-use perfusion bioreactor, which operates at a 2 mL working volume and achieve densities in excess of 100e6 cells/mL. We have demonstrated that the perfusion system can perform in-place activation, transduction, and expansion. We show that with improved media exchange rates, cell expansion performance is improved, achieving nearly patient dose levels with more than 400-fold expansion from 0.6 million cells at the point of transduction to more than 200 million cells at 14 days post-transduction at consistently high cell viability of above 95%. These data show that the Breez platform is well suited for cell therapy process development and process characterization studies, and is promising for the production of a cell dosage that is almost sufficient for a patient infusion.
12:10 – 12:50 PM	**Lunch**
12:50 – 1:20 PM	**Richard Anderson** *Senior Director, Manufacturing Science and Technology* **Fate Therapeutics** **Manufacturing of Next-Generation Cellular Immunotherapies using a Novel Induced Pluripotent Stem Cell Platform** Fate Therapeutics (Nasdaq: FATE) is a clinical-stage biopharmaceutical company dedicated to the development of next-generation cellular immunotherapies for cancer and immune disorders. We are pioneering a revolutionary approach to cell therapy – we use renewable master induced pluripotent stem cell (iPSC) lines generated from our proprietary iPSC

	platform to derive cell therapy product candidates that can be delivered off-the-shelf for the treatment of a large number of patients. Our novel manufacturing platform and its application to the production of candidate clinical cell therapy products will be presented. Specific challenges in the scale-up and commercialization of off-the-shelf cell therapies will be discussed. Our programs reflect our dedication and commitment to pioneering ground-breaking science to address severe, life-threatening diseases where the unmet need is significant and the treatment options are limited. Development and application of innovative manufacturing technologies and processes will be pivotal in scaling-up and bringing our novel products to all patients in need.
1:20 – 1:50 PM	**Philip Lee** *Co-Founder and Chief Technology Officer* **Senti Bio** **The Potential of Gene Circuits and the Importance of Building Innovative Cell Therapy Manufacturing Capabilities** With the growing adoption of cell and gene therapies, there is an increased need for gene circuit technologies to control therapeutic activities. We developed four classes of gene circuits that address key limitations in current therapeutic approaches. First, logic gating gene circuits integrate multiple targets to pinpoint diseased cells and spare healthy ones. Second, multi-arming gene circuits can hit multiple disease pathways to reduce disease evasion. Third, regulator dial gene circuits dynamically control activity *in vivo* to address narrow therapeutic windows. Fourth, smart sensor gene circuits precisely detect and respond to disease environments. As Senti Bio's gene circuit platform technologies are applied into clinical applications, a key consideration is the ability to efficiently manufacture these sophisticated potential product candidates at appropriate scale and quality. We are building GMP manufacturing capabilities to focus on gene circuit-enabled allogeneic cell therapies, with an initial objective to flexibly support initial clinical trials for our lead product candidates. Our allogeneic cell process produces over 100 doses in a single clinical batch, with the potential to expand to thousands of doses at future commercial scale. We believe the combination of gene circuit technology with advanced manufacturing capabilities is critical to next generation cell and gene therapies.
1:50 – 2:20 PM	**Krystyn J. Van Vliet** *Associate Provost and Associate Vice President for Research; Michael (1949) and Sonja Koerner Professor, Departments of Materials Science and Engineering and Biological Engineering* **Massachusetts Institute of Technology** **Making Cell Therapies Work for Patients: Defining and Driving Label-Free Critical Quality Attributes** Manufacturing of cell therapies includes a persistent challenge shared by allogeneic and autologous approaches, for a range of target disease and injury indications. What are the attributes of the cell therapy product that map to quality, and more specifically to identity, potency, and therapeutic efficacy? Critical quality attributes can be used to enable real-time and endpoint product release, but also have the potential to enable process analytics that adapt to promote those CQAs during production. Imagine the capacity to monitor and moderate those attributes during production, without the need for labeling cells and with the throughput that qualifies all the cells in the final product. Here we will discuss opportunities and progress in identifying label-free CQAs, including those based on biophysical attributes of the cells, with an eye toward in-line approaches facilitating adaptive culture and real-time release. We

	will focus on mesenchymal stromal cells for regenerative medicine and genetically modified T cells for blood cancers, to illustrate concepts and technologies that complement current at-line and endpoint product characterization.
2:20 – 2:50 PM	**Jongyoon Han** *Professor, Departments of Electrical Engineering & Computer Science & Biological Engineering* **Massachusetts Institute of Technology** **Adventitious Agent Detection in Cell Therapies** In the detection of adventitious agents in bioprocessing, it is necessary to detect the lowest abundance of virus or bacterial cells, often contained in a large volume of the original sample. The current sample preparation workflow is not adequate to handle this challenge, therefore limiting the lower limit of detection regardless of the downstream sensing methodologies used. In this presentation, I will demonstrate that we can address this sample preparation challenge directly by introducing an efficient electrokinetic concentration system, which can concentrate dilute detection targets (various adventitious agents) from a large sample volume (~100mL) into a small volume (as small as ~10pL), achieving an extremely high level of effective signal enhancement for downstream detection. This may allow direct, non-amplifying detection of the target biomolecules, which could enable rapid, real-time monitoring of various targets. Using the system, we have demonstrated that low abundance viral and bacterial targets below ~1CFU/ml can be concentrated and detected reliably by collecting low abundance targets from a large volume of the original sample (1~100mL). Interfacing with both amplifying and non-amplifying detection modalities is showcased**.**
2:50 – 3:00 PM	**Closing Remarks** **Stacy L. Springs** *Senior Director of Programs, Executive Director, Biomanufacturing Initiatives* **MIT Center for Biomedical Innovation**