CMaT

NSF Engineering Research Center
for Cell Manufacturing Technologies

Strategic Plan

May 8, 2018

NCMC: National Cell Manufacturing Consortium;
CQA: Critical Quality Attributes; CPP: Critical Process Parameters

CMaT Logic Model – Center Level

= Research
= Engineering Workforce Development
= Diversity and Inclusion
= Innovation Ecosystem

CMaT

Resources/Inputs

- NSF funding and ERC program resources
- NCMC Roadmap: 4 years of input from industry and clinical practitioners; current state of technology
- Talented faculty, trainees, & dedicated staff
- Excellent research and training facilities, infrastructure, GMP/GLP
- Existing and new relationships with K-12, technical colleges,& URM outreach programs
- Existing and new industry and clinical partnerships
- High-quality undergraduate and graduate programs
- Dedicated experts and researchers synergistically leading all key programs
- Biomanufacturing resources from Marcus Center and Waisman Center
- Existing and new programs for diversity and inclusion, industry ecosystem, & entrepreneurship training
- Advisory boards, NIST, FDA, SCB, patient groups, reimbursement experts
- Feedback from and engagement with regulatory and standards agencies
- Integrated and continuous evaluation

Activities

- Comprehensive cell and process characterization, big data analytics, & predictive computational modeling for all Test-Beds
- New technology development for monitoring and assessing CQA, CPP, potency, and safety during manufacturing in all Test-Beds
- Systems optimization and process improvement; scalability; new models and theory for supply chain and logistics for all Test-Beds
- Integrate real-time monitoring of CQAs and CPPs into scalable, quality-controlled manufacturing processes for each Test-Bed

- Provide center-wide implicit bias and cultural competency training
- Share best practices across institutions and beyond
- Recruit, retain, & mentor trainees and faculty from underrepresented groups

- Provide continuous and broad professional development opportunities for faculty & trainees at all levels
- Bio-manufacturing curriculum development and dissemination – for pre-college, technical college, university, professional education
- Certificate and degree programs at technical colleges & universities
- International training program

- Continuous engagement of industry practitioners in research, innovation, inclusivity, & workforce development
- Develop and nurture a culture of translation, entrepreneurship, and commercialization

Outputs

- Novel biological insights resulting in robust analytical, computational, and workflow tools for identifying CQAs & CPPs; Identified CQAs & CPPs for specific Test-Beds
- New theories, models, and technologies for rapid, high-throughput, or real-time measurement of cell quality, CQAs, and CPPs across Test-Beds
- New theories, models, & technologies for scalable Test-Bed production and distribution
- Center-wide vision of cross-cutting engineered system of closed-loop manufacturing with real-time analytics, potency measurements, and feedback process control for Test-Beds

- Center-wide, embedded culture of inclusion
- Best practices in diversity and inclusion implemented across CMaT partners and disseminated internationally
- Increased number of faculty and students from underrepresented groups active in the broader CMaT ecosystem

- Increased number of CMaT faculty and students trained in broad professional skills
- Inclusive precollege & technical college programs, entrepreneurship enrichment modules, & teacher experience programs developed in cell manufacturing
- Inclusive, industry-driven technical college and university certificate programs developed for cell manufacturing
- Strong international program focused on training a globally engaged workforce

- Diverse portfolio of highly engaged member companies across value chain
- Best practices leading to increased technology licensing, startups, & innovation

Outcomes

Short (1-3 years)	Mid (4-7 years)	Long (8-10 years and beyond)
CMaT ecosystem advances knowledge and enables innovations that result in publications, filed patents, & new industry collaborations	Industry & clinical input results in shorter technology/process development cycle and new research directions and projects	CQA/CPP driven Engineered system with rapid, real-time analytics to enable large-scale, reproducible manufacturing of high-quality cells disseminated to clinicians and industry in the U.S. and internationally
New research talent from associated fields begin working on areas supported by CMaT	CMaT researchers leverage CMaT projects and other infrastructure to receive additional funding from federal, state, philanthropic, or industry sources	CMaT faculty & trainees spin-off new U.S. companies or license technologies to other companies
Diverse perspectives, multi-disciplinary expertise, and input from industry and clinicians synergizes to enhance R&D activities and training in CMaT	CMaT's international program results in more globally engaged, holistic researchers and increases new research collaborations	Faculty and trainees from traditionally underrepresented groups populate and remain in career fields supported by CMaT
A sustainable ecosystem links industry, global institutions, K-12 schools, technical colleges, & universities to address the current and future needs of the cell manufacturing workforce	CMaT trainees begin impacting industry ecosystem through diversity and inclusion, cross-disciplinary expertise, policy and regulatory awareness, and diversity	Industry-relevant bio-manufacturing training becomes part of engineering curricula nationwide
Traditionally underrepresented groups make distinct scientific contributions and interface with clinicians and industry	Training based on industry need and emphasizing global perspectives becomes an embedded part of CMaT's culture	CMaT's best practices for workforce training, innovation ecosystem, and culture of inclusion become exemplars for other programs at partner institutions and nationally
New courses, modules, and outreach across all levels raise awareness and enthusiasm for cell and biomanufacturing careers	CMaT impacts establishment of best practices and standards internationally	
CMaT is recognized as a global leader in cell manufacturing technology development and training	CMaT impacts regional economic development and industrial competitiveness	CMaT sustainability post-NSF funding
Faculty and trainees engage in more industry-relevant research	Increased quantity, quality, and filing-speed of invention disclosures	Accelerated innovation and increased commercialization

Societal Impacts

- Improved availability and access to reliable, high-quality, cell-based therapies
- Reduced cost of cell therapy products
- Change in clinical practice — cell therapies become more routine for clinical care
- A robust, sustainable cell manufacturing industry with a well-trained, diverse, and global workforce
- Better health outcomes regardless of socio-economic status

Logic Model – Engineering Workforce Development

CMaT

Resources/ Inputs

- NSF funding and ERC program resources
- NCMC Roadmap with 4 years of input from industry and clinical practitioners
- Excellent research and training facilities and world-class infrastructure, Marcus and Waisman center ecosystem
- Dedicated GMP/GLP facility for training
- Talented faculty, trainees, and dedicated staff
- Industry-driven research strategies and results
- High-quality undergraduate and graduate programs
- Engaged industry, and clinical partners, regulatory and standards experts, & CMaT Advisory boards
- Existing and new relationships with K-12, technical colleges, and URM outreach programs

Activities

- High school research internships, RET, and flipped RET programs, supported by mentoring programs
- Technical college course modules, mentoring partnerships
- Undergraduate course modules, REU programs, MSI partnerships
- Inter-institutional graduate courses; new credentials if desirable
- Partnerships to develop professional education course modules for retraining current workforce
- CMaT virtual symposium, annual retreat, SLC, inter-institutional courses, research exchanges, mentoring network
- International exchange and training program
- Internships and entrepreneurship training opportunities

Outputs

- Pre-college implementation of CMaT-related curricula and enrichment experiences, pre-college student participation
- CMaT content integrated into technical college coursework; technical college student and instructor participation
- CMaT content integrated into undergraduate and graduate programs; diverse group of trainees
- Student understanding of industry and clinical challenges and regulatory, standards, ethical, legal, economic, & policy issues
- CMaT course modules and training content from all levels and best practices disseminated internationally
- Inclusive inter-institutional research collaborations, co-presentations, co-publications, co-mentoring
- Increased number of faculty and students from underrepresented groups active in the broader CMaT ecosystem
- Students trained in global industry and research culture, regulatory and standards issues, and global entrepreneurship
- Positive student and mentor satisfaction ratings and clear goals for internship and entrepreneurship experiences

Outcomes

Short (1-3 years)	Mid (4-7 years)	Long (8-10 years … and beyond)
New programs attract student interest in engineering and biomanufacturing at the pre-college, technical college, and college levels, especially among underrepresented groups in engineering	Mature programs increase student commitment to engineering and biomanufacturing at the pre-college, technical college, and college levels, especially among underrepresented groups in engineering	Sustainable programs across CMaT drive increased student commitment to biomanufacturing at all levels, especially among underrepresented groups in engineering; CMaT training used as an exemplar nationwide
Industry-relevant curricula, pedagogical approaches, technical and professional skills, and strategies for broadening participation are developed at all levels	Industry-relevant curricula, pedagogy, technical & professional skills, and broadening participation strategies are enacted and revised at all levels at partner sites and by technical colleges and K-12 schools	Industry-relevant curricula, pedagogy, technical & professional skills, and strategies for broadening participation are adopted as exemplars at institutions beyond CMaT
Increased number of underrepresented students at preparatory colleges enter programs for careers in biomanufacturing	Increased number of underrepresented students entering and graduating from preparatory colleges prepared for careers in biomanufacturing	Steady flow of underrepresented students entering and graduating from preparatory colleges prepared for evolving careers in biomanufacturing
Increased numbers of diverse undergraduate and graduate engineers begin receiving key technical and professional skills necessary to transform the nascent cell manufacturing industry	Increased numbers of diverse undergraduate and graduate engineers graduating with key technical and professional skills necessary to transform the cell manufacturing industry	Steady flow of undergraduate and graduate engineers with key technical and professional skills necessary to transform the nascent cell manufacturing industry
An ecosystem of sustainable partnerships begins to link industry, global research partners, K-12 schools, technical colleges, and universities to address current and future workforce needs	An ecosystem of sustainable partnerships strengthens and expands links among all stakeholders to address current and future needs of the global cell manufacturing workforce	A sustained ecosystem of partnerships ensures strong links among all stakeholders to address current and future needs of the cell manufacturing workforce
Precollege, technical college, & college instructors' initial engagement with CMaT builds enthusiasm for initial infusion of cell manufacturing concepts into engineering education at all levels	Instructors' ongoing engagement with CMaT furthers continued infusion of cell manufacturing concepts into engineering education at all levels	Instructor engagement with CMaT at all levels is institutionalized, becoming an exemplar for infusion of cell manufacturing concepts into engineering education at all levels

Contents

The CMaT Team

Introduction

During the four months since its launch, the National Science Foundation (NSF) Engineering Research Center (ERC) for Cell Manufacturing Technologies (CMaT) has further refined its overall vision, goals, and comprehensive strategic plan through input from all CMaT participants, NSF reviewers and program officers, and a diverse group of external stakeholders—including industry leaders, standards experts, and clinicians. This strategic plan leverages CMaT's unparalleled infrastructure and resources to integrate the four foundational pillars—research, engineering workforce development, diversity and inclusion, and innovation ecosystem—into a cohesive and synergistic set of activities that will achieve CMaT's overall vision. The plan places a dynamic management structure around an inclusive team of international leaders who will continually use formative and summative assessments along with stakeholder feedback to refine, adjust, and improve CMaT's direction to achieve maximum impact. The following section details this strategic plan.

Vision

CMaT's vision is to transform the manufacture of cell-based therapeutics into a large-scale, low-cost, reproducible, and high-quality engineered system for broad industry and clinical use. CMaT will become a visionary and strategic international resource and an exemplar for developing new knowledge, transformative technologies, an inclusive well-trained workforce, and enabling standards for cell production and characterization processes.

Goals

CMaT will be recognized as a **Diverse and Inclusive Innovation Hub** for:

- **Creating fundamental new knowledge and transformative engineered systems** that enable predictive cell-quality determination and robust, low-cost, scalable cell manufacturing processes
- **Inventing and translating new and transformative tools and technologies** for affordable, reproducible, and high-quality cell production
- **Disseminating best practices and standards to all stakeholders** throughout the cell manufacturing ecosystem
- **Training an inclusive cell manufacturing workforce across the value chain**—including trainings on policy, ethics, regulations, and healthcare economics—and involving undergraduate students, graduate students, and post-doctoral fellows, underrepresented students and teachers from middle and high schools, students with disabilities, veterans, and technical and community college students and teachers

What's New and Current Status

Since submission of the CMaT proposal and the 10-page response to site visit questions, CMaT has made a number of strategic changes based on feedback from the blue-ribbon panel, discussions with stakeholders, the roadmap update meeting of the National Cell Manufacturing Consortium (NCMC) in May 2017, feedback from the CMaT kick-off meeting in November 2017, and other discussions with ERC

program managers. Below is a summary of key adjustments; additional aspects are discussed in the sections that follow.

GT trainees	19
UGA trainees	15
UW trainees	14
UPRM trainees	9
Gladstone trainees	2
Total	59

High school students	1
UG students	13
Gradute students	37
Post-docs	8

Number of Females	29
Number of URMs	17

a. Inclusion of payer and regulatory experts in the Scientific Advisory Board (SAB) in addition to scientists, engineers, and clinicians. We have reached out to these stakeholders and expect them to be on the SAB by this summer.

b. Detailed strategic plans for all Thrusts were developed, with Test-Beds integrated and embedded in each project. We engaged Nexight Group to develop the detailed strategic plan and performance criteria (deliverables) for every project in every Thrust and ensure that all Test-Beds are well represented across projects.

c. Developed a "Quick Win" validation project for Thrust 1 in close collaboration with industry and clinical stakeholders. Theresa Kotanchek, CEO of Evolved Analytics (a Tier 3 industry member of CMaT), and Bruce Levine from the Abramson Cancer Center at the University of Pennsylvania (instrumental in developing the first approved chimeric antigen receptor T cell [CAR-T] product in the United States through Novartis) were directly involved in developing the Thrust 1 strategic plan and the quick win project involving T cells. This project will help establish the workflow and demonstrate the utility of various data analytics and computational methods for Thrust 1. Additional input came from discussions with T cell therapy companies, including Celgene, Pfizer, Novartis, and Juno Therapeutics. A similar project using mesenchymal stem cells (MSCs), proteomics, and high-content imaging is also under way in Thrust 1. These projects are currently in the experimental data collection phase; for example, the T Cell project is employing a design of experiment (DOE) approach to identify critical process parameters (CPPs) for high-quality T cells and will further correlate them with secretome, metabolome, and transcriptome data to identify early predictors of quality and eventually surrogate critical quality attributes (CQAs) in later years. The projects are designed to be 2-year demonstration projects as discussed during the kick-off meeting.

d. As of January 2018, 43 trainees are working on CMaT projects using CMaT funding, and a total of 59 trainees are working on CMaT projects with additional leveraging funds (e.g., Marcus Center, various fellowships). The number of undergraduate and high school students will significantly increase over the summer and beyond as we recruit them in a more targeted manner. The current demographic of these students is shown in the Table above, demonstrating that CMaT has already put together a highly diverse and inclusive group of trainees across multiple disciplines.

e. As of January 2018, CMaT has started 12 projects across the 3 Thrusts and 3 Test-Beds. An abstract, milestones, and deliverables chart for each project, as well as a list of participants, are provided in Appendix A. All CMaT projects span multiple disciplines, areas of expertise, and academic partners. All projects were selected and milestones developed through close interaction with industry and clinicians both through our original roadmap and also subsequently through the roadmap update meeting and subsequent discussions.

f. We have developed a comprehensive summative and formative assessment plan for outputs and outcomes in each of the four pillars. A summary of this plan for the overall center is included later in this strategic plan.

g. We have engaged with 28 companies—spanning the whole cell manufacturing value chain—including big pharma, tools and supply chain companies, as well as small and medium businesses. This level of engagement is double the number of companies engaged during the proposal phase. These companies are going through their legal due diligence on our membership agreement and bylaws (attached). Based on current conversations and feedback, we expect a significant number of these companies will become CMaT members in Year 1. A list of companies, where they fit in the value chain, and conferences where we conducted outreach activities are listed later in the document.

Foundations of the ERC

In this start-up phase, CMaT used an external strategic planning consulting firm, Nexight Group (using funding from the Georgia Research Alliance), to develop a comprehensive strategic plan that seamlessly integrates and synergizes the four pillars—research, engineering workforce development, diversity and inclusion, and innovation ecosystem—based on the following overarching principles:

a. Leverage our foundation and bring all stakeholders together
b. Build on existing partnerships and forge new strategic partnerships
c. Ensure an embedded, deeply-rooted, inclusive culture
d. Nurture a mentorship-driven, inclusive management structure
e. Fully assimilate, expand, and implement the 3-Plane strategy and roadmap
f. Implement impactful and feedback-driven workforce training
g. Leverage NSF's deep investments as well as other complementary infrastructure and training programs in all partner institutions, focusing on implementing best practices and lessons learned
h. Develop an engaged, inclusive, and adaptive innovation ecosystem

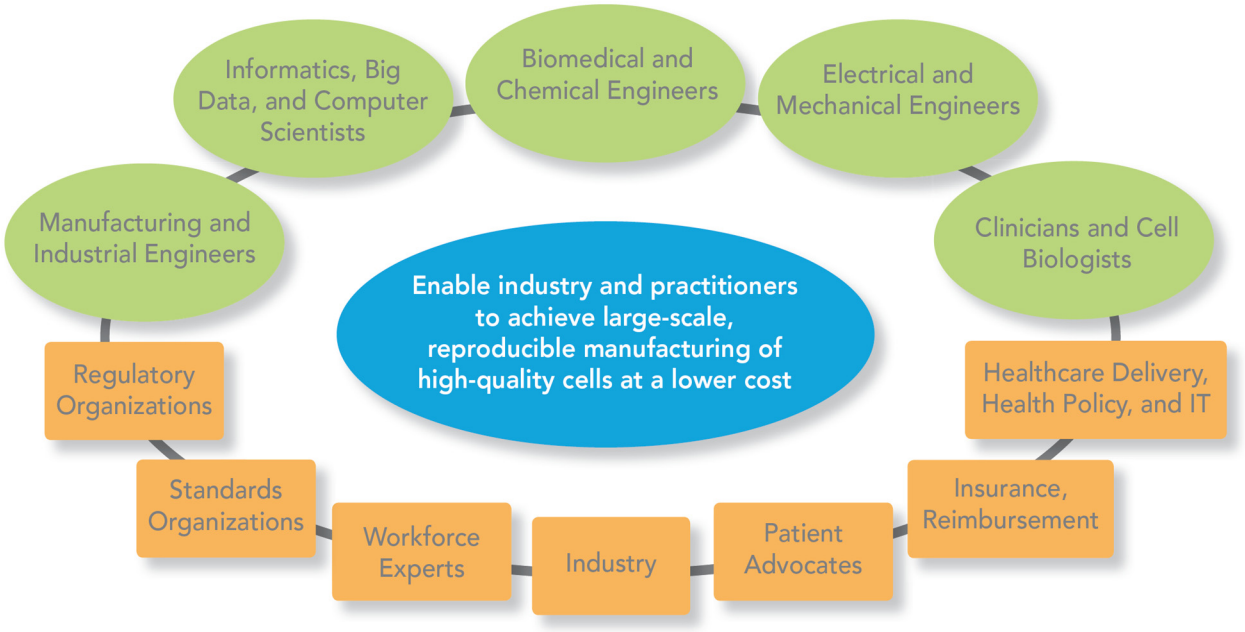
CMaT will extensively leverage the National Cell Manufacturing Consortium's industry-driven 10-year roadmap that outlines the barriers and challenges in cell manufacturing and identifies needs for innovation and new technologies. This roadmap (**Figure 1**), originally published in 2016 and updated again in the summer of 2017, was written with input from over 30 industry partners, 16 academic and clinical partner institutions, GMP manufacturers, standards experts, regulatory experts, and other stakeholders.

The roadmap serves as a foundation for CMaT activities and will also be regularly updated by CMaT through continuous stakeholder input and assessment of ongoing activities.

FIGURE 1. National Cell Manufacturing Consortium Roadmap

Another key aspect of CMaT's overall strategy is to be the international entity that converges stakeholders from all components of the cell manufacturing value chain to enable CMaT's vision. As shown in **Figure 2**, CMaT will synthesize expertise, advice, and viewpoints from diverse communities.

FIGURE 2. CMaT Stakeholders



CMaT also strategically leverages existing infrastructure. As shown in **Figure 3**, CMaT helps synergize the deep infrastructure and leveraging funding of all its partner and affiliate institutions, including:

- Georgia Institute of Technology (Georgia Tech): The Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M), with its new 4,000 sq. ft. GLP/GMP facility and $23 million in philanthropic and state investment, The Georgia Tech Manufacturing Institute, and the Parker H. Petit Institute for Bioengineering and Bioscience

- University of Georgia (UGA): The Regenerative Bioscience Center
- The tri-institutional Regenerative Engineering and Medicine Center between Georgia Tech, UGA, and Emory University
- The Georgia ImmunoEngineering Consortium between Georgia Tech and Emory University
- University of Wisconsin: The Stem Cell and Regenerative Medicine Center and the Waisman Biomanufacturing Center
- University of Puerto Rico at Mayagüez (UPRM): The Bioprocess Development and Training Center
- University of Pennsylvania: Clinical and GMP facilities at the Abramson Cancer Center
- Gladstone: The Rodenberry Stem Cell Center

FIGURE 3. CMaT Partners

In addition, CMaT's strategic plan also leverages NSF's deep investment at all partner institutions and the best practices that have emerged as a result. **Figure 4** shows a partial list of these NSF-funded programs that provide, along with other highly successful programs, the foundation of CMaT's workforce training, innovation ecosystem, and diversity/inclusion programs. These programs will be strongly leveraged to ensure CMaT's success.

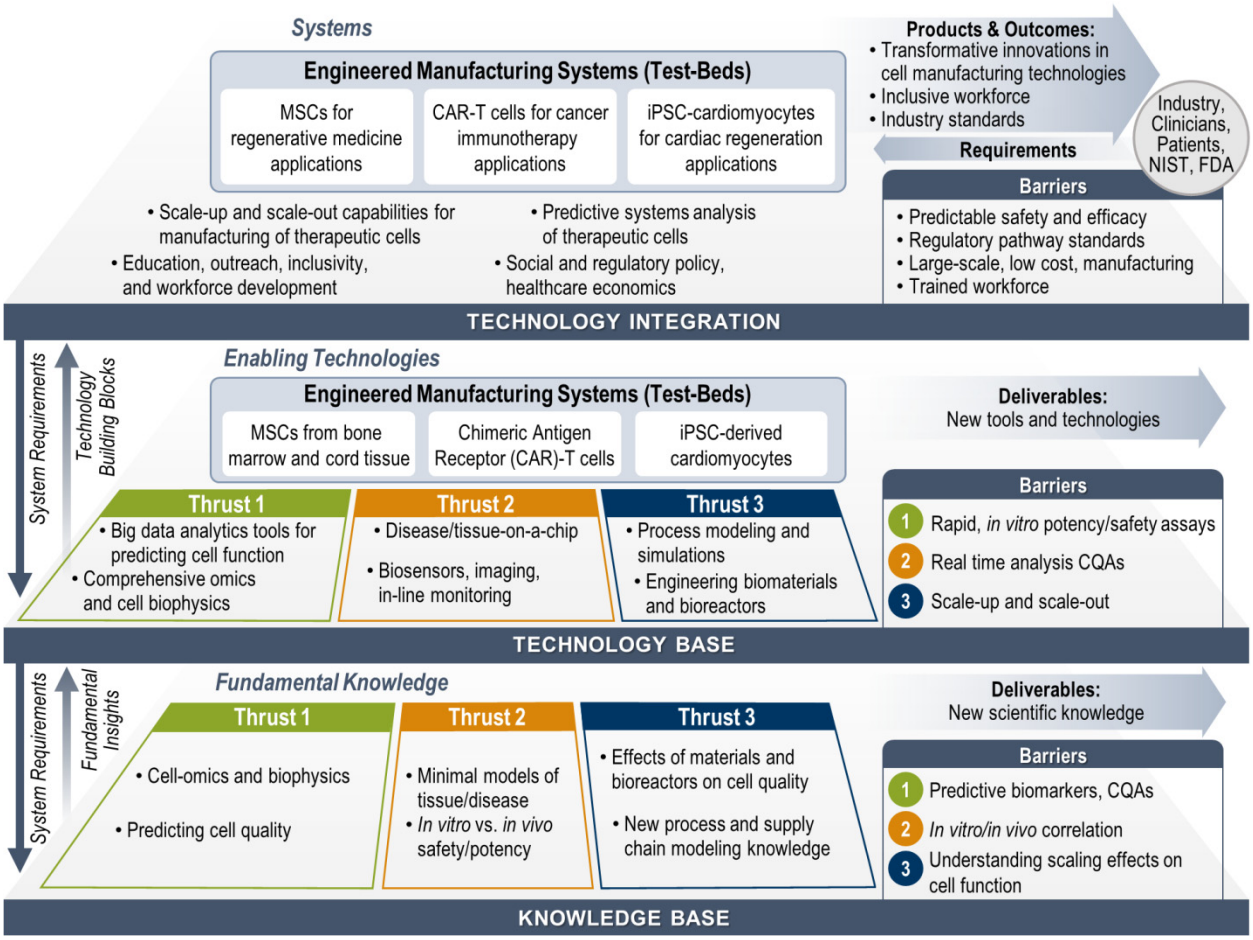
FIGURE 4. NSF-Funded Programs Leveraged by CMaT

The following sections provide detailed strategic plans for each of the foundational pillars of CMaT and demonstrate how they are integrated and synergized.

Research

Figure 5, the 3-Plane Chart of CMaT, demonstrates that CMaT will enable transformative changes in health, economy, and the manufacturing workforce of the nation and have a global impact.

FIGURE 5. ERC 3-Plane Chart



CMaT will employ broad, multi-disciplinary *SMART* (***S**pecific, **M**easurable, **A**daptive and **A**chievable, **R**esponsive and **R**ealistic, and **T**ransformative and **T**imely*) strategies to gain fundamental knowledge, develop technologies, and overcome barriers identified in the NCMC Roadmap.

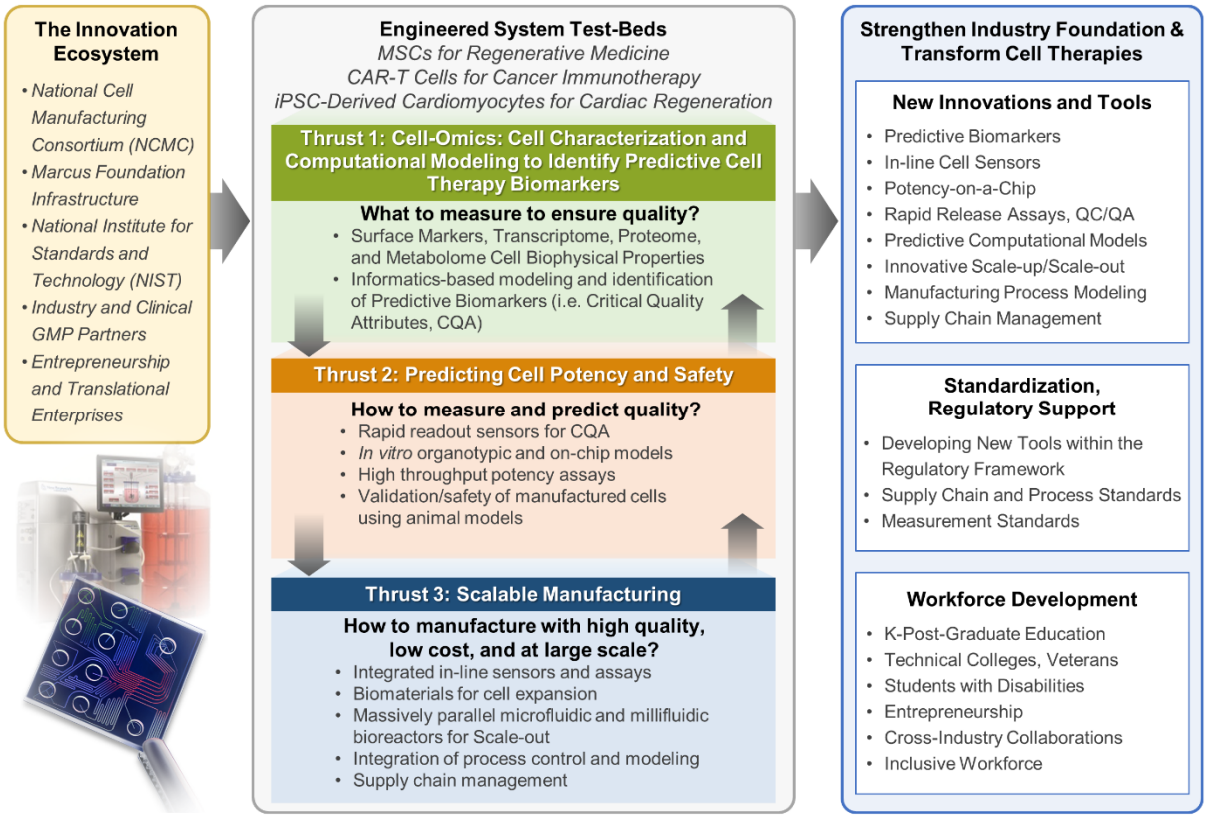
First, new fundamental knowledge will be gained about how manufacturing processes affect cell quality to catapult scalable cell manufacturing, especially in areas of critical quality attributes (CQA), i.e., the properties or biomarkers of a given type of cell that "predict' its safety, efficacy, or potency. The lack of reliable CQAs is major barrier in the success of cell therapies as well as their reproducibility across clinical centers and industry. There is also little correlation between *in vitro* and *in vivo* potency-safety (i.e., quality) measurements. Furthermore, not much is known on how scaling of the manufacturing process affects cell function. In collaboration with NIST and the Standards Coordinating Body (SCB), we will use measurement science approaches in all aspects of cell characterization and process development, enabling standards development for the broader cell manufacturing industry. Second, CMaT will develop new enabling tools and technologies that would be broadly applicable to all Test-Beds as well as other cell therapies and biomanufacturing platforms. Such tools and technologies include rapid, in-line testing of critical cell attributes through multiplexed sensors and imaging probes; organ/disease-on-a-chip models for rapid, low-cost, potency testing; big-data analytics to model cell quality; as well as engineered biomaterials and bioreactors coupled with advanced process modeling and supply chain innovation and integration. Third, at the Engineered Systems level, CMaT will address key barriers in each Test-Bed:

predicting safety and efficacy on industry relevant Test-Beds; large-scale, low-cost manufacturing; lack of industry standards and a trained workforce, and regulatory and social policy as related to large-scale cell therapies. Finally, CMaT will nurture an inclusive, industry-academia-clinician-government ecosystem to achieve its goals. This broad strategy, driven by needs from industry, academics, clinicians, patients, and regulatory agencies, will collectively enable large-scale, low-cost, reproducible manufacturing of high-quality therapeutic cells.

Through these efforts, CMaT will reduce the cost, increase access to, and improve the efficacy and reproducibility of cell therapies, which will enable industry growth, alleviate patient suffering, improve the healthcare economy, and transform how we routinely treat incurable and chronic diseases.

CMaT's overall research plan and its impact on industry and workforce is shown in Figure 6. This strategic plan is structured around a broad stakeholder-driven ecosystem with three inter-dependent and convergent Thrusts, and three industry-relevant Test-Beds (Engineered Systems) that are integrated and cross-cutting across all three Thrust areas. As shown, CMaT will have tremendous impact in strengthening the nascent industry.

FIGURE 6. The Ecosystem, Overall Strategic Plan, and Outcomes of CMaT

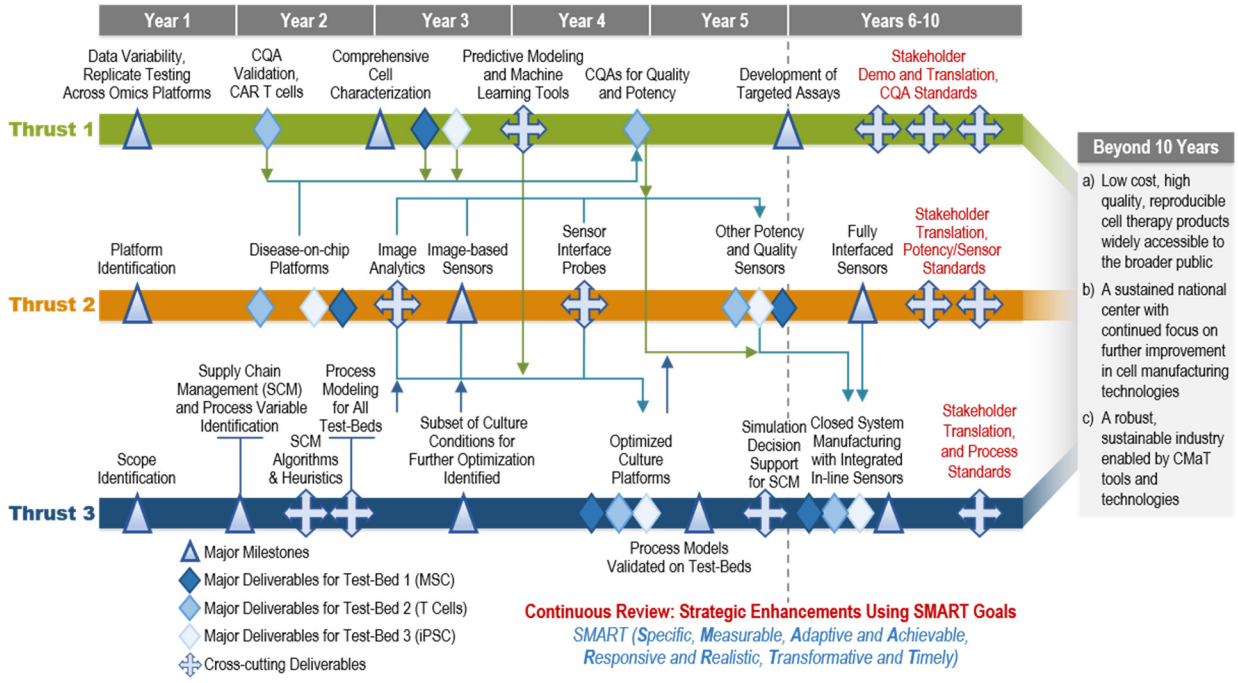


CMaT's technology development strategy builds on a strong foundation of fundamental knowledge in manufacturing technologies, process engineering, computational modeling, and cell engineering to develop and integrate an array of enabling tools and technologies that will lead to high-quality, scalable, cost-effective manufacturing systems for three transformative cell therapy platforms (Test-Beds). Barriers at the fundamental knowledge, enabling technologies, and systems levels have been identified though

stakeholder engagement. In each thrust, we will continually engage our IPAB and SAB to identify roadblocks in manufacturing of each Test-Bed and to assist us in setting quantitative goals for the key technical metrics related to our engineered system.

Figure 7 presents the 10-year milestones and deliverables chart. As shown, CMaT will take a convergence-science approach, with integrated, inter-connected, and synergistic Thrusts and Test-Beds to address the roadmap-identified barriers in scalable cell manufacturing.

FIGURE 7. CMaT 10-Year Milestones and Deliverables



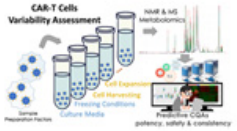
The three proposed Engineered System Test-Beds reflect current clinical and commercial interests (T cell immunotherapy and MSCs for regenerative medicine), as well as longer-term emerging therapies (induced pluripotent stem cell-derived cardiomyocytes [iPSC-CM] for cardiac repair). We have chosen to focus on Chimeric Antigen Receptor (CAR)-T cell and MSC (from bone marrow or cord tissue, BM-MSC/C-MSC) manufacturing systems because their large-scale production is severely limited by barriers in current manufacturing technologies and our team has deep expertise in these areas. We anticipate the most rapid translation of CMaT research into these two Test-Beds given access to clinical data and industry partners working with these cells. Our choice of iPSC-CMs as the third Test-Bed is due both to our collective expertise in this area and because of rapidly growing interest and transformative clinical potential of reprogrammed, patient-matched, adult cells for regenerative medicine. Although widespread use of pluripotent stem cell therapies may be years away, clinical trials for some diseases, including heart failure, are under way, and there will be critical need for scalable manufacturing technologies in the next 10 years and beyond. Our work on iPSC-CMs will impact how manufacturing develops in early-stage clinical implementation of these cells and other cell types that require differentiation during manufacturing. Importantly, although we have chosen three cell therapy Test-Beds based on current clinical needs and emerging innovation opportunities, the platform technologies, models, and knowledge

Engineered System Vision

Cross-cutting thrusts with independent, transformative deliverables

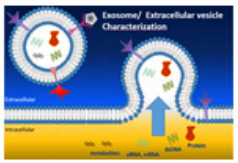
Project 1, Thrust 1, TB = T Cells (Edison, Roy, Fernandez, Saha, Levine, Kotancheck, Torres-Garcia)

Variability assessment and omics characterization of CAR-T cells through an integrative computational pipeline



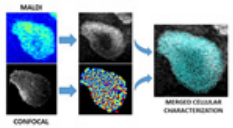
Project 2, Thrust 1, TB = MSC (Stice, Kemp, Platt, Edison, Fernandez)

Exosome protein and cell surface signature: a critical quality attribute for MSCs



Project 3, Thrust 1, TB = All (Kemp, Fernandez, McDevitt, Palecek, Mortensen)

Integration of imaging modalities with omics characterization



Applied to each Test-Bed

Cross-cutting Engineered System:

Closed-loop cell manufacturing platform with integrated, real-time analytics, potency measurement, and feedback process control

Source cells, materials, and reagents → Initial culture for purification, and selection → Cell transduction, gene-modification, genome editing → Cell expansion and/or differentiation → Harvesting, pooling, separation and enrichment → Formulation and filling → Release testing, delivery and administration

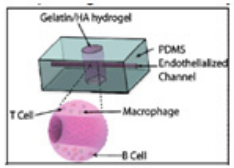
Cryopreservation, storage, release, transportation, delivery

Downstream Processing

Upstream Processing

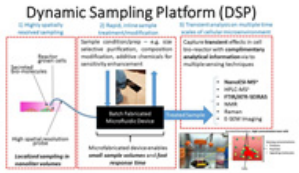
Project 1, Thrust 2, TB = T Cells (Saha, Roy, Karumbiah, Torres-logo)

Predictive CAR-T Potency assay for solid tumors using tumor-on-a-chip models



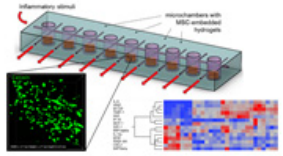
Project 2, Thrust 2, TB = All (Fedorov, Resto, Guldberg)

Dynamic Sampling Platform (DSP) for Cell State Analysis and Bioreactor Monitoring



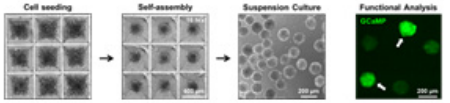
Project 3, Thrust 2, TB = MSC (Garcia, Lam, Mortensen)

Tissue-on-a-Chip Platform for Mesenchymal Stem Cell Potency



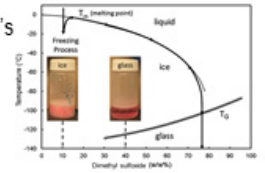
Joint Project, Thrust 2 and 3, TB = iPSC-CM (Palecek, Domenech, Kamp, Kane. McDevitt, Torres-Lugo, De la Fuente)

Improving the Quality of iPSC-derived Cardiomyocytes by Providing Intercellular Cues during Scalable Manufacturing



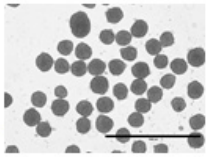
Project 1, Thrust 3, TB = T Cell / iPSC (Ashton, Kam, Levine, Brockbank)

Analysis of Cryopreservation's Effect on Cell Isolates and Manufactured Therapeutic Phenotypes



Project 3, Thrust 3, TB = MSC (Temenoff, Murphy, Galipeau, Karumbiah, Guldberg)

Effects of Culture Substrate Parameters on MSC Secretome



Project 2, Thrust 3, TB = All (Wang, White, Levine, Ashton, Saha, Roy, Levine)

Development of Novel Supply Chain and Process Modeling Algorithms, Methods, and Tools for Cell Therapy Manufacturing and Distribution

developed in CMaT will be adaptable to other manufactured cell systems as the needs of the industry evolve.

Crucial to the CMaT vision is the recognition that cell manufacturing and all related engineering innovations must be embedded within the social and regulatory policy environment—a key challenge identified by industry in the NCMC Roadmap. To help cell manufacturing reach its transformative potential, CMaT has included faculty in relevant social sciences (e.g., public policy and ethics – Levine A., Saha, and Hogle) and will support high-quality research that addresses critical barriers (e.g., regulatory policy harmonization, intellectual property, and global access to therapies). In fact, one of the start-up projects in Thrust 3 involves collaboration with Dr. Aaron Levine and his graduate students in public policy.

Detailed strategic plans for each Thrust are provided below. A brief description of each research project—including aims, milestones, and the multi-disciplinary multi-institutional team involved—is provided in Appendix A.

Thrust 1 — Cell-Omics: Comprehensive Characterization, Big-Data Analytics, and Computational Modeling to Identify Predictive Cell Therapy Biomarkers

The goal of Thrust 1—Cell-Omics: Comprehensive Characterization, Big-Data Analytics, and Computational Modeling to Identify Predictive Cell Therapy Biomarkers—is to work synergistically with Thrusts 2 and 3 to develop robust, reproducible, and predictive analytical measurements and models using comprehensive cell-omics. The analytical data and analysis from Thrust 1 will complement quantitative phenotypic data from other CMaT groups. This approach will allow Thrust 1 to develop multi-omics integrated maps of cell types from each Test-Bed to measure critical quality attributes (CQAs) that can be tied to safety, consistency, and/or *in vivo* activity.

The computational infrastructure quick-start project has achieved its short-term goals of establishing data acquisition, sharing, and analysis pipelines. Five Thrust 1 strategic plan projects have been designed to enable CQA identification, initially focusing primarily on engineered T-cells and MSCs. The overall approach for discovery and data sharing, computation and analysis, and tool integration will permeate through CMaT and across different cell types. The team has expertise in -omics analysis, imaging, machine learning and multi-omics data integration, computational infrastructure, and systems biology modeling. With input from our IPAB and SAB, this team is well-qualified to achieve all goals in Thrust 1.

These multi-omics integrated maps are being developed through a two-phase process:

Discovery Phase

- Understand variance in sample preparations
- Identify what to measure
- Standardize cell quality control metrics
- Assess characteristics that are predictive

Implementation Phase

- Integrate multi-omics maps in large-scale production
- Establish pipeline that industry can use to measure and assess CQAs

R&D Activities

Legend for Cross-Center Integration		
1 **Thrust 1:** Cell-Omics – Cell Characterization and Computational Modeling to Identify Predictive Cell Therapy Biomarkers	1 **Test-Bed 1:** MSCs for Regenerative Medicine	**Workforce Development**
2 **Thrust 2:** Monitoring Cell Potency and Safety – Sensors, Potency-on-a-Chip, and Modeling	2 **Test-Bed 2:** CAR-T Cells for Cancer Immunotherapy	**Innovation Ecosystem**
3 **Thrust 3:** Systems Optimization for Scalable Manufacturing	3 **Test-Bed 3:** iPSC-Derived Cardiomyocytes for Cardiac Regeneration	**Diversity and Inclusion**

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Quick-Start Project (Year 1) CAR-T Project (Years 2–5)	**Test-Bed 2: CAR-T**					
	Performance target: • Q2: Establish regulatory procedures and agreements for cell sharing (MTA, IRB) • Q2: Acquire "play" cells (currently available at GT) to optimize sample preparation for NMR/LC-MS/RNAseq • Q2: Establish a standard computational protocol for pre-processing and merging multi-omics datasets • Q4: Starting with available GT samples, generate initial CAR-T dataset. Compare rich and minimal culture conditions using NMR and LC-MS data from media and cell extracts (e.g., for reproducibility and sample preparation data). Provide data to computation groups to develop modeling approaches • Q4: Complete statistical power analysis for CAR-T quick-start project to distinguish responder/non-responder populations by metabolomics	Performance target: • Q2: Establish a standard protocol for pre-processing and merging multi-omics datasets • Q2: Generate a second experimental dataset of CAR-T cells using one culture condition and an inter-lab comparison • Q3: Extract a reduced set of relevant features that are linked to a response (or responses) • Q3: Develop a computational methodology to rank important patterns from ensemble methods using multi-omics data • Q4: Improve statistical power and establish other important factors for potency and safety of CAR-T cells • Q4: Implement statistical learning, data mining, and/or machine-learning algorithms to identify important rules (i.e., patterns) to predict outcome using pilot data	Performance target: • Q2: Expand the examination of variables to cover clinical needs (discussions with clinical and industrial partners) • Q4: Refine the predictive models as a function of all variables	Performance target: • Q2: Design an industrially and clinically relevant study of individuals undergoing clinical trials from industrial partner • Q4: Collect data on clinical CAR-T study	Performance target: • Q2: Model the clinical data to determine CQAs predictive of CAR-T efficacy • Q4: Identify unknown CQAs to improve mechanistic understanding and establish baseline for developing targeted approaches in the next 5 years	Identification of CQAs predictive of CAR-T efficacy will allow for screening out of non-efficacious cell batches and/or improvement of processes to achieve these CQAs in each batch. This will improve the quality of the cell therapy produced, leading to improved clinical outcomes.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
		• Q4: Implement the ranking model to rank important patterns from diverse set of models using pilot data				
Exosome Critical Quality Attribute Discovery and Modeling Project	**Overarching Goals Across Test-Beds**					
			Cross-Test-Bed Goal: • Expand approaches developed in years 1 and 2 to iPSC	Cross-Test-Bed Goal: • Expand approaches developed in years 1 and 2 to CAR-T	Cross-Test-Bed Goal: • Expand approaches developed in years 1 and 2 to add other Thrust measurements	Identification of CQAs predicted by exosomes derived from each cell type will allow for the improvement of processes to produce exosomes with these CQAs in each batch. This will improve the quality of the exosome therapy produced, leading to improved clinical outcomes
	Test-Bed 1: MSCs					
	Performance target: • Q2: Grow initial set of 10 MSC samples under 2 conditions and optimize sample preparation • Q4: Collect complete dataset (CD surface markers, spent media, exosomes, and cell pellet) by NMR and LC-MS • Q4: Develop initial model to determine correlation structure of dataset	Performance target: • Q2: Optimize culture conditions and sample size • Q4: Collect new datasets (CD surface markers, spent media, exosomes, cell pellet by NMR and LC-MS) • Q4: Refine computational model to determine correlation structure of dataset	Performance target: • Q2-Q4: Show phenotypic relationship between exosomes and clinical phenotype • Q2–Q4: Determine the most important analytical measurements to support model and determine CQAs	Performance target: • Q2–Q4: Show phenotypic relationship between exosomes and clinical phenotype • Q2–Q4: Determine the most important analytical measurements to support model and determine CQAs • Q4: Develop targeted features to predict CQAs	Performance target: • Q2–Q4: Test the targeted model by designing new study and measuring a limited number of important CQAs • Q2–Q4: Model targeted measurements to determine predictive value of potency	Identification of CQAs predicted by MSC exosomes will allow for the improvement of processes to produce exosomes with these CQAs in each batch. This will improve the quality of the exosome therapy produced, leading to improved clinical outcomes

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Integration of Imaging Modalities with Omics Characterization	**Overarching Goals Across Test-Beds**					
	Cross-Test-Bed Goal: • Engineer a label-free, non-destructive, low-cost imaging method to identify predictive measures of donor quality and cell potency that can be customized for all CMaT Test-Beds • Develop an analytical pipeline that provides single-cell positional information by merging MALDI data with confocal imaging for evaluating spatial metabolic heterogeneity among 2D colonies and 3D aggregates	Performance target: • Establish data processing pipeline for 2D colony characterization	Performance target: • Establish data processing pipeline for 3D aggregate characterization			This label-free, non-destructive, low-cost imaging method will enable in-line, real time sensing of cell quality in order to provide early detection of batches that are out of specification, (and perhaps correction to improve the quality of the batch). This will improve the overall quality of each batch produced
	Test-Bed 1: MSCs					
	Establish image feature extraction and orthogonal polynomial characterization using cultured MSC populations with known high and low potency Performance target: • Quantitative phase imaging of MSC topography	Performance target: • Logistic regression and principal component analysis (PCA) on MSC populations	Develop machine-learning algorithms to identify topographical feature distributions for biomanufactured MSCs Performance target: • Conduct full study to screen blinded test donors	Performance target: • Coordinate with Thrust 2 on development of in-line, label-free imaging; relate data generated to CQAs via modeling		Same as general description above

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	Test-Bed 2: CAR-T					
			Identify CAR-T cell feature extraction for preliminary test population and high and low potency cell populations using orthogonal polynomials to separate cells by high and low potency as described by CAR-T specialists Performance target: • Pilot study for separation of T cell potency	Performance target: • Conduct full study to screen blinded test donors	Performance target: • Coordinate with Thrust 2 on development of in-line, label-free imaging; relate data generated to CQAs via modeling	Same as general description above
	Test-Bed 3: iPSCs					
	Apply pipeline to iPSC-cardiomyocyte Test-Bed Performance target: • Assess metabolic heterogeneity in baseline iPSCs to CQA of mesoderm lineage potential	Performance target: • Extract spatial metrics associated with cardiomyocyte population	Performance target: • Assess maturation heterogeneity as a function of time in cardiomyocytes	Performance target: • Narrow down the variable space for predictive biomarkers to perform more directed, hypotheses-driven tests for CQAs	Performance target: • Develop targeted assays that selectively monitor targets for potency and efficacy	Same as general description above
Quality Assurance/ Quality Control and Standards	**Overarching Goals Across Test-Beds**					
	Cross-Test-Bed Goal: • Formalize specific QA/QC protocols for NMR and LC-MS that are appropriate for the sample sizes and types in CMaT Cross-Test-Bed Goal: • Establish an intermediate external reference standard that can serve as a reference material for batch normalization until more robust material is developed	Cross-Test-Bed Goal: • Apply to the most advanced Test-Bed from other Thrust 1 projects	Cross-Test-Bed Goal: • Develop cell-specific reference material with NIST partners	Cross-Test-Bed Goal: • Validate a cell-specific reference material standard that can be used by industry and academics	Cross-Test-Bed Goal: • Apply to other Test-Beds	Reference materials will be developed for each cell type that will allow comparison of NMR and LC-MS data gathered worldwide on different equipment

Computational Infrastructure	Overarching Goals Across Test-Beds					
	Develop a computational infrastructure with efficient data sharing; robust, secure, and HIPAA-compliant data storage with full back-ups; scalable computational nodes and software that can access the data; software and algorithm sharing tools; a protocol site for CMaT members to develop and share protocols and eventually make them public; efficient team communication software; and shared electronic notebooks <u>Cross-Test-Bed Goal:</u> • Establish a CMaT Slack channel • Establish a CMaT GitHub account for efficient software development and sharing • Establish a simple and sharable computing notebook that can be used by all CMaT members	<u>Cross-Test-Bed Goal:</u> • Develop a protocol sharing area on the CMaT website or another more appropriate place • Develop a common data storage system that is HIPAA compliant and backed up • Create a common computing cluster that can easily access the stored data and tools that will be common to CMaT members and partners				CMaT researchers will be able to easily access and share data in standardized formats to facilitate data mining from all experiments conducted in the center

Thrust 2 — Monitoring Cell Potency and Safety: Sensors, Potency-on-a-Chip, and Modeling

The goal of Thrust 2—Monitoring Cell Potency and Safety: Sensors, Potency-on-a-Chip, and Modeling—is to engineer robust, reproducible, and predictive measurement and assay technologies that enable batch and continuous monitoring of both process conditions and cell state during manufacturing across the three CMaT Test-Beds. Data from this Thrust will feed into Thrust 1 to discover new predictive CQAs, and technologies from this Thrust will be applied to Thrust 3 to fully describe the cell state during large-scale manufacturing. As new CQAs are identified in Thrust 1, they will also feed into this Thrust.

This Thrust aims to achieve the following outcomes:

- Ability to rapidly and cost-effectively evaluate potency and safety of cells during the manufacturing process
- Availability of rapid and cheap potency and safety assays that accurately mimic human disease conditions
- Integration of innovative monitoring technologies—including in-line sampling and real-time omics measurement, reporters and sensors, and "organ/disease-on-a-chip" platforms—in bioreactors

R&D Activities

Legend for Cross-Center Integration		
1 **Thrust 1:** Cell-Omics – Cell Characterization and Computational Modeling to Identify Predictive Cell Therapy Biomarkers	1 **Test-Bed 1:** MSCs for Regenerative Medicine	**Workforce Development**
2 **Thrust 2:** Monitoring Cell Potency and Safety – Sensors, Potency-on-a-Chip, and Modeling	2 **Test-Bed 2:** CAR-T Cells for Cancer Immunotherapy	**Innovation Ecosystem**
3 **Thrust 3:** Systems Optimization for Scalable Manufacturing	3 **Test-Bed 3:** iPSC-Derived Cardiomyocytes for Cardiac Regeneration	**Diversity and Inclusion**

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Non-Destructive, In-Line, Closed-System Measurement and Assay Technologies	**Test-Bed 1: MSCs**					
	Develop the Dynamic Sampling Platform (DSP), coupled to a multi-mode analytical sensor such as MS and FTIR, for cell reactor characterization that can also integrate directly into therapeutic cell manufacturing quality control approaches Performance target: • Define probe specs for engineering design and fabrication • Design DSP probe and develop/fabricate monolithic microfabricated probes	Performance target: • Integrate DSP with HPLC-nano-ESI-MS and demonstrate secretome sampling/analysis • Integrate and demonstrate DSP/ATR-FTIR high-throughput characterization of small molecules in cell culture • Analyze MSC secretome evolution on the time scale relevant to local secretome change	Performance target: • Characterize DSP performance (time response and sampling volume), in combination with label-free nano-ESI MS and ATR-SEIRAS detection • Use DSP with ATR-SEIRAS detection for monitoring MSCs and MSC culture supernatant grown under different bioreactor conditions	Performance target: • Demonstrate DSP-HPLC-nano-ESI-MS sensitivity to detect variability in MSC donor secretome profiles • Relate secretome profiles measured via DSP with HPLC-nano-ESI-MS to differences in MSC function *in vitro*	Performance target: • Correlate higher-throughput ATR data to higher-sensitivity MS data for closed-loop cell manufacturing system • Relate DSP measured secretome profiles to differences in MSC function *in vivo* (a stretch goal)	This technology will enable inline determination of cellular potency during culture, resulting in increased consistency from batch to batch and higher quality of cells produced from the overall process.
	Test-Bed 2: CAR-T					
	Design in-line sensors for CAR-T to measure cytotoxic activity Performance target: • Integrate into bioreactors on small scale • Run in parallel to morphology techs (4Q18)	Integrate sensors with microfluidic cell-transduction platform for CAR-T manufacturing to monitor transduction efficiency Performance target: • # of CAR-T cells transduced				This technology will result in higher transduction efficiency and therefore higher potency of each batch of cells produced.
	Refine microfluidic CAR-T transduction platform					This technology (really a part of the technology in the row above) will result in higher potency of cells produced.
	Apply CRISPR/Cas9 genome editing to construct cell lines that act as sentinels (i.e., cells that representatively report quality by being inside the bioprocess, but that can be	Performance target: • Sentinel cell matches established cells • Develop assays for protein expression level	Performance target: • Assess effect of scale-up on sensor through large bioreactor testing			This technology will enable determination of cellular potency during culture, resulting in increased consistency from batch to batch and higher quality of

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	easily separated out at the end of bioprocessing) Performance target: • Report on CAR-transgene level or other alternative critical marker to get rid of or track (2Q18) • Add cell lines in bioreactor (4Q18)					cells produced from the overall process.
	Test-Bed 3: iPSCs					
	Construct sentinel cells with GFP tags on CM-specific genes Performance target: • Validate expression of GFP during CM differentiation	Devise method for elimination of sentinel cells after manufacturing Performance target: • Achieve no detectable sentinel cells after elimination	Construct reporter lines to enable monitoring of cell potency and safety Performance target: • Validate ability to detect	Construct reporter lines to enable detection of cardiac gene isoform switching in a single line Performance target: • Validate detection of isoform switching by qPCR and flow cytometry	Demonstrate use and elimination of sentinel cells in a manufacturing-scale process Performance target: • Achieve 10^9 CMs manufactured in a process using sentinel cells to monitor differentiation progression	This technology will enable inline determination of cellular maturity during culture, resulting in increased consistency from batch to batch and higher maturity of cells produced from the overall process.
	Construct epigenetic sensors of cardiac cell differentiation Performance target: • Validate sensors using standard histone acetylation assays	Performance target: • Implement quantitative, real-time imaging of epigenetic sensors during cardiac cell differentiation and correlate with label-free chromatin analysis to identify CQAs	Performance target: • Test the effect of engineered, functionalized biomaterials and/or organoid culture on CQAs associated with cardiac cell differentiation and potency	Performance target: • Identify transcriptomic and epigenetic signatures of cell potency and correlate with CQAs and high-content, label-free chromatin analysis to monitor cell potency during scaled-up cell manufacturing	Performance target: • Develop non-invasive strategies for the analysis of cardiac cell differentiation and cell potency during large-scale biomanufacturing	This technology will enable inline determination of cellular maturity during culture, resulting in increased consistency from batch to batch and higher maturity of cells produced from the overall process.
	Develop the DSP, coupled to a multi-mode analytical sensor such as MS and FTIR, for cell reactor characterization that can also integrate directly into therapeutic cell	Performance target: • N/A- technology development initially with MSC Test-Bed	Performance target: • N/A- technology development initially with MSC Test-Bed	Performance target: • Apply and characterize DSP performance (i.e., time response and sampling volume), in combination with label-free nano-ESI	Performance target: 1 • Achieve highly local (i.e., on the scale of a single cell) measurements of transcription factors and CQAs (indicative of the gene expression level determined in Thrust 1)	This technology will enable determination of cellular maturity during culture, resulting in increased consistency from batch to batch and higher maturity of cells produced from the overall process.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	manufacturing quality control approaches <u>Performance target</u>: • N/A- technology development initially with MSC Test-Bed			MS and ATR-SEIRAS detection, for monitoring iPSCs	• Use internal standards/calibrants in application of DSP-nano-ESI-MS and FTIR-ATR/SEIRAS for quantitative measurements	
Disease/Tissue-on-a-Chip Models	**Test-Bed 1: MSCs**					
	Engineer tissue-on-a-chip platforms to evaluate MSC potency in response to defined inflammatory stimuli <u>Performance target</u>: • Engineer basic perfusable chip with only human MSCs • Characterize cytokine profile of basal cells vs inflammatory stimuli cells	<u>Performance target</u>: • Correlate MSC morphological features with *in vitro* secretory profiles • Engineer perfusable chip with immune cells • Correlate perfusable chip from *in vitro* to *in vivo*	<u>Performance target</u>: • Correlate perfusable combo chip from *in vitro* to *in vivo*	<u>Performance target</u>: • Correlate perfusable combo chip from *in vitro* to *in vivo* in different MSC patient sources (2-year activity) • Test unknown patient samples		Establishing surrogate platforms for cell potency and safety will enable low-cost screening for each batch and thus increase the safety and quality of cells produced through scale-up production. Such assays could also inform the development of standards for assessing potency of cell-based therapies.
					<u>Performance target</u>: • Test predictive power with new set of patient samples	
	Test-Bed 2: CAR-T					
	Develop two models: one with a central vascular channel surrounded by a tumor and one with a tumor model with a distributed vascular model <u>Performance target</u>: • Generate optical metabolic imaging (OMI) data set on CAR-T cell batches • Isolate and characterize invasive glioblastoma stem cell subpopulations using 3D matrices	Test therapeutic potency of CAR-T cells, either as a monotherapy or as combination therapies using the on-chip models <u>Performance target</u>: • Characterize glioma 3D organoid within chip • Identify metabolic states correlating with low potency • Conduct on-chip potency testing of CAR-T cell products	Integrate additional inline sensors for CAR-T to measure potency <u>Performance target</u>: • Integrate morphology imaging and analysis • Examine invasive potential and chemotherapeutic drug resistance using glioma-on-chip assays • Perform mass spectrometry, metabolite, and other –	Evaluate CAR-T product safety by profiling cytokine release and off-target cytotoxicity <u>Performance target</u>: • Perform cytokine profiling on-chip • Integrate healthy tissue chips to model off-target toxicity	Integrate microfluidic transduction platform and cellular sensors into chip <u>Performance target</u>: • Optimize fluidics and sensors in the integrated system • Integrate into bioreactors on small scale	<u>See above.</u>

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	• Synthesize and characterize collagen-based thermoresponsive hydrogel		omics profiling of these models			
					Performance target: • Test predictive power with new set of patient samples	See above
	Test-Bed 3: iPSCs					
	Identify prototyping process (replicate testing) platform and evaluate its robustness for the establishment of an *in vitro* organoid-disease model of cardiac tissue injury Performance target: • Assess cell function • Achieve coupling of cells: 2Q18					See above

Thrust 3 — Systems Optimization for Scalable Manufacturing

Thrust 3—Systems Optimization for Scalable Manufacturing—will focus on developing new technologies for scale-up/scale-out of therapeutic cells. In this Thrust, which emphasizes "how to scale," information about "what to measure" (Thrust 1) and "how to monitor" (Thrust 2) will be integrated using technologies such as new bioreactors/biomaterials, process control, and industrial models for supply chain management and reduction of product variability and cost. To produce large numbers of high-quality cells for all three Test-Beds with well-managed supply chain constraints, Thrust 3 will focus on achieving the following outcomes:

- Implementation of robust supply chain and process modeling algorithms to ensure product reproducibility and cost effectiveness
- Development of new bioreactors/biomaterials with in-line sensing capabilities to expand and/or differentiate cells in a closed system
- Deployment and integration of real-time sensors that generate feedback data to reduce variability in quality/quantity of the product

R&D Activities

Overarching goals for each Test-Bed in the order in which they would be executed include the following (exact timeline varies depending on the Test-Bed):

1. Develop Supply Chain Manufacturing Process model:
    a. Determine process boundary conditions and variables
    b. Identify undefined/unknown variable
    c. Meet with appropriate industrial partners to fill in knowledge gaps and validate model structure
2. Leverage high-throughput screening to maximize yield of therapeutic cell phenotype
3. Develop novel bioreactors for acquisition, maintenance, and expansion of therapeutic cell phenotype
4. Update supply chain manufacturing process model with new technologies developed in Thrust
5. Quantitatively benchmark improvement in cost, robustness, and accessibility

Legend for Cross-Center Integration		
1 **Thrust 1:** Cell-Omics – Cell Characterization and Modeling to Identify Predictive Biomarkers	1 **Test-Bed 1:** MSCs for Regenerative Medicine	**Workforce Development**
2 **Thrust 2:** Monitoring Cell Potency and Safety – Sensors, Potency-on-a-Chip, and Modeling	2 **Test-Bed 2:** CAR-T Cells for Cancer Immunotherapy	**Innovation Ecosystem**
3 **Thrust 3:** Systems Optimization for Scalable Manufacturing	3 **Test-Bed 3:** iPSC-Derived Cardiomyocytes	**Diversity and Inclusion**

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
High Throughput Screening for Scale-up/ Development of Responsive Culture	**Test-Bed 1: MSCs**					
	Develop culture substrates that will provide key biochemical signals to improve expansion and potency of MSCs in serum-free culture. In particular, we will alter the following parameters in our arrays: a. GAG (heparin and chondroitin sulfate) sulfation patterns b. Peptides to engage different ligands (engaging integrins vs cadherins) c. Stiffness <u>Performance target</u>: • Determine cell source, work, and materials flow between participating investigators • Adapt current high-throughput technology available between investigators to incorporate all biomolecules listed above • Incorporate materials into dotted arrays and determine MSC adhesion and cell viability via microscopy	<u>Performance target</u>: • Produce larger materials from "hits" from Aim 1 to examine effects of substrate on MSC secretome (using a bead-based multiplex cytokine assay kit) in serum and serum-free conditions • Generate a multivariate model to better understand/predict the effects of substrate parameters on MSC secretome	Iterate on substrate parameters based on multivariate model and input from Thrust 1 <u>Performance target</u>: • Further optimize culture conditions to show increase in anti-inflammatory secretome without sacrificing proliferation • Incorporate measurements of other CQAs from Thrust 1 on subset of hits from Y1-Y2 that show the greatest proliferation and anti-inflammatory secretome	Iterate on substrate parameters based on input from Thrust 1 <u>Performance target</u>: • Incorporate measurements of other CQAs from Thrust 1 on subset of hits from Y1-Y3 that show the greatest proliferation and anti-inflammatory secretome • Examine effects of substrate parameters on composition of exosomes produced (based on results of Thrust 1 for the ideal type/amount of exosomes) • Examine effects of substrate parameters on MSC response (using CQAs identified thus far) to exosome exposure • Validate trends seen (and associated computational models) with other sources of MSCs	Iterate on substrate parameters based on input from Thrust 1 <u>Performance target</u>: • Further refine substrates to optimize composition of exosomes produced (based on results of Thrust 1 for the ideal type/amount of exosomes) • Further refine substrates to optimize MSC response (using CQAs identified thus far) to exosome exposure • Continue to validate observed data trends (and associated computational models) with other sources of MSCs • Demonstrate proof-of-concept that shows how the best substrates identified in Y1-Y4 would be integrated into a standard bioreactor/culture flask	Culture substrates derived from this project will enhance the number (scale-up) of high-quality MSCs.
					Use data produced on 2D substrates to create array of "best-guess" particles for scale-up culture <u>Performance target</u>: • Incorporate materials into particles and determine adhesion and cell viability	Culture substrates derived from this project will enhance the number of high-quality MSCs.
				Incorporate in-line sensors for CQAs identified thus far <u>Performance target</u>: • Use "good" and "bad" surfaces from array data to validate sensors and markers	Incorporate in-line sensors for CQAs identified thus far <u>Performance target</u>: • Use "good" and "bad" surfaces from array data to validate sensors and markers	Data derived from this project will be used to validate sensors and markers developed in

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
						Thrusts 1-2, thereby accelerating progress on improving scale-up of high-quality MSCs.
	Test-Bed 3: iPSCs					
	Identify process for differentiating iPSCs to cardiac fibroblasts Performance target: • Compare efficiency of epicardial-derived cardiac fibroblasts vs. Kamp protocol to achieve virtually pure cardiac fibroblasts	Assess effects of co-culture on iPSC-CM phenotypes in 2D Performance target: • Achieve improved structural, electromechanical, and metabolic maturation compared to monoculture control	Scale suspension culture of myocardial organoids Performance target: • Achieve production of 10^8 iPSC-CMs in aggregate culture	Assess effects of organoid composition on iPSC-CM phenotypes Performance target: • Achieve improved structural, electromechanical, and metabolic maturation compared to CM monoculture and CM:CF organoids	Scale suspension culture of myocardial organoids Performance target: • Achieve production of 10^9 iPSC-CMs in aggregate culture	Culture substrates and conditions developed in this project will improve the number and quality of cardiomyocytes produced.
	Design media and matrices for CM/CF co-culture Performance target: • Identify conditions that permit controlled ratios of CM:CF in 2D culture	Assess effects of organoid composition on iPSC-CM phenotypes Performance target: • Achieve improved structural, electromechanical, and metabolic maturation compared to monoculture control	Incorporate endothelial and epicardial cells in cardiac organoids Performance target: • Achieve physiologic ratio of CMs, CFs, EC, and EpiCs in engineered myocardial organoids			Culture substrates and conditions developed in this project will improve the number and quality of cardiomyocytes produced.
	Identify suitable scaffolds for organoid formation and culture Performance target: • Achieve CM and CF survival in 3D culture for > 2 weeks	Design materials for iPSC-CM differentiation in suspension Performance target: • Identify materials with suitable transition temperatures • Identify materials that have culture survival	Design materials for iPSC-CM differentiation in suspension; add new ligands/materials to improve survival without compromising transition temperatures Performance target: • Screen at least 10 second-generation	Design materials for iPSC-CM differentiation in suspension; assess effects of scaffold composition on iPSC-CM phenotypes Performance target: • Achieve improved structural, electromechanical, and metabolic maturation compared to plastic control	Design materials for iPSC-CM differentiation in suspension; scale scaffold-mediated suspension production of myocardial organoids Performance target: • Modify scaffold for prolonged culture, and achieve improved structural, electromechanical, and	Culture substrates developed in this project will improve the number and quality of cardiomyocytes produced.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
		of at least > 1 week	materials • Achieve two-fold increase in survival		metabolic maturation compared to suspended organoids	
	Design scaffolds that align cardiac cells in 3D Performance target: • Achieve >50% of cells with major axes aligned					Culture substrates developed in this project will improve the number and quality of cardiomyocytes produced.
Process and Supply Chain Modeling Algorithms	**Test-Bed 1: MSCs**					
			Study sources of variability, i.e., the causal and temporal relationships of controllable variables (such as time in culture, media composition, and culture substrate type) in the manufacturing process and the CQAs Performance Target: • Define baseline of current practice • Identify knowledge gaps in process characterization	Design and implement uncertainty quantification methods for complex biological processes to bridge gaps between conventional manufacturing process modeling techniques and cell manufacturing processes Performance Target: • Define functional uncertainty quantification methods	Build and implement a sub-scaled closed-system control bioreactor that demonstrates minimal variability in product with a low implementation cost for in-line sensing Performance Target: • Demonstrate efficacy of control strategy on a sub-scaled prototype production unit • Conduct cost/benefit analysis: increased operation cost vs. less variability	Models and control systems developed in this project will result in a closed-system bioreactor to allow improved scale-up of MSCs.
			Design concepts of closed-system manufacturing that implement real-time data from in-line sensors to provide a controlled, real-time responsive environment Performance Target:	Design temporal, multi-stage state-space modeling techniques that integrate real-time data from in-line sensors to predict product quality by assessing and controlling the temporal impact on process variability and throughput (i.e., tracking and reducing production lead time)	Build and implement a sub-scaled, closed-system control bioreactor that demonstrates minimal variability in product with a low implementation cost for in-line sensing Performance Target: • Demonstrate efficacy of control strategy on a sub-	Models and control systems developed in this project will result in a closed-system bioreactor to allow improved scale-up of MSCs.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
			• Develop conceptual designs	Performance Target: • Test results through prototype • Establish protocol and validated methods for estimating product quality of any given manufacturing process with in-line monitoring data	scaled prototype production unit • Conduct cost/benefit analysis: increased operation cost vs. less variability	
			Develop and validate single bio-manufacturing facility simulations to understand the impact of processing and QA on needle-to-needle lead-time, patient benefit, and cost at the facility level Performance target: • Understand dynamics • Develop baseline model • Complete validation and assessment with industry and academic partners' data	Demonstrate decision-making in manufacturing configurations given real-time patient information Performance target: • Estimate the impact of real-time reconfiguration on patient benefits (e.g., efficacy, cost, risk)	Develop dynamic dispatching and routing decision support models for multiple types of cell products based on real-time patient conditions and state of cells. *(This will be a cross-test-bed activity for all three cell types.)* Performance target: • Demonstrate full integration of Thrust 2 real-time sensor data related to cost minimization and risk mitigation via real-time network-facility optimization	Simulations developed in this project will enhance efficiency of scale-up of MSCs.
				Validate system-wide supply chain network model and assess efficacy Performance target: • Complete validation and assessment using industry partners' data (e.g., fill rates, delivery reliability, responsiveness)	Develop dynamic dispatching and routing decision support models for multiple types of cell products based on real-time patient conditions and state of cells *(This will be a cross-test-bed activity for all three cell types.)* Performance target: • Show proof of concept related to cost minimization and risk mitigation via real-time network-facility	Supply chain network models developed in this project will provide ways to reduce cost and patient risk, thus improving the efficacy and availability of cell-based therapies.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
					optimization	
			Identify policy barriers and opportunities to promote efficient and equitable translation of MSCs Performance Target: • Develop policy proposals regarding MSCs	Identify policy barriers and opportunities to promote efficient and equitable translation of MSCs Performance Target: • Develop policy proposals and roadmap of MSCs		Policy analysis arising from this project will provide suggestions to improve availability of cell-based therapies.
	Test-Bed 2: CAR-T					
	Study sources of variability, i.e., the causal and temporal relationships of controllable variables (such as time in culture, media composition, and culture substrate type) in the manufacturing process and the CQAs Performance Target: • Define baseline of current practice • Identify knowledge gaps in process characterization	Design concepts of closed-system manufacturing that implement real-time data from in-line sensors to provide a controlled, real-time responsive environment Performance Target: • Develop conceptual designs	Design and implement uncertainty quantification methods for complex biological processes to bridge gaps between conventional manufacturing process modeling techniques and cell manufacturing processes Performance Target: • Define functional uncertainty quantification methods	Design temporal, multi-stage state-space modeling techniques that integrate real-time data from in-line sensors to predict product quality by assessing and controlling the temporal impact on process variability and throughput (i.e., tracking and reducing production lead time) Performance Target: • Test results through prototype • Establish protocol and validated methods for estimating product quality of any given manufacturing process with in-line monitoring data	Build and implement a sub-scaled, closed-system control bioreactor that demonstrates minimal variability in product with a low implementation cost for in-line sensing Performance Target: • Demonstrate efficacy of control strategy on a sub-scaled prototype production unit • Conduct cost/benefit analysis: increased operation cost vs. less variability	Models and control systems developed in this project will result in a closed-system bioreactor to allow improved scale-up of CAR-T cells.
	Develop and validate single bio-manufacturing facility simulations to understand the impact of processing and QA on needle-to-needle lead-time, patient benefit, and cost at the facility level Performance target: • Understand dynamics • Develop baseline model	Develop simulations for supply chain operating strategies to minimize needle-to-needle lead times, risk and costs (production, inventory, transportation) Performance target: • Test with current levels of demand and	Demonstrate decision-making in manufacturing configurations given real-time patient information Performance target: • Estimate the impact of real-time reconfiguration on			Simulations developed in this project will enhance efficiency of scale-up of therapeutic cells.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	• Complete validation and assessment with industry and academic partners' data	supply forecast accuracy for CAR-T cells	patient benefits (e.g., efficacy, cost, risk)			
	Develop system-wide, network-level supply chain simulations <u>Performance target</u>: • Identify best supply chain configurations: optimal number of bio-manufacturing facilities and their locations	Validate system-wide supply chain network model and assess efficacy <u>Performance target</u>: • Complete validation and assessment using industry partners' data (e.g., fill rates, delivery reliability, responsiveness)	Develop dynamic dispatching and routing decision support models for multiple types of cell products based on real-time patient conditions and state of cells *(This will be a cross-test-bed activity for all three cell types.)* <u>Performance target:</u> • Show proof of concept related to cost minimization and risk mitigation via real-time network-facility optimization	Develop dynamic dispatching and routing decision support models for multiple types of cell products based on real-time patient conditions and state of cells *(This will be a cross-test-bed activity for all three cell types.)* <u>Performance target:</u> • Demonstrate full integration of Thrust 2 real-time sensor data related to cost minimization and risk mitigation via real-time network-facility optimization		Supply chain network models developed in this project will provide ways to reduce cost and patient risk, thus improving the efficacy and availability of cell-based therapies.
	Identify policy barriers and opportunities to promote efficient and equitable translation of CAR-T cells <u>Performance target</u>: • Develop roadmap for CAR-T cells	<u>Performance target</u>: • Provide suggestions on policy making based on promotion roadmap of CAR-T cells				Policy analysis arising from this project will provide suggestions to improve availability of cell-based therapies.
	Test-Bed 3: iPSCs					
			Study sources of variability, i.e., the causal and temporal relationships of controllable variables (such as time in culture, media composition, and culture substrate type)	Design and implement uncertainty quantification methods for complex biological processes to bridge gaps between conventional manufacturing process modeling techniques and cell manufacturing processes	Build and implement a sub-scaled, closed-system control bioreactor that demonstrates minimal variability in product with a low implementation cost for in-line sensing <u>Performance Target:</u> • Demonstrate efficacy of control strategy on a sub-	Models and control systems developed in this project will result in a closed-system bioreactor to allow improved scale-up of iPSC-

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
			in the manufacturing process and the CQAs <u>Performance Target:</u> • Define baseline of current practice • Identify knowledge gaps in process characterization	<u>Performance Target:</u> • Define functional uncertainty quantification methods	scaled prototype production unit • Conduct cost/benefit analysis: increased operation cost vs. less variability	cardiomyocytes.
			Design concepts of closed-system manufacturing that implement real-time data from in-line sensors to provide a controlled, real-time responsive environment <u>Performance Target:</u> • Develop conceptual designs	Design temporal, multi-stage state-space modeling techniques that integrate real-time data from in-line sensors to predict product quality by assessing and controlling the temporal impact on process variability and throughput (i.e., tracking and reducing production lead time) <u>Performance Target:</u> • Test results through prototype • Establish protocol and validated methods for estimating product quality of any given manufacturing process with in-line monitoring data	Build and implement a sub-scaled, closed-system control bioreactor that demonstrates minimal variability in product with a low implementation cost for in-line sensing <u>Performance Target:</u> • Demonstrate efficacy of control strategy on a sub-scaled prototype production unit Conduct cost/benefit analysis: increased operation cost vs. less variability	Models and control systems developed in this project will result in a closed-system bioreactor to allow improved scale-up of iPSC-cardiomyocytes.
			Develop and validate single bio-manufacturing facility simulations to understand the impact of processing and QA on needle-to-needle lead-time, patient benefit, and cost at the facility level <u>Performance target:</u> • Understand dynamics • Develop baseline model	Demonstrate decision-making in manufacturing configurations given real-time patient information <u>Performance target:</u> • Estimate the impact of real-time reconfiguration on patient benefits (e.g., efficacy, cost, risk.)	Develop dynamic dispatching and routing decision support models for multiple types of cell products based on real-time patient conditions and state of cells. *(This will be a cross-test-bed activity for all three cell types.)* <u>Performance target</u>: • Demonstrate full integration of Thrust 2 real-time sensor data related to cost minimization and risk mitigation via real-time	Simulations developed in this project will enhance efficiency of scale-up of iPSC-cardiomyocytes.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
			• Complete validation and assessment with industry and academic partners' data		network-facility optimization	
			Develop and validate system-wide, network-level supply chain simulations <u>Performance target</u>: • Identify best supply chain configurations: optimal number of bio-manufacturing facilities and their locations • Complete validation and assessment using industry partners' data (e.g., fill rates, delivery reliability, responsiveness)	Develop simulations for supply chain operating strategies to minimize needle-to-needle lead times and costs (production, inventory, transportation) <u>Performance target:</u> • Test with current levels of demand and supply forecast accuracy for iPSCs		Supply chain network models developed in this project will provide ways to reduce cost and patient risk, thus improving the efficacy and availability of cell-based therapies.
					Identify policy barriers and opportunities to promote efficient and equitable translation of iPSCs <u>Performance target</u>: • Develop proposed policy and promotion roadmap of iPSCs	Policy analysis arising from this project will provide suggestions to improve availability of cell-based therapies.

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Technology for Transport	**Test-Bed 1: MSCs**					
			Determine the impact of cryopreservation on viability, phenotypical distribution, and molecular profile of patient bone marrow aspirates Performance target: • Test samples from 4 patients, comparing before and after cryopreservation • Test 3 different cryopreservation protocols • Use CQAs from Thrust 1	Evaluate how changes in viability, phenotypical distribution, and molecular profile of bone marrow aspirates samples affect MSC manufacture Performance target: • Test efficiency of MSC manufacture on 4 patient samples	Optimize cryopreservation protocols or develop post-thaw culture protocol to improve MSC manufacture and efficacy Performance target: • Maintain 70% efficacy in cryopreserved versus fresh MSC batches • Integrate Thrust 2 assays to evaluate efficacy of MSC cell product	Information gathered in this project will result in improved freezing and culture handling techniques that will increase the number of high-quality MSCs.
			Determine the impact of cryopreservation on viability, secretome profile, and molecular profile of MSCs Performance target: • Test samples from 4 patients, comparing before and after cryopreservation • Test 3 different cryopreservation protocols • Use CQAs from Thrust 1	Evaluate how changes in viability, secretome profile, and molecular profile affects MSC efficacy Performance target: • Maintain 70% efficacy in cryopreserved versus fresh MSC cell batches • Integrate Thrust 2 assays to evaluate efficacy of MSC product		
	Test-Bed 2: CAR-T					
	Determine the impact of cryopreservation on the viability and phenotypical distribution of patient leukapheresis samples Performance target: • Test samples from 4 patients,	Determine the impact of cryopreservation on the molecular profile of patient leukapheresis samples Performance target:	Evaluate how changes in viability, phenotypical distribution, and molecular profile of leukapheresis samples affects CAR-T cell	Optimize cryopreservation protocols or develop post-thaw culture protocol to improve persistence of T-cells and efficiency of CAR-T cell manufacture	Compare CAR-T cell efficacy before and after cryopreservation pipeline using *in vivo* model Performance target: • Maintain 70% efficacy in	Information gathered in this project will result in improved freezing and

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	comparing before and after cryopreservation • Test 3 different cryopreservation protocols	• Conduct RNA-seq on samples from 4 patients, comparing before and after cryopreservation	manufacture <u>Performance target</u>: • Test efficiency of CAR-T manufacture on 4 patient samples	<u>Performance target</u>: • Integrate Thrust 2 assays to evaluate efficacy of CAR-T cell product • Maintain 70% viability of target T-cell populations • Optimize CAR-T cell manufacture efficiency	cryopreserved versus fresh CAR-T cell batches	culture handling techniques that will increase the number of high-quality CAR-T cells.
	Determine the impact of cryopreservation on the viability and activation state of CAR-T cells <u>Performance target:</u> • Test on 4 different CAR-T cell batches before and after cryopreservation • Test 3 different cryopreservation protocols	Determine the impact of cryopreservation on the molecular profile of CAR-T cells <u>Performance target</u>: • Conduct RNA-seq on 4 different CAR-T cell batches before and after cryopreservation	Evaluate how changes in viability, activation state, and molecular profile affects CAR-T cell efficacy <u>Performance target</u>: • Maintain 70% efficacy in cryopreserved versus fresh CAR-T cell batches • Integrate Thrust 2 assays to evaluate efficacy of CAR-T cell product	Optimize cryopreservation protocols or develop post-thaw culture protocol to improve persistence of T-cells and efficiency of CAR-T cell manufacture <u>Performance target</u>: • Maintain 70% efficacy in cryopreserved versus fresh CAR-T cell batches		Information gathered in this project will result in improved freezing and culture handling techniques that will increase the number of high-quality CAR-T cells.
	Test-Bed 3: iPSC-CM					
	Determine the impact of cryopreservation on the viability, cell attachment, and functional activity of iPSC-CMs <u>Performance target</u>: • Test on 4 different iPSC-CM batches before and after cryopreservation • Test 3 different cryopreservation protocols	Determine the impact of cryopreservation on the molecular profile of iPSC-CMs <u>Performance target</u>: • Conduct RNA-seq on 4 different iPSC-CM batches before and after cryopreservation	Evaluate how changes in viability, molecular profile, and functional activity affect iPSC-CM efficacy <u>Performance target</u>: • Maintain 70% efficacy in cryopreserved versus fresh iPSC-CMs • Integrate Thrust 2 assays to evaluate efficacy of iPSC-CM product	Optimize cryopreservation protocols or develop post-thaw culture protocol to improve iPSC-CM efficacy <u>Performance target</u>: • Maintain 70% efficacy in cryopreserved versus fresh iPSC-CMs • Integrate Thrust 2 assays to evaluate efficacy iPSC-CM product	Compare iPSC-CM cell efficacy before and after cryopreservation pipeline using *in vivo* model <u>Performance target</u>: • Maintain 70% efficacy in cryopreserved versus fresh iPSC-CMs	Information gathered in this project will result in improved freezing and culture handling techniques that will increase the number of high-quality cardiomyocytes.

Engineering Workforce Development

CMaT's workforce development program is designed to recruit, inspire, and train a highly inclusive group of next-generation engineering innovators and leaders with broad, convergent expertise in biomanufacturing and, specifically, cell manufacturing technologies. Drawing on evidence-based approaches and established best practices, the Engineering Workforce Development program will train technically-skilled, globally competitive, and culturally aware engineers prepared to advance cell manufacturing (**Figure 8**).

The plan addresses critical workforce needs identified by our industry partners in the 10-year NCMC national roadmap. We propose to develop new research, training, and outreach experiences designed to accomplish three overarching goals:

1. Produce a diverse group of undergraduate and graduate engineers with a unique set of key technical and professional skills necessary to transform cell manufacturing
2. Prepare students from two-year colleges (e.g., technical and community colleges) for careers in the biomanufacturing industry
3. Build upon the excitement surrounding cell therapies to stimulate student interest in bioengineering at the pre-college and college levels, especially among underrepresented groups

Both our university education and our pre-college education programs will include targeted recruiting and outreach to underrepresented students—including students of color, women, veterans, English learners, and students with disabilities—to broaden participation and develop a culture of inclusion within the cell manufacturing stakeholder community. We will leverage existing successful partnerships and local and state resources (described below) to bring talented undergraduate and high school students to CMaT labs at each partner institution for hands-on training experiences. We will connect all CMaT trainees with their peers at other institutions, CMaT faculty, and industry-clinical stakeholders through collaborative research projects, education programs, and an annual CMaT Virtual Symposium. Finally, we will work with the industry/practitioner advisory board (IPAB) and professional associations to identify key continuing education needs and develop professional education programs to support the industry.

Regional Strategies: While CMaT's EWD efforts are center-wide, each CMaT institution has its own unique strengths and is located within the context of a larger regional economy. As a result, we are prioritizing and tailoring EWD activities across the CMaT ecosystem to maximize their impact.

Georgia	We are building on state investments to support advanced bio-science training by prioritizing our partnership with the Technical College System of Georgia (TCSG) through summer research experiences for both instructors and students and long-term internships for students. We will partner with TCSG instructors to develop new curricular materials for two-year colleges to help meet the workforce needs identified by our industry partners.
Wisconsin	We are prioritizing work with an existing stem cell technologies certificate offered by the Madison Area Technical College and are working to integrate cell manufacturing content into this successful program.
Puerto Rico	We are focusing on our partnership with the local public school system, especially at the high school level. These efforts aim to engage students in the fields of cell- and bio-manufacturing both to build a pipeline of students interested in these areas and to help prepare students to contribute to rebuilding the island's pharmaceutical and bio-manufacturing sector following Hurricane Maria.

Ultimately, these efforts will contribute to a new, innovative, diverse, and skilled engineering workforce. Throughout, we will use SMART (Specific, Measurable, Achievable, Relevant, and Timely) goals, systematic data collection, and input from internal and external experts to continually assess and improve our approach and will identify best practices to disseminate across the broader stakeholder community. The workforce development leaders, Buxton (UGA, lead), Levine A. (GT, co-lead), Hogle (U-Wisc) and Padovani (UPRM), collectively are experts in education and training, as well as regulatory, healthcare, and social policy related to cell therapies. They will work closely with CMaT's diversity experts, the IPAB, and innovation-entrepreneurship experts to implement this strategic plan. CMaT faculty are fully committed to training an inclusive workforce.

CMaT is well positioned to integrate our efforts in the pillars of workforce development, diversity & inclusion, and innovation ecosystem to produce outputs that are unique to the goals of CMaT. Specifically, three of these unique outputs focus on: 1) our plans for building unique partnerships with technical colleges; 2) our plans to integrate entrepreneurship as it relates to cell manufacturing at all education levels from elementary school through graduate school; and 3) our development and implementation of CMaT implicit bias training (see Culture of Inclusion section).

1. **Technical college partnerships** - While our partnerships with technical colleges across CMaT sites were already built into the initial CMaT strategic plan, in the interim we received a supplemental Research Experience and Mentoring (REM) award that we will use to jumpstart our collaboration with our technical college colleagues. We envision this collaboration leading to unique and highly relevant outputs for CMaT, given the critical role that technical colleges must play in training a diverse, innovative, and skilled technical workforce for the emerging cell manufacturing industry. Several innovative features of the partnership that the REM will help us to build and strengthen include:

- Working directly with technical college instructors to enhance their understanding of cell manufacturing and to support their efforts to integrate novel cell manufacturing concepts into existing courses at their institutions.
- Working directly with technical college students to introduce the field of cell manufacturing and encourage them to pursue training and careers in this field and share what they are learning about this field with other technical college students and K-12 students through school visits.

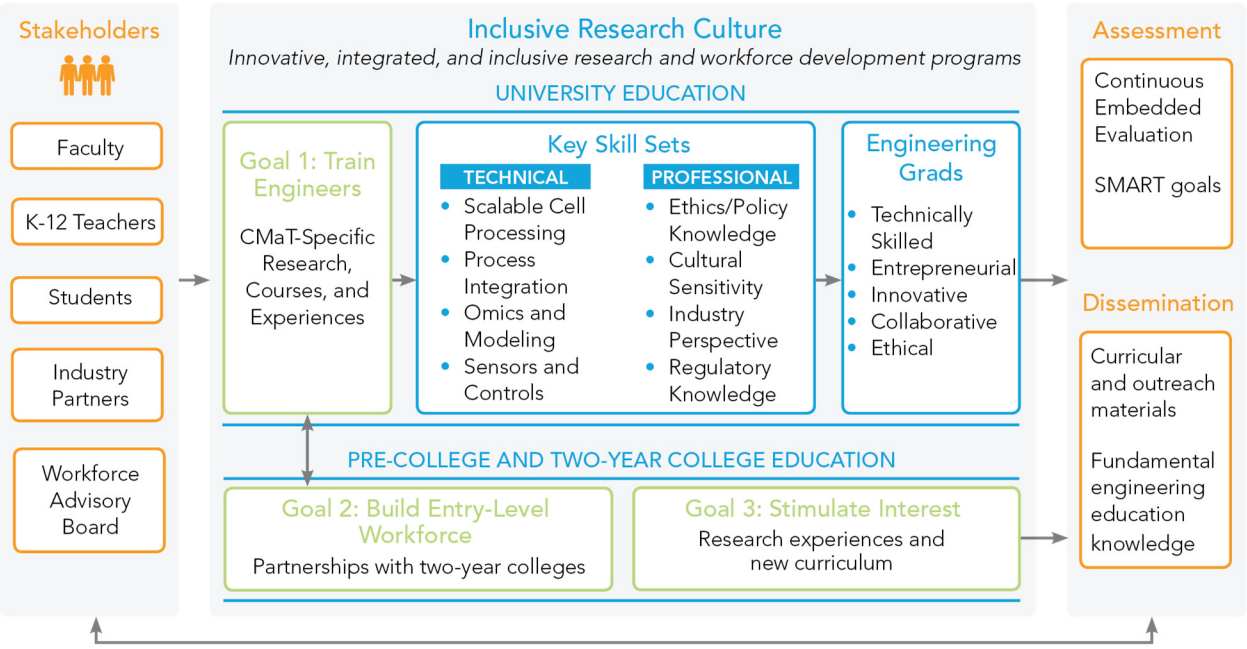
- Leveraging the partnership between CMaT institutions and technical colleges to integrate CMaT professional and technical skill sets that are needed for the cell manufacturing workforce into both the technical college and the university curriculum.
- Diversifying the pool of future engineers and scientists through recruitment of participants from underrepresented groups in engineering into technical college pathways.
- Providing mentor training for faculty and for students at the technical colleges and CMaT institutions to ensure high-quality experiences for all participants while deepening these partnerships to enhance project sustainability.

2. Integrated entrepreneurship experiences - Providing high-quality internships and entrepreneurship opportunities for students is central to the work of all ERCs. However, an output in this area that will make CMaT unique is our effort to integrate entrepreneurship experiences into all education levels from elementary school to graduate school. We believe that many of today's young people still in the K-12 education system have an entrepreneurial spirit that typically goes unrecognized and undeveloped in K-12 school contexts or even in undergraduate education in STEM fields. CMaT has the potential to engage and motivate these students to think in new ways about the future of biomanufacturing and the possible roles they could play in developing this emerging field. In the short term, this requires building new partnerships across precollege, technical college, university, and industry to foster enthusiasm for the entrepreneurial possibilities of cell manufacturing. This can be done through school presentations, field trips, and classroom conversations about entrepreneurship as it relates to STEM fields generally and biomanufacturing specifically. In the midterm, we envision a range of partnerships between CMaT industry partners and students at all levels of education such that cell manufacturing concepts and engineering education more generally are included in the curriculum and through internship experiences in ways that move beyond the science and engineering content to also focus on the innovation and excitement that comes from entrepreneurship and industrial opportunities.

In the long term, our goal is for CMaT to become an exemplar for infusion of entrepreneurship experiences at all education levels as a way to advance the cell manufacturing field while expanding students' ideas about what STEM professionals do to include business and entrepreneurship opportunities.

A more detailed strategic plan follows.

FIGURE 8. Overall Strategic Plan of CMaT's Engineering Workforce Development



Engineering Workforce Development Strategic Plan

The Workforce Development program will facilitate new research, training, and outreach experiences to achieve the following outcomes:

- A diverse group of undergraduate and graduate engineers with a unique set of key technical and professional skills necessary to transform the cell manufacturing industry
- Students from two-year technical colleges prepared for careers in biomanufacturing
- Increased student interest in bioengineering and cell manufacturing at the pre-college and college levels, especially among underrepresented groups in engineering
- Teachers and instructors at all levels—from K-12 to graduate education—who use new curricular materials, new pedagogical approaches, and new strategies for broadening participation
- An ecosystem of sustainable partnerships that link industry, global institutions, K-12 schools, technical colleges, and universities to address the current and future needs of the cell manufacturing workforce

R&D Activities

Legend for Cross-Center Integration		
1 **Thrust 1:** Cell-Omics – Cell Characterization and Computational Modeling to Identify Predictive Cell Therapy Biomarkers	1 **Test-Bed 1:** MSCs for Regenerative Medicine	**Workforce Development**
2 **Thrust 2:** Monitoring Cell Potency and Safety – Sensors, Potency-on-a-Chip, and Modeling	2 **Test-Bed 2:** CAR-T Cells for Cancer Immunotherapy	**Innovation Ecosystem**
3 **Thrust 3:** Systems Optimization for Scalable Manufacturing	3 **Test-Bed 3:** iPSC-Derived Cardiomyocytes for Cardiac Regeneration	**Diversity and Inclusion**

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Cross-Cutting Workforce Development	Engage with the CMaT industry/practitioner advisory board (IPAB) and Workforce Development Advisory Board (WFAB) to identify continually evolving education needs and modify courses and modules accordingly Performance target: • Use the NCMC roadmap as a starting point; update at IPAB and WFAB meetings	Performance target: • Facilitate sessions on evolving workforce needs at IPAB, WFAB, and the Annual Retreat • Design CMaT courses and modules to reflect updated workforce needs	Performance target: • Facilitate sessions on evolving workforce needs at IPAB, WFAB, and the Annual Retreat • Modify CMaT courses and modules to reflect updated workforce needs	Performance target: • Facilitate sessions on evolving workforce needs at IPAB, WFAB, and the Annual Retreat • Modify CMaT courses and modules to reflect updated workforce needs	Performance target: • Facilitate sessions on evolving workforce needs at IPAB, WFAB, and the Annual Retreat • Modify CMaT courses and modules to reflect updated workforce needs	CMaT students continue to receive state-of-the-art workforce preparation
	Host annual CMaT Student Virtual Symposium and Annual Meeting to share student research, provide mentoring, and foster CMaT identity Performance target: • Plan format and logistics for annual virtual symposia and EWD component of Annual Meeting to include presentations of student research and CMaT results, and best practices for workforce development and mentoring	Performance target: • Host initial annual CMaT Student Virtual Symposium and Annual Meeting • Gather feedback on initial meetings and use to modify plans for 2020 symposium and Annual Meeting	Performance target: • Host 2nd annual CMaT Student Virtual Symposium and Annual Meeting • Gather feedback on meetings and use to modify plans for 2021 symposium and Annual Meeting	Performance target: • Host 3rd annual CMaT Student Virtual Symposium and Annual Meeting • Gather feedback on meetings and use to modify plans for 2022 symposium and Annual Meeting	Performance target: • Host 4th annual CMaT Student Virtual Symposium and Annual Meeting • Gather feedback on meetings and use to modify plans for future symposia and Annual Meetings	Graduate and undergraduate students develop and sustain CMaT identity, and learn to share results of their participation
	Partner with existing evidence-based entrepreneurship training and industry partners to provide CMaT students with internships and entrepreneurial opportunities Performance target: • Each site to update list of relevant programs by 3Q18 • Market to CMaT students by 4Q2018	Performance target: • 3+ students participate in internships with industry partners or other firms working in cell manufacturing • Update list of opportunities for 2020 and market to CMaT students	Performance target: • 5+ students participate in internships with industry partners or other firms working in cell manufacturing • Update list of opportunities for 2021 and market to CMaT students	Performance target: • 7+ students participate in internships with industry partners or other firms working in cell manufacturing • Update list of opportunities for 2022 and market to CMaT students	Performance target: • 7+ students participate in internships with industry partners or other firms working in cell manufacturing • Update list of opportunities for 2023 and market to CMaT students	Graduate and undergraduate students gain real-world experience in the cell manufacturing industry
	Establish cross-institutional and diverse undergraduate-graduate	Performance target:	Performance target:	Performance target:	Performance target:	Students at all levels and from all partner

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	student organization and Student Leadership Council (SLC) to provide feedback, advise CMaT from student perspectives, and promote CMaT identity and ecosystem <u>Performance target:</u> • Launch a diverse student leadership team • Perform preliminary SWOT analyses of CMaT activities and conduct training workshops and seminars	• Recruit undergraduate and graduate students from all partner institutions to join CMaT student organization • Student organization plans student activities for Virtual Symposium and Annual Meeting • SLC gathers and provides feedback to leadership team	• Recruit students from all education levels and all partner institutions to join CMaT student organization • Student organization plans student activities for Virtual Symposium and Annual Meeting • SLC gathers and provides feedback to leadership team	• Recruit students from all education levels and all partner institutions to join CMaT student organization • Student organization plans student activities for Virtual Symposium and Annual Meeting • SLC gathers and provides feedback to leadership team	• Recruit students from all education levels and all partner institutions to join CMaT student organization • Student organization plans student activities for Virtual Symposium and Annual Meeting • SLC gathers and provides feedback to leadership team	institutions engage in CMaT activities in ways that shape student identity while supporting the goals of the Center
Graduate Programs	Develop an inter-institutional graduate course on "Best Practices and Current Challenges in Cell Manufacturing" with focus on industry case studies and real-world problems <u>Performance target</u>: • Developed by Q4 2018	<u>Performance target:</u> • Integrate courses into existing MS and PhD engineering programs at all CMaT partner institutions using synchronous virtual classroom technology • 10+ students enrolled in this course across campuses • 2+ industry presenters / case studies integrated into course	<u>Performance target:</u> • 15+ students enrolled in this course across campuses • 3+ industry presenters / case studies integrated into course	<u>Performance target:</u> • 15+ students enrolled in this course across campuses • 3+ industry presenters / case studies integrated into course	<u>Performance target:</u> • 15+ students enrolled in this course across campuses • 3+ industry presenters / case studies integrated into course	Graduate students gain industry perspective and appreciation of current state of cell manufacturing
	Develop inter-institutional graduate course on "Cell Manufacturing and Society" focused on relevant regulatory, ethical, legal, economic, healthcare, and policy issues <u>Performance target</u>: • Developed by Q2 2018	<u>Performance target:</u> • Integrate courses into existing MS and PhD engineering programs at all CMaT partner institutions using synchronous virtual classroom technology • 10+ students enrolled in this course across campuses • 2+ outside experts (e.g., regulatory, reimbursement, health economics, ethics) participate in course	<u>Performance target:</u> • 15+ students enrolled in this course across campuses • 3+ outside experts (e.g., regulatory, reimbursement, health economics, ethics) participate in course	<u>Performance target:</u> • 15+ students enrolled in this course across campuses • 3+ outside experts (e.g., regulatory, reimbursement, health economics, ethics) participate in course	<u>Performance target:</u> • 15+ students enrolled in this course across campuses • 3+ outside experts (e.g., regulatory, reimbursement, health economics, ethics) participate in course	Graduate students gain broader social perspective (including awareness of ethical considerations, policy environment) in cell manufacturing

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	Assess demand for graduate credentials (e.g., graduate certificate, professional master's degree) in cell manufacturing and, if demand merits, develop one or more new credentials <u>Performance target</u>: • Assess needs and value proposition for graduate credentials in cell manufacturing with IPAB and WFAB • Conduct needs and interest assessment on each campus	<u>Performance target:</u> • Work with relevant faculty at each campus to develop framework for potential graduate certificate and/or professional master's in cell manufacturing	<u>Performance target</u>: • (If demand merits) Establish pilot graduate certificate in cell manufacturing at one CMaT university	<u>Performance target:</u> • (If demand merits) Expand graduate certificates in cell manufacturing to additional CMaT partner universities • Update demand assessment for potential professional master's	<u>Performance target:</u> • (If demand merits) Develop new professional master's degree in cell manufacturing at one CMaT university	Provide access to new opportunities for graduate students at each campus to gain credential in cell manufacturing
	Establish mentoring ecosystem with graduate students serving both as mentors and mentees <u>Performance target</u>: • 2+ CMaT graduate students participate in mentor training • 2+ graduate students participate as mentors in summer research experiences (e.g., REU, RET, REM)	<u>Performance target:</u> • 4+ CMaT graduate students participate in mentor training • 4+ graduate students participate as mentors in summer research experiences (e.g., REU, RET, REM)	<u>Performance target:</u> • 4+ CMaT graduate students participate in mentor training • 4+ graduate students participate as mentors in summer research experiences (e.g., REU, RET, REM)	<u>Performance target:</u> • 4+ CMaT graduate students participate in mentor training • 4+ graduate students participate as mentors in summer research experiences (e.g., REU, RET, REM)	<u>Performance target:</u> • 4+ CMaT graduate students participate in mentor training • 4+ graduate students participate as mentors in summer research experiences (e.g., REU, RET, REM)	Graduate students learn and practice the skills and dispositions of effective mentoring through both receiving and providing mentoring
	Establish international research exchanges for CMaT students with our global partners <u>Performance target</u>: • Create framework for exchanges with international partners • Work with faculty across institutions to identify and match specific exchange partners	<u>Performance target:</u> • 2+ CMaT students participate in international research exchange • Evaluate initial research exchange and modify framework and plans based on feedback	<u>Performance target:</u> • 3+ CMaT students participate in international research exchange • Evaluate second research exchange and modify framework and plans based on feedback	<u>Performance target:</u> • 4+ CMaT students participate in international research exchange • Evaluate third research exchange and modify framework and plans based on feedback	<u>Performance target:</u> • 4+ CMaT students participate in international research exchange • Evaluate fourth research exchange and modify framework and plans based on feedback	Graduate students gain global perspective, skills, and experience through international exchanges

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Undergraduate and Veterans Programs CMaT to identify what modules include and how to get them used (e.g., cross-CMaT material development)	Develop educational modules for integration into existing undergraduate engineering courses Performance target: • CMaT faculty identify what to include in modules and the initial courses for pilot testing • CMaT faculty and graduate students work to develop 3 initial modules to pilot test in courses • CMaT leadership team recruits faculty to pilot test modules	Performance target: • Pilot and assess initial modules at GT • Revise modules based on feedback and share with faculty at other CMaT institutions	Performance target: • Utilize modules in undergraduate programs at CMaT partner universities • Revise modules based on feedback • Develop 1-2 additional modules	Performance target: • Revise modules based on feedback • Pilot and assess new modules at GT • Integrate updated ethical, economic, and policy information; career prospects; and industry trends	Performance target: • Revise modules based on feedback • Disseminate and promote use of modules outside of CMaT	Undergraduate students gain opportunities to learn about cell manufacturing as an exciting growth area in bioengineering
	Launch new CMaT Research experience for undergraduates (REU) and integrate cell manufacturing into ongoing REUs (e.g., REVAMP focused on veterans) Performance target: • Pilot integration of cell manufacturing opportunities into existing REUs at GT to identify best practices • Coordinate with CMaT faculty at all institutions to launch CMaT-specific REU program	Performance target: • 8+ students participate in CMaT REUs (across all four campuses), recruiting an inclusive group of engineering students, including students of color, women, veterans, and those with disabilities • 1-2 students in existing REUs focus on cell manufacturing research experiences • Evaluate and revise to improve REU experience as needed	Performance target: • 8+ students participate in CMaT REUs (across all four campuses), recruiting an inclusive group of engineering students, including students of color, women, veterans, and those with disabilities • 3-4 students in existing REUs focus on cell manufacturing research experiences	Performance target: • 10+ students participate in CMaT REUs (across all four campuses), recruiting an inclusive group of engineering students, including students of color, women, veterans, and those with disabilities • 3-4 students in existing REUs focus on cell manufacturing research experiences	Performance target: • 10+ students participate in CMaT REUs (across all four campuses), recruiting an inclusive group of engineering students, including students of color, women, veterans, and those with disabilities • 3-4 students in existing REUs focus on cell manufacturing research experiences	Undergraduate students gain robust research experiences and mentoring through participation in CMaT and related REUs

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	Integrate cell manufacturing research experiences into existing regional Minority Serving Institution (MSI) Partnerships <u>Performance target:</u> • Coordinate with existing academic year program for students at Atlanta-area HBCUs to identify opportunities to integrate cell manufacturing	<u>Performance target:</u> • 2+ students participate in cell manufacturing research experiences through existing MSI program for students at GT • Evaluate and revise efforts to integrate CMaT topics into this existing program	<u>Performance target:</u> • 4+ students participate in cell manufacturing research experiences through existing MSI program for students at GT • Assess demand and feasibility for expanding program to additional CMaT universities	<u>Performance target:</u> • 4+ students participate in cell manufacturing research experiences through existing MSI program for students at GT • Pilot program at additional CMaT university	<u>Performance target:</u> • 4+ students participate in cell manufacturing research experiences through existing MSI programs for students at GT and/or other CMaT universities • Evaluate and revise efforts to integrate CMaT topics	Undergrad students at MSIs gain opportunities to learn about and work on research connected to CMaT
Technical Colleges	Work with regional partners, the Technical College System of Georgia (TCSG), and Madison Area Technical College (MATC), to develop educational modules for integration into existing biotechnology courses <u>Performance target:</u> • CMaT faculty work with technical college faculty to identify what to include in modules and courses in which they fit • CMaT faculty and graduate students work with technical college faculty to develop 2 initial modules to pilot test in courses	<u>Performance target:</u> • Pilot and assess initial modules in courses at 2 technical colleges • Revise modules based on feedback and share with faculty at other technical colleges in Georgia and Wisconsin	<u>Performance target:</u> • Utilize modules in courses at 3+ technical colleges • Revise modules based on feedback from instructors • Integrate updated material and develop additional modules	<u>Performance target:</u> • Utilize modules in courses at 4+ technical colleges • Revise modules based on feedback from instructors	<u>Performance target:</u> • Utilize modules in courses at 4+ technical colleges • Revise modules based on feedback from instructors • Integrate updated materials into modules	Technical college students gain opportunities to learn about cell manufacturing as an exciting growth area in biotechnology
	Collaborate with regional partners, TCSG, and MATC, to create a long-term, part-time cell manufacturing internship for students pursuing 2-year degrees near GT, UGA, and UW <u>Performance target:</u>	<u>Performance target:</u> • 2+ technical college students participate in pilot of internships in CMaT research labs, career education, and mentoring • Evaluate and revise internship plan based on	<u>Performance target:</u> • 3+ technical college students participate in 2nd year of internships in CMaT research labs, career education, and mentoring	<u>Performance target:</u> • 4+ technical college students participate in 3rd year of internships in CMaT research labs, career education, and mentoring	<u>Performance target:</u> • 4+ technical college students participate in 4th year of internships in CMaT research labs, career education, and mentoring	Technical college students gain robust research experiences and career education and mentoring through participation in CMaT research

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	• CMaT faculty work with technical college faculty to design internship experience that aligns with both goals of CMaT and goals of technical college program • Technical college faculty and CMaT team develop plan to recruit students from underrepresented groups • Follow REM model to build mentoring experiences into internship plan	experiences of students and mentors in the pilot	• Evaluate and revise internships based on experiences of students and mentors	• Evaluate and revise internships based on experiences of students and mentors	• Evaluate and revise internships based on experiences of students and mentors	
	Partner with GATech's Excel Program and new UGA program to bring students with disabilities to CMaT sites for professional education <u>Performance target:</u> • CMaT faculty work with Excel directors to design professional education experience that aligns with goals of CMaT and Excel • Excel directors and CMaT team develop recruitment plan to recruit students from Excel for CMaT professional education experience	<u>Performance target:</u> • 1–2 students from Excel program participate in CMaT professional education experience • Evaluate and revise program based on experiences of students in the pilot • Share model and lessons with UGA program	<u>Performance target:</u> • 2+ students from Excel program and/or UGA program participate in CMaT professional education experience • Evaluate and revise program based on experiences of students • Assess feasibility of expanding beyond GT and UGA	<u>Performance target:</u> • 2+ students from Excel program and/or analogous programs at other CMaT universities participate in CMaT professional education experience • Evaluate and revise program based on experiences of students	<u>Performance target:</u> • 2+ students from Excel program and/or analogous programs at other CMaT universities participate in CMaT professional education experience • Evaluate and revise program based on experiences of students	Students with disabilities gain robust professional education experience through participation in CMaT
	Technical college instructors and students in GA and WI participate in research and mentoring in CMaT labs through new REM initiative <u>Performance target:</u> • 3 pairs of technical college instructors and students participate in summer research experience and academic year mentoring experience	<u>Performance target:</u> • Apply for continued supplemental funding from REM • Recruit 3 new pairs of technical college instructors and students to participate in summer research experience and academic year mentoring experience at GT, UGA, and UW	<u>Performance target:</u> • Apply for continued supplemental funding from REM • Recruit 3 new pairs of technical college instructors and students to participate in summer research experience and academic year	<u>Performance target:</u> • Apply for continued supplemental funding from REM • Recruit 3 new pairs of technical college instructors and students to participate in summer research experience and academic year	<u>Performance target:</u> • Apply for continued supplemental funding from REM • Recruit 3 new pairs of technical college instructors and students to participate in summer research experience and	Technical college instructors and students gain robust research experiences and mentoring through participation in CMaT research

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	• Students and instructors recruited following a plan to maximize participation of underrepresented groups • Evaluate effectiveness of research and mentoring components of REM	• Evaluate effectiveness of research and mentoring components of REM and as needed, revise to improve program	mentoring experience at GATech, UGA, and UW • Evaluate effectiveness of research and mentoring components of REM	mentoring experience at GATech, UGA, and UW • Evaluate effectiveness of research and mentoring components of REM	academic year mentoring experience at GATech, UGA, and UW • Evaluate effectiveness of research and mentoring components of REM	
Pre-College	Provide a cell manufacturing research experience program for high school teachers (RET) from local region <u>Performance target:</u> • CMaT faculty work with high school teachers to design a summer research experience that aligns with both the goals of CMaT and high school science standards • Develop recruitment plan to recruit teachers from underrepresented groups • Teachers develop curriculum units based on research experience to integrate into high school curriculum	<u>Performance target:</u> • 2+ teachers participate in summer research experience in CMaT research labs • Teacher-led development of 1-2 related curriculum units for integration into high school curriculum • Evaluate and revise RET plan based on experiences of teachers and mentors	<u>Performance target:</u> • 3+ teachers participate in summer research experience in CMaT research labs and develop related curriculum unit • New curriculum integrated into 2+ schools across CMaT partner institutions • Evaluate and revise RET plan based on experiences of teachers and mentors	<u>Performance target:</u> • 4 teachers participate in summer research experience in CMaT research labs and develop related curriculum unit • New curriculum integrated into 4+ schools across CMaT partner institutions • Evaluate and revise RET plan based on experiences of teachers and mentors	<u>Performance target:</u> • 4 teachers participate in summer research experience in CMaT research labs and develop related curriculum unit • New curriculum integrated into 5+ schools across CMaT partner institutions • Evaluate and revise RET plan based on experiences of teachers and mentors	Teachers gain robust research experiences and take new ideas and activities to their classrooms through participation in CMaT research
	Develop and test a "flipped" RET model to bring knowledge and experiences from the CMaT research labs to groups of high school teachers through summer workshops and module development <u>Performance target:</u> • CMaT graduate students and faculty develop flipped RET	<u>Performance target:</u> • 10 teachers participate in summer flipped RET workshop experience at school sites and develop related curriculum units • Evaluate and revise flipped RET plan based on experiences of teachers and instructors	<u>Performance target:</u> • 10 teachers participate in summer flipped RET workshop experience at school sites and develop related curriculum units • Evaluate and revise flipped RET plan based on experiences	<u>Performance target:</u> • 10 teachers participate in summer flipped RET workshop experience at school sites and develop related curriculum units • Evaluate and revise flipped RET plan based on experiences of teachers and instructors	<u>Performance target:</u> • 10 teachers participate in summer flipped RET workshop experience at school sites and develop related curriculum units • Evaluate and revise flipped RET plan based on	Teachers gain robust lab skills and take new ideas and activities to their classrooms through participation in CMaT workshop

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	workshop in consultation with high school teachers • Workshops highlight knowledge and skills from research in cell manufacturing that are aligned with relevant state and national science standards • Develop plan to recruit teachers from underrepresented groups • Teachers develop curriculum units based on workshop experience to integrate into high school curriculum		of teachers and instructors		experiences of teachers and instructors	
	Engage high school teachers and students in Puerto Rico in research and mentoring in CMaT labs at UPRM through new REM initiative Performance target: • 1 triad of a high school teacher and 2 students participate in summer research experience and academic year mentoring experience at UPRM • Students and teacher recruited following a plan to maximize participation of underrepresented groups • Evaluate effectiveness of research and mentoring components of REM	Performance target: • Apply for continued supplemental funding from REM • Recruit new triad of a teacher and 2 students in PR to participate in summer research experience and academic year mentoring experience at UPRM • Evaluate effectiveness of research and mentoring components of REM and revise to improve program as needed	Performance target: • Apply for continued supplemental funding from REM • Recruit new triad of a teacher and 2 students in PR to participate in summer research experience and academic year mentoring experience at UPRM • Evaluate effectiveness of research and mentoring components of REM	Performance target: • Apply for continued supplemental funding from REM • Recruit new triad of a teacher and 2 students in PR to participate in summer research experience and academic year mentoring experience at UPRM • Evaluate effectiveness of research and mentoring components of REM	Performance target: • Apply for continued supplemental funding from REM • Recruit new triad of a teacher and 2 students in PR to participate in summer research experience and academic year mentoring experience at UPRM • Evaluate effectiveness of research and mentoring components of REM	Teacher and students gain robust research experiences and mentoring through participation in CMaT research
	Train high school student researchers from underrepresented groups with extended cell manufacturing research experience through Project ENGAGES (Initially at	Performance target: • 4 CMaT funded high school scholars participate in summer research experience in CMaT research labs that continues throughout the academic year at	Performance target: • 4 CMaT funded scholars participate in summer research experience in CMaT research labs that continues throughout the academic year at	Performance target: • 4 CMaT funded scholars participate in summer research experience in CMaT research labs that continues throughout the academic year at	Performance target: • 4 CMaT funded scholars participate in summer research experience in CMaT research labs that continues throughout the	Students from underrepresented groups gain robust research experiences, successfully compete in science fair/scholarship competitions, and obtain

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	GATech, but plan for roll out at other institutions) <u>Performance target:</u> • CMaT faculty/postdocs/graduate students work with high school students to develop research projects based on CMaT goals • Develop recruitment plan to recruit students from underrepresented groups from all local school systems • Develop assessment criteria and MOU to include a school system or a particular school for recruitment into ENGAGES applicant pool • Teachers develop curriculum units based on research experience to integrate into high school curriculum	participating CMaT institutions • Develop CMaT related modules to be taught at the Biotechnology Boot Camp that precedes ENGAGES research experience; create adaptable modules that can also be transitioned to the high school classroom • Evaluate and revise Boot Camp and CMaT identity for these students	participating CMaT institutions • Roll out CMaT related modules to be taught at the Biotechnology Boot Camp that precedes ENGAGES research experience • Expand CMaT ENGAGES to additional university • Evaluate and revise CMaT ENGAGES scholars' experiences with researchers and mentors	participating CMaT institutions • Assess feasibility of expanding to additional university • Develop new CMaT related teaching modules for Boot Camps • Create adaptable modules that can also be transitioned to the high school classroom • Evaluate and revise plan based on experiences of mentors, faculty, and local school systems	academic year at participating CMaT institutions • Develop new CMaT related teaching modules for Boot Camp • Create adaptable modules that can also be transitioned to the high school classroom	STEM degrees upon college matriculation

Innovation Ecosystem

The vision of CMaT's innovation ecosystem is to achieve global intellectual leadership, national industrial competitiveness, and lasting economic impact. The mission is to pioneer a vibrant environment for collaboration and entrepreneurship, effective knowledge transfer, and value exchange based on mutually-beneficial partnerships. The strategic goals of the CMaT Innovation Ecosystem are to:

1. Engage a diverse group of innovation leaders, entrepreneurs, industry, and practitioners in all aspects of the ERC
2. Partner with non-traditional stakeholders (standards bodies, regulatory experts, policy forums, reimbursement industry, and clinicians) to ensure that engineering innovations happen in the context of standardization, regulatory policies, and reimbursement framework, and they are relevant and translatable
3. Nurture the ecosystem through a series of enriching meetings and programs that foster two-way exchange of knowledge and value across all stakeholders
4. Enable students and faculty with skills necessary to be entrepreneurs and create ecosystem for new start-ups
5. Develop sustainable partnerships and business models for CMaT to flourish beyond NSF support

CMaT and our industry/practitioner partners share the same vision and commitment to developing an innovative, diverse, and inclusive cell manufacturing workforce. As such, we will leverage our IPAB meetings that bring together faculty, students, administrators from partner universities, and industry and practitioners to share best practices, lessons learned, perspectives, and broader impacts of diversity and inclusion.

Innovation Ecosystem Strategic Plan

CMaT seeks a balanced representation of small, medium, and large companies across the cell manufacturing value chain that will actively participate in the Center's research, innovation, workforce development, and knowledge transfer programs. As such, our strategy to recruit industry partners is to have CMaT faculty, staff, and students identify prospective members through participation in relevant initiatives like the National Cell Manufacturing Consortium (NCMC), Phacilitate, The Bioprocessing Summit, Cell & Gene Therapy Bioprocessing & Commercialization, and the World Stem Cell Summit. In addition, CMaT's ILOs attend relevant industry-focused conferences, such as the International Society for Cellular Therapy, Meeting on the Mesa, and CBI Optimization of Cell and Gene Therapy Production, to elevate the visibility of the Center and recruit new members. Each of these conferences and initiatives cover different dimensions of the industry value chain and some have more participation from small companies than others, thereby providing valuable connections and outreach to a broader portfolio of companies. This strategy has already resulted in many new leads, new partnerships, and a diverse pipeline of potential member companies across the value chain of CMaT.

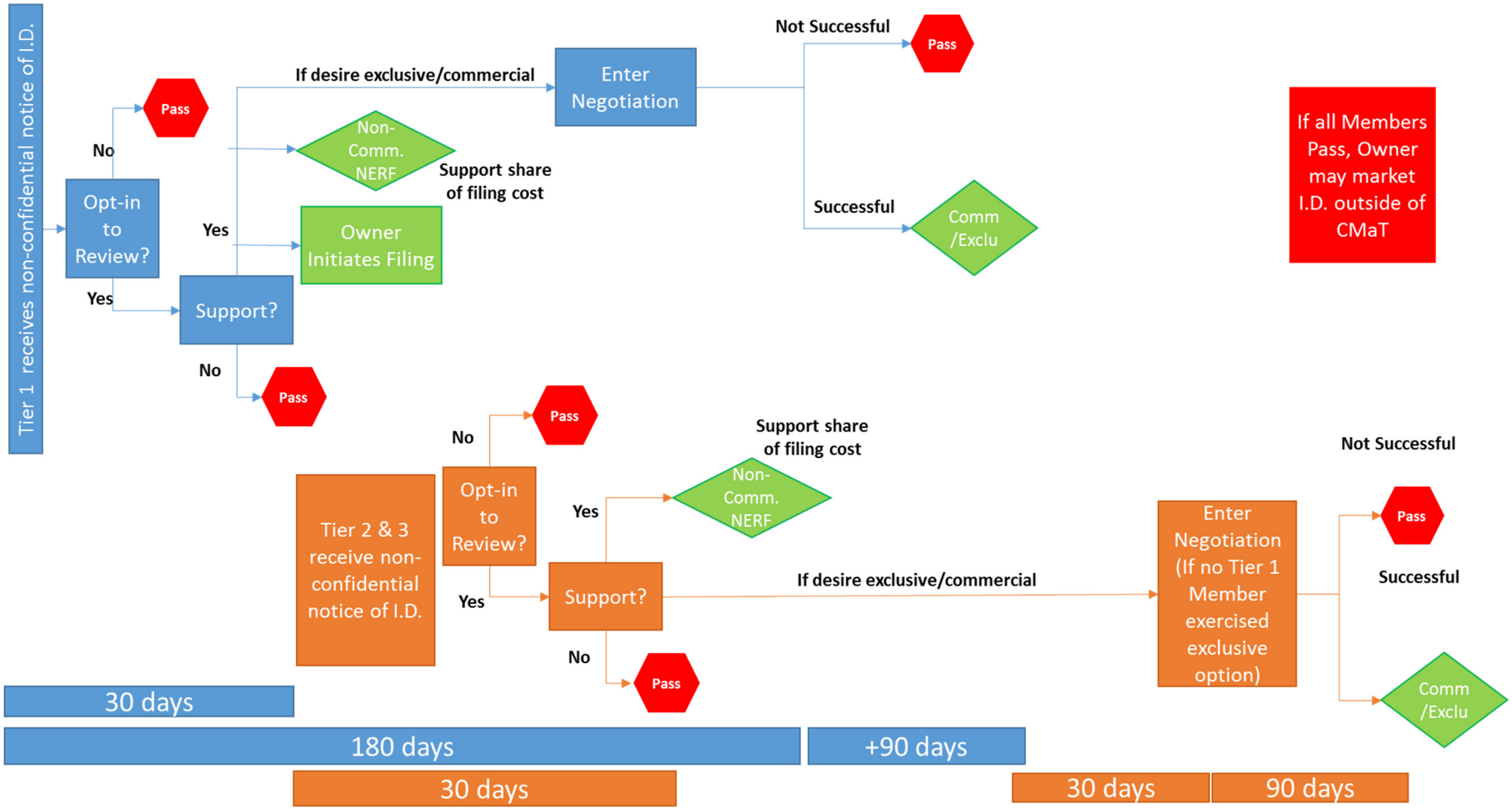
To enable broad participation of diverse stakeholders, CMaT has established a fee-based membership program where participating industry members contribute financial and in-kind support. The fees and benefits are tiered to facilitate collaborations with companies in different parts of the value chain, of diverse sizes, differing capacity for participation, and varied interests.

Membership	Contributions	Benefits
Full (Tier 1)	**$100K Total Annually** ($50K Cash + $50K in-kind)	• Priority option to exclusively license CMaT IP for commercial application* • Priority networking opportunities • Priority to engage in one-on-one research • Option of named student fellowship ***Plus all Associate Member Benefits***
Associate (Tier 2)	**$75K Total Annually** ($25K Cash + $50K in-kind)	• Priority Test-Bed participation • Priority workforce access • Priority access to infrastructure • Priority access to short courses & workshops ***Plus all Affiliate Member Benefits***
Affiliate (Tier 3)	**$50K Total Annually** (Combination of cash and in-kind, or All in-kind)	• Participation on IPAB — influence research directions, project support • Priority involvement in standards development • Option to secure non-exclusive, non-commercial, royalty-free license for any CMaT IP • Option to exclusively license CMaT IP for commercial application if full and associate members do not opt-in* • Logo on website

**for detailed terms, please see membership agreement bylaws*

Technology transfer to the IPAB members will be the first option for research commercialization. In the event that members do not exercise the option to license promising CMaT-generated intellectual property (IP), the Center may choose to pursue other commercialization partnerships. These may include large and/or small companies who are committed to bringing the IP to market, student/faculty-based startups, or translational research partnerships with small-business member or non-member firms. When appropriate, translational research programs like Small Business Technology Transfer (STTR), Small Business Innovation Research (SBIR), Small-Business/ERC Collaborative Opportunity (SECO), and Partnership for Innovation (PFI) support will be pursued. The framework for commercialization is captured in the membership agreement and in the IP management flow diagram below.

IP Management Flow Diagram



The expected size of the industry affiliates program is 10 companies the first year, growing to 18 companies by year 5. CMaT expects some turnover in industry membership over the course of the ERC due to changes in business needs, company reorganizations, and mergers/acquisitions. The key to company retention will be active and deep engagement, attention to company needs and expectations, and regular communication. CMaT plans to listen to the voice of the customer and devise a customized plan that addresses each company's needs aligned with the Center benefits of most value (i.e., access to students, faculty expertise, research, workforce development, specialized facilities, environment to interact with industry colleagues, and intellectual property). This plan will be revisited during the year and a progress report will be provided at the end of the membership period to ensure that we are delivering value to our members. We will actively engage companies in IPAB meetings twice a year where they will have an opportunity to provide feedback on research direction and interact with faculty and students. Student engagement activities such as a mentoring program for CMaT students, judging student "perfect pitch" competitions, and internships will also keep companies engaged and provide value to CMaT. Companies involved in research will be encouraged to interact regularly and provide guidance and feedback to project teams. Knowledge and intellectual property produced by CMaT will encourage retention, since companies will want to exercise their IP rights and priority review under the membership agreement. CMaT-related proprietary sponsored research will further engage companies and allow them to customize CMaT technologies to their own manufacturing processes/products.

Regional and CMaT-wide Synergies: Wisconsin, Georgia, Puerto Rico, and the local cities/counties/communities where our core university partners reside each have their own unique regional innovation ecosystems and support networks to propel cell manufacturing forward. In addition, there is synergy between the regional nodes and cross-CMaT capabilities that are shared, such as the cell characterization, translational research, and scale-up process development capabilities of the Marcus Center for Therapeutic Cell Characterization & Manufacturing and the Waisman Biomanufacturing Center. Our strategy is to leverage these regional innovation capabilities and cross-CMaT competencies to accelerate commercialization and advance local economic impact. The innovation ecosystem team, SAB, IPAB, CAB, Council of Deans, and Executive Committee all assist in coordinating the regional and national synergy. Adding to the regional synergy, we have already observed that many of the small companies that CMaT has in the membership pipeline are clustered near our partner institutions.

The anticipated outcomes of Innovation Ecosystem activities include the following:

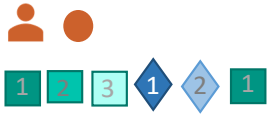
- An extensive network of industrial and practitioner partnerships to help guide research priorities, set research targets, maximize the impact of research outputs, and sustain CMaT beyond NSF support
- Accelerated speed of commercialization and realization of the impacts of innovations through licensing to industry leaders, formation of startup companies, and effective knowledge transfer
- Broader access to cell therapies by enabling an industry capable of large-scale manufacturing of high-quality therapeutic cells
- A diverse, inclusive, innovative, and industry-ready workforce with the cell manufacturing knowledge, skills, and culture to serve as global leaders, impact national competitiveness, and attain local economic benefits

R&D Activities

Legend for Cross-Center Integration		
1 **Thrust 1:** Cell-Omics – Cell Characterization and Computational Modeling to Identify Predictive Cell Therapy Biomarkers	1 **Test-Bed 1:** MSCs for Regenerative Medicine	**Workforce Development**
2 **Thrust 2:** Monitoring Cell Potency and Safety – Sensors, Potency-on-a-Chip, and Modeling	2 **Test-Bed 2:** CAR-T Cells for Cancer Immunotherapy	**Innovation Ecosystem**
3 **Thrust 3:** Systems Optimization for Scalable Manufacturing	3 **Test-Bed 3:** iPSC-Derived Cardiomyocytes for Cardiac Regeneration	**Diversity and Inclusion**

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Industry Engagement	Finalize membership agreement and intellectual property policy Performance target: Complete in 4Q17					Agreements that effectively govern mutually-beneficial industry-university collaboration
	Finalize inter-institutional agreement (IIA) with conflict of interest management policy Performance target: Complete in 2018					Policies that effectively foster transparency, promote inter-institutional collaboration, and manage conflict of interest
	Implement an industry outreach strategy to recruit and retain a diverse portfolio of industry members across the value chain Performance targets: • 10 member companies	Performance targets: • 12 member companies	Performance targets: • 14 member companies	Performance targets: • 16 member companies	Performance targets: • 18 member companies	A diverse portfolio of small, medium, and large member companies with representation across the cell manufacturing value chain
	Actively engage industry and practitioners in advancing CMaT goals Performance Targets: • Convene 2 effective IPAB meetings led by IPAB officers • IPAB to conduct actionable SWOT analysis with CMaT response • Engage IPAB in planning, executing, and evaluating research, Test-Beds, and translational research • 1–2 sponsored/associated research projects with industry/practitioners leveraging CMaT's core research capabilities	Performance targets: • Convene 2 effective IPAB meetings led by IPAB officers • IPAB to conduct actionable SWOT analysis with CMaT response • Engage IPAB in planning, executing, and evaluating research, Test-Beds, and translational research	Performance targets: • Convene 2 effective IPAB meetings led by IPAB officers • IPAB to conduct actionable SWOT analysis with CMaT response • Engage IPAB in planning, executing, and evaluating research, Test-Beds, and translational research	Performance targets: • Convene 2 effective IPAB meetings led by IPAB officers • IPAB to conduct actionable SWOT analysis with CMaT response • Engage IPAB in planning, executing, and evaluating research, Test-Beds, and translational research	Performance targets: • Convene 2 effective IPAB meetings led by IPAB officers • IPAB to conduct actionable SWOT analysis with CMaT response • Engage IPAB in planning, executing, and evaluating research, Test-Beds, and translational research	IPAB that is effectively engaged in imparting industry perspectives, guiding research priorities, and providing actionable feedback Sponsored / associated projects that advance the cell manufacturing / cell therapy industry Successful knowledge transfer in the form of publications co-authored with industry/practitioners

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	• Each member company has opportunity to mentor 1 or more research projects 	• Maintain 2–3 sponsored/associated research projects with industry/practitioners leveraging CMaT's core research capabilities • 1–2 publications co-authored with industry/practitioners • Each member company has opportunity to mentor 1 or more research projects	• Maintain 2–3 sponsored/associated research projects with industry/practitioners leveraging CMaT's core research capabilities • 2–3 publications co-authored with industry/practitioners • Each member company has opportunity to mentor 1 or more research projects	• Maintain 2–3 sponsored/associated research projects with industry/practitioners leveraging CMaT's core research capabilities • 2–3 publications co-authored with industry/practitioners • Each member company has opportunity to mentor 1 or more research projects	• Maintain 2–3 sponsored/associated research projects with industry/practitioners leveraging CMaT's core research capabilities • 3–4 publications co-authored with industry/practitioners • Each member company has opportunity to mentor 1 or more research projects	and industry mentors for projects
	Facilitate student-industry interactions via events and activities <u>Performance targets:</u> • At least 2 student-industry networking events or industry perspective sessions at IPAB meetings per year • Establish a voluntary mentorship program between industry and 2 students	<u>Performance target</u>: • At least 2 student-industry networking events or industry perspective sessions at IPAB meetings per year • Grow voluntary mentorship program with industry to 4 students	<u>Performance target</u>: • At least 2 student-industry networking events or industry perspective sessions at IPAB meetings per year • Grow voluntary mentorship program with industry to 6 students	<u>Performance target</u>: • At least 2 student-industry networking events or industry perspective sessions at IPAB meetings per year • Grow voluntary mentorship program with industry to 8 students	<u>Performance target</u>: • At least 2 student-industry networking events or industry perspective sessions at IPAB meetings per year • Maintain voluntary mentorship program with industry at 8 students	Students with well-rounded industry perspectives and expanded professional networks
	Develop and execute a marketing and communication strategy to raise visibility of CMaT and enhance knowledge transfer with industry/practitioners <u>Performance target</u>: • Develop marketing and communication strategy (2Q18)					Visibility and branding as the global thought leader in cell manufacturing, and effective knowledge transfer to industry, practitioners, the general public, and other stakeholders

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	• Disseminate CMaT information at 4 conferences or workshops (regional, national, international) 	Performance target: • Annual review of marketing and communication strategy to enhance branding as global thought leaders and maximize knowledge transfer • Disseminate CMaT information at 5 conferences or workshops (regional, national, international)	Performance target: • Annual review of marketing and communication strategy to enhance branding as global thought leaders and maximize knowledge transfer • Disseminate CMaT information at 6 conferences or workshops (regional, national, international)	Performance target: • Annual review of marketing and communication strategy to enhance branding as global thought leaders and maximize knowledge transfer • Disseminate CMaT information at 7 conferences or workshops (regional, national, international)	Performance target: • Annual review of marketing and communication strategy to enhance branding as global thought leaders and maximize knowledge transfer • Disseminate CMaT information at 8 conferences or workshops (regional, national, international) • Organize an international forum on cell manufacturing research, innovation, and commercialization	
Non-Industry Partnership Development	Engage a diverse group of non-traditional partners on the Scientific and Clinical Advisory Board (SAB) that includes third-party payers/health insurance industry, clinicians, hospital administrators, patient advocates, and standards bodies (e.g., NIST, FDA, NIH) Performance target: • At least one representative from each area on SAB by June 2018 	Performance target: • Maintain at least one representative from each area	Performance target: • Maintain at least one representative from each area	Performance target: • Maintain at least one representative from each area	Performance target: • Maintain at least one representative from each area	Partnerships to guide research strategies, innovation, workforce development, and knowledge transfer in the context of standardization, regulatory policies, clinical compatibility, reimbursement frameworks, well-being of patients, and best practices
	Engage with state groups to leverage available resources Performance target: • Engage with state groups on new cell manufacturing			Performance target: • Obtain formal state support in terms of new		Obtain formal state support in preparation for post-NSF sustainability and guide

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	legislation and/or obtain proclamations of support			legislation in cell manufacturing and/or proclamations of support		local economic development
	Impact the development of standards, regulations, and policy 	Performance target: • Identify key partners and targets for development of standards, regulations, and policy			Performance target: • Impact one standard, regulation, or policy	Standardization within the emerging cell manufacturing industry to enable large-scale, low-cost, and high-quality manufacturing of therapeutic cells
Commercialization (addresses both	Establish an IP support framework for CMaT researchers that facilitates increased high-quality IP disclosures Performance target: • Establish IP practicum and/or attorney office hours at GATech 	Performance target: • Establish appropriate IP support framework at UWM, UGA, and UPRM • 3 invention disclosures	Performance target: • Establish appropriate IP support framework at other partners (domestic and international) • 6 additional invention disclosures (9 total)	Performance target: • 8 additional invention disclosures (17 total)	Performance target: • 10 additional invention disclosures (27 total)	Increased quantity, quality, and speed of filing invention disclosures

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	Establish a Commercialization Advisory Board (CAB) to help de-risk commercialization projects (i.e., technology, market, IP, people, regulatory, reimbursement, and financial risks) and maximize potential commercialization impact by: 1) guiding IP protection and commercialization strategies, 2) fostering the launch of viable start-up companies, and 3) leveraging local/state/CMaT/national resources 	Performance target: • CAB organized and processes developed for review of inventions/innovations • Review all inventions/innovations and make commercialization recommendations • 1 commercialization project de-risked	Performance target: • Review all inventions/innovations and make commercialization recommendations • 3 commercialization projects de-risked	Performance target: • Review all inventions/innovations and make commercialization recommendations • 4 commercialization projects de-risked	Performance target: • Review all inventions/innovations and make commercialization recommendations • 4 commercialization projects de-risked	Accelerated innovation and increased commercialization impacts driven by CAB of experts (including investors, venture capitalists, and angels) and by leveraging the unique resources of regional, cross-CMaT, and national innovation ecosystems
Industry Engagement in Workforce Development	Engage industry/practitioners in development and delivery of education Performance target: • Engage at least 2 industry members/practitioners in workforce development advisory board • Facilitate industry mentoring of 1 capstone project • Arrange for industry to host 1 internship 	Performance target: • Engage at least 2 industry members/practitioners in workforce development advisory board • Facilitate industry mentoring of 2 additional capstone projects • Arrange for industry to host 2 additional internships	Performance target: • Engage at least 2 industry members/practitioners in workforce development advisory board • Facilitate industry mentoring of 2 additional capstone projects • Arrange for industry to host 4 additional internships	Performance target: • Engage at least 2 industry members/practitioners in workforce development advisory board • Facilitate industry mentoring of 2 additional capstone projects • Arrange for industry to host 4 additional internships	Performance target: • Engage at least 2 industry members/practitioners in workforce development advisory board • Facilitate industry mentoring of 2 additional capstone projects • Arrange for industry to host 4 additional internships	Industry involved in shaping a diverse, inclusive, innovative, and industry-ready workforce with the cell manufacturing knowledge, skills, and culture to be global leaders, impact national competitiveness, and attain local economic benefits
	Facilitate and capture industry/practitioner lectures in CMaT-wide courses for broader dissemination 					Shared industry perspectives with students and broader

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	Performance target: • Curate 5 industry talks in database	Performance target: • Curate 5 additional industry talks in database	Performance target: • Curate 5 additional industry talks in database	Performance target: • Curate 5 additional industry talks in database	Performance target: • Curate 5 additional industry talks in database	impacts of educational materials
	Engage industry in a "Perfect Pitch" competition to teach students how to deliver an elevator pitch and demonstrate a compelling value proposition specific to their own research and for cell manufacturing in general 	Performance target: • All students trained • 5 projects selected for semi-finals • 1 perfect pitch presentation at ERC Biennial Meeting		Performance target: • All students trained • 5 projects selected for semi-finals • 1 perfect pitch presentation at ERC Biennial Meeting		All students trained on how to deliver an elevator pitch about their research project and cell manufacturing in lay terms with a compelling value proposition
	Engage teams of business school students in commercialization evaluation, market analysis, economic development impact studies, value-chain and supply-chain transformation projection, and IP valuation projects based on IPAB recommendations and CMaT leadership approval of relevance 	Performance target: • 1 project at UPRM	Performance target: • 1 project at UGA	Performance target: • 1 project at UWM	Performance target: • 1 project at GATech	Enhanced workforce by training a pool of business students in the context of the cell manufacturing industry
	Leverage international partnerships to educate students in global industry/practitioner perspectives, provide study/work/research abroad experiences, and establish a network for commercialization pathways to other parts of the world 	Performance target: • 1 global industry perspectives seminar • 3 work/study/research abroad experiences for students	Performance target: • 1 additional global industry perspectives seminar • 5 additional work/study/research abroad experiences for students • 1 global commercialization project de-risked	Performance target: • 1 additional global industry perspectives seminar • 7 additional work/study/research abroad experiences for students • 1 additional global commercialization project de-risked	Performance target: • 1 additional global industry perspectives seminar • 7 additional work/study/research abroad experiences for students • 1 additional global commercialization project de-risked	Workforce with relevant international knowledge, skills, and networks to lead the global cell manufacturing industry

Culture of Inclusion

CMaT has a strong vision of a deeply embedded culture of inclusivity across all partners and affiliates to recruit and retain participation of groups that are underrepresented in engineering, and especially manufacturing. Benton-Johnson at GT, an expert on minorities in engineering, a member of the Board of Directors of NAMEPA (The National Association for Multicultural Engineering Program Advocates) and Director of the Center for Engineering Education and Diversity (CEED) will co-direct CMaT's Diversity programs with Fitzpatrick at U-Wisc, an expert on Women in Engineering and Engineering-Outreach and the Director of Diversity Research and Initiatives in the College of Engineering. All CMaT institutions have a strong history and a deep commitment toward diversity and have fully endorsed CMaT's inclusivity plan. Higher Education Magazine in 2015 ranked GT #1 in graduating Minority Engineers at the B.S. and Ph.D. levels, including #1 in African American and Hispanic doctorates and #2 in African American bachelor's degrees. U-Wisc and UGA have increasing populations of underrepresented groups. A goal is to significantly increase diversity among all CMaT participants, but particularly at these universities.

A more detailed strategic plan follows.

Culture of Inclusion Strategic Plan

Diversity and inclusion are at the core of CMaT and are central to achieving CMaT's goals and objectives. These initiatives will facilitate an ecosystem-wide culture of inclusion and are integral to CMaT's workforce development and engagement. Our mission is to be the "best-in-class" engineering research consortium by infusing the values of diversity and inclusion at each educational level and across all program components. CMaT's diversity and inclusion strategy will be centered around a *collaborative* and *multiple touch point* model to achieve the engagement of underrepresented groups within CMaT.

Collaborative: Peer/Group, Team and Tiered strategies will be utilized with students, faculty, labs, and industry for effective mentoring/modeling;

Multiple Touch Points: will include on-going communication via email, workshops, social media, newsletters; engagement in multiple CMaT initiatives/activities for recruitment, retention, and training

These strategies will guide CMaT's focus on the following **three objectives** across CMaT.

Objective 1: Ensure that CMaT's **leadership, researchers, and students represent a diverse group** across ALL institutional partners, and promote a **welcoming and inclusive** culture in all we do.

- Hiring/staffing – An ongoing and annual review for inclusion will be conducted and will include participation from new/replacement hires
- Implicit Bias and Cultural Competency Training – All members of the CMaT consortium will engage in ongoing training to support a culture of inclusion. Training will focus on aspects of activities most susceptible to influences of implicit bias, for example, in student evaluation and selection, classroom and lab interactions, mentoring, and hiring. CMaT participants (faculty, students, and staff) may participate in multiple implicit bias and cultural competency workshops based on different roles and environments, and will be offered continuing education to allow for ongoing engagement. This unique program will begin to ensure that CMaT's leadership, researchers, and students represent a diverse group across ALL institutional partners and promote a welcoming and inclusive culture in all we do. Educational training will include 1–2 hour workshops and videos that focus on recognizing bias in the admissions process, lab groups, classrooms, etc.; an Implicit Bias Series; and other specific activities that focus on defining diversity and inclusion and building an inclusive culture.

Objective 2: Share and leverage strengths (SLS) from CMaT unique geographical positioning to the individual institutional diversity and inclusion programs across partners to train minority, women, and disabled students in cell manufacturing engineering from the pre-college through post-doctorate pipeline.

- Geographical Relevance – We are partnering with EWD efforts and tailoring our diversity and inclusion activities across the CMaT ecosystem to maximize their impact based on partner geographical positions. These educational pipelines and programs were identified, set up, and highlighted because they offer opportunities to non-traditional, low income, and diverse students.

  Georgia: At Georgia Tech and the University of Georgia, we are building on state investments to support advanced bio-science training by prioritizing our partnership with the Technical College System of Georgia through summer research experiences for both instructors and students and long-term internships for students during the academic year. As a part of this program, we plan to work with these students and, especially, instructors in a mentoring capacity to identify and increase access to regionally-based cell manufacturing industries/businesses. Moreover, this group will meet virtually with the groups from the other regional locations of CMaT every two weeks during the program in a more formalized mentorship and professional development program.

  Wisconsin: At University of Wisconsin, we have identified an existing stem cell technologies certificate program offered by the Madison College and are working with this program to integrate cell manufacturing content. As a part of this program, we plan to work with these students and, especially, instructors in a mentoring capacity to identify and increase access to regionally-based cell manufacturing industries/businesses. Moreover, this group will meet virtually with the groups from the other regional locations of CMaT every two weeks during the program in a more formalized mentorship and professional development program.

  Puerto Rico: At the University of Puerto Rico – Mayaguez, we are prioritizing our outreach efforts with the local public-school system, especially at the high school level. As a part of this program, we plan to work with these students and, especially, instructors in a mentoring capacity to identify and increase access to regionally-based cell manufacturing industries/businesses. Moreover, this group will meet virtually with the groups from the other regional locations of CMaT every two weeks during the program in a more formalized mentorship and professional development program.

Program	Home Location	Expanding		Rollout Priority
Internship – Technical College (faculty/students)	Georgia	Wisconsin	50K Coalition (AISES, NSBE, SHPE, SWE)	Year 2–3
Certification Program	Wisconsin	Georgia	Puerto Rico	Year 4–6
Outreach	Puerto Rico	Georgia	Wisconsin	Year 7–10

- Louis Stokes Alliance for Minority Participation (LSAMP) – all CMaT institutions are participants of the NSF LSAMP. This extensive network will offer an outstanding pipeline of CMaT opportunities to talented minority students in engineering. In addition, LSAMP networks have individual strengths (e.g., mentoring, outreach, and professional development) that will be evaluated for sharing with or developing at partner CMaT institutions.

- Institutional Offices and Programs – There are engineering and campus offices and programs across CMaT institutions that focus on recruiting, retaining, and training underrepresented and non-traditional students in engineering/STEM. CMaT will collaborate with these offices and programs to access their student pipelines and provide opportunities within CMaT, and to replicate high-performing programs where they do not exist at CMaT partners.
- Collaboration with Education/Workforce Development – This close collaboration is critical to infuse CMaT curriculum in existing educational programs (pre-college, two-year college, undergraduate, and graduate) at each institution, enhancing reach to and access for underrepresented minority students

Objective 3: Identify, train, and mentor **specific groups of students, such as veterans, mildly disabled students,** or other non-traditional students who could be successful in manufacturing careers with targeted CMaT industry training.

- Veteran and Disabled Student Program Initiatives – GT and University of Georgia currently support veterans engineering education through the Regent's Engineering Transfer Program (RETP), and Expanding Career, Education and Leadership for Students with Intellectual and Developmental Disabilities (Excel) certificates. These programs offer unique opportunities that CMaT can leverage at multiple education levels (certificate, two-year degrees, and four-year degrees), and may be exemplar templates for replication at other CMaT institutions.

R&D Activities

Legend for Cross-Center Integration		
1 **Thrust 1:** Cell-Omics – Cell Characterization and Computational Modeling to Identify Predictive Cell Therapy Biomarkers	1 **Test-Bed 1:** MSCs for Regenerative Medicine	**Workforce Development**
2 **Thrust 2:** Monitoring Cell Potency and Safety – Sensors, Potency-on-a-Chip, and Modeling	2 **Test-Bed 2:** CAR-T Cells for Cancer Immunotherapy	**Innovation Ecosystem**
3 **Thrust 3:** Systems Optimization for Scalable Manufacturing	1 **Test-Bed 3:** iPSC-Derived Cardiomyocytes for Cardiac Regeneration	**Diversity and Inclusion**

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Objective 1: Culture of Inclusion	Conduct CMaT-wide implicit bias and cultural competency training Performance targets: • Research and identify curriculum • Identify evaluation approach • Test curriculum with CMaT leadership • Establish process for facilitator and participant certification	Performance target: • Disseminate materials across CMaT • Develop continuing education modules • 50% CMaT lab groups complete training	Performance target: • 75% of CMaT lab groups have participated in training • 50% of initial CMaT trainees participate in continuing education/ engagement	Performance target: • Establish process for training new CMaT hires • Initiate collaboration with industry diversity training programs	Performance target: • Collaborate with at least 2 industry diversity training programs • 100% of CMaT initial cohort participate in continuing education	Center-wide language and understanding around processes, effects, and methods to alleviate bias; demonstrated center-wide commitment to inclusivity
Objective 2: Share and Leverage Strengths	Create shared CMaT educational/recruitment presentations and deliver to pre-college (summer), undergraduate, and graduate student populations in existing institutional pipeline programs Performance target: • Pilot materials at 1 pre-college and 1 undergraduate program	Performance target: • Present CMaT materials at 20% of all pre-college and institutional pipeline programs • Develop graduate-level recruitment materials	Performance target: • Present at 30% of all diversity pipeline programs across CMaT institutions	Performance target: • Present at 60% of diversity pipeline programs across CMaT institutions	Performance target: • Present at 80% of diversity pipeline programs across CMaT institutions	Demonstrate robust flow of candidates and hires from institutional diversity programs to CMaT educational and workforce programs
	Broadly share CMaT opportunities through electronic "opportunity board" Performance target • Pilot opportunity board via list-serve or website job board	Performance target: • Include undergraduate and graduate research opportunities • Initiate methods for tracking candidates to inform hires	Performance target: • Include RET and pre-college opportunities	Performance target: • Include industry internship and staff position opportunities	Performance target: • Opportunity board is fully operational, with tracking mechanisms in place	Improved awareness of CMaT opportunities across institutions and corporate partners
	Collaborate with LSAMP at CMaT institutions to develop shared CMaT programming and match LSAMP students with research opportunities Performance targets: • Identify 1–2 short-term CMaT research projects to engage LSAMP summer students	Performance target: • Host 1 LSAMP scholar in CMaT lab at 1 institution	Performance target: • Host 1 LSAMP scholar in CMaT lab at 2 institutions	Performance target: • Host 1 LSAMP scholar in CMaT lab at 3 of 4 institutions	Performance target: • 6 LSAMP scholars hosted across CMaT institutions	Fully leverage LSAMP infrastructure and integrate CMaT educational programming across Georgia, Puerto Rico, and Wisconsin networks to identify, engage, and train talented students

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
	Identify and recruit CMaT underrepresented undergraduate/graduate students through CMaT student, post-doc, faculty, and director attendance at national or regional affinity engineering conferences (e.g., ERN, ABRCMS, BMES, SACNAS, SHPE and NSBE) Performance target: • CMaT faculty or director attends 2 national conferences and presents CMaT opportunities	Performance target: • 3 REU students attend/present • 2 CMaT directors, faculty, or post-docs attend/present	Performance target: • 4 REU students attend/present • 3 CMaT directors, faculty, or post-docs attend/present	Performance target: • 5 REU students attend/present • 4 CMaT directors, faculty, or post-docs attend/present	Performance target: • 5 REU students attend/present • 5 CMaT directors, faculty, or post-docs attend/present	Increased awareness and engagement of affinity student and professional organizations with CMaT research and workforce opportunities
	Support up to four minority undergraduate students per year from minority-serving institutions external to CMaT to attend CMaT institution for year-long mentored research experiences Performance target: • Identify minority-serving institutions close to CMaT partners with relevant undergraduate programs • Initiate recruitment and application process	Performance target: • Host 2–4 research students within CMaT lab/institution	Performance target: • Host 4 students (total) at 2 CMaT labs/institutions • CMaT corporate partners host 1 undergraduate for summer internship	Performance target: • Host 4 students (total) at 2 CMaT labs/institutions • CMaT corporate partners host 1 undergraduate for summer internship	Performance target: • Host 4 students (total) at 2 CMaT labs/institutions • CMaT corporate partners host 2 undergraduates for summer internship	Tight collaboration with MSI and CMaT education and innovation ecosystem

Activity Area	2018	2019	2020	2021	2022	Overall Outcomes
Objective 3: Identify, train, and mentor students from special populations	In collaboration with EWD, utilize RETP and Excel to identify, train, and mentor disabled students and veterans Performance target: • Share program operation and evaluation data of these two programs across CMaT institutions • Evaluate opportunity for replication at other CMaT institutions • Develop specialized curriculum as needed	Performance target: • 2 students from RETP and/or Excel participate in CMaT professional education experience	Performance target: • 4 students from RETP and/or Excel participate in CMaT professional education experience	Performance target: • 6 students from RETP and/or Excel participate in CMaT professional education experience • Create RETP pilot program at UPR or UW	Performance target: • 6 students from RETP and/or Excel participate in CMaT professional education experience • Create pilot program of Excel at UGA, UPR, or UW	Create workforce pipeline for non-traditional students that meets industry needs for non-degreed employees

Logic Model and Evaluation Plan

The Center's overall Logic Model and a specific logic model for Workforce and innovation are shown below in **Figure 9 and 10**.

FIGURE 9. Center-Level Logic Model

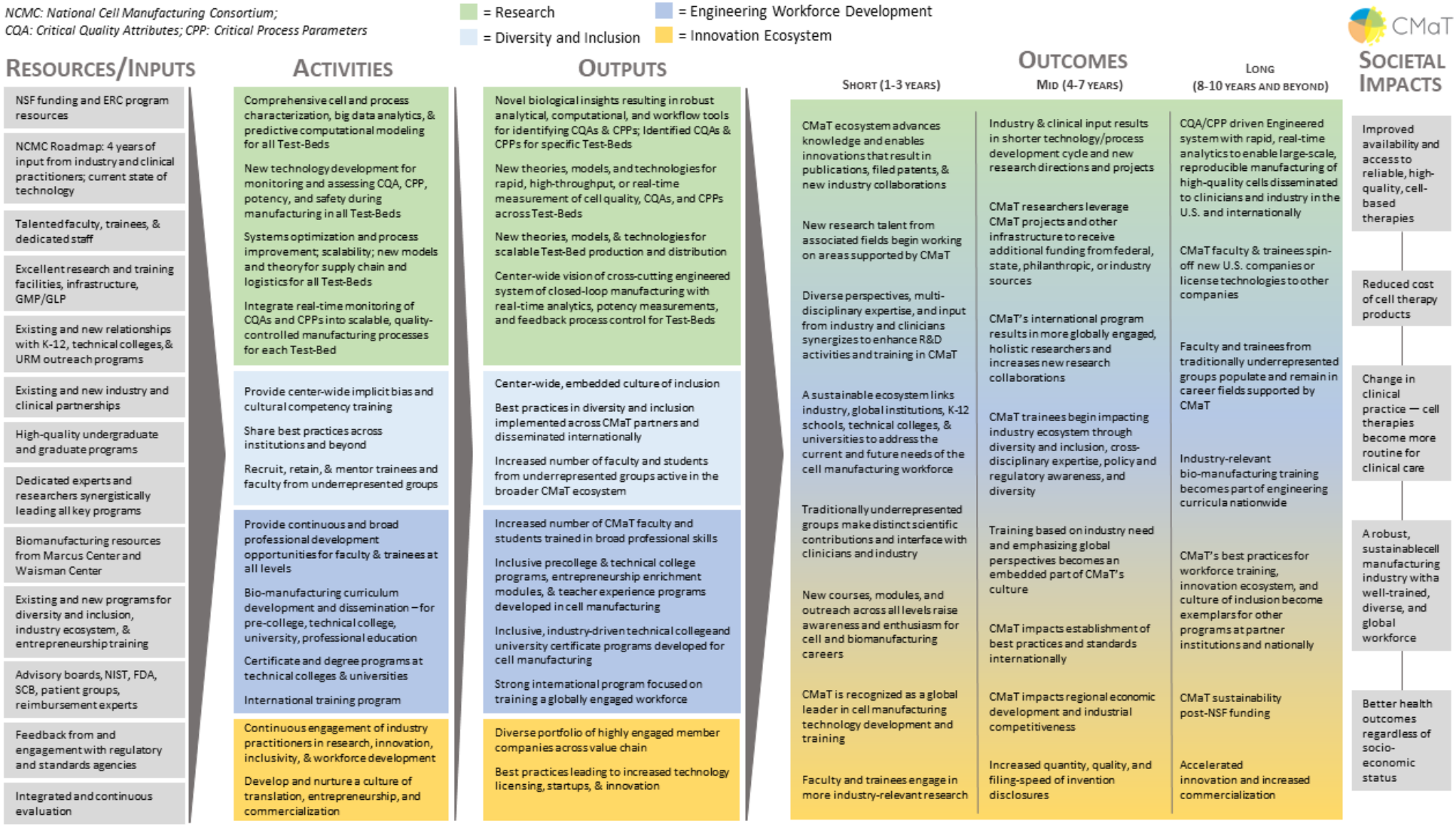
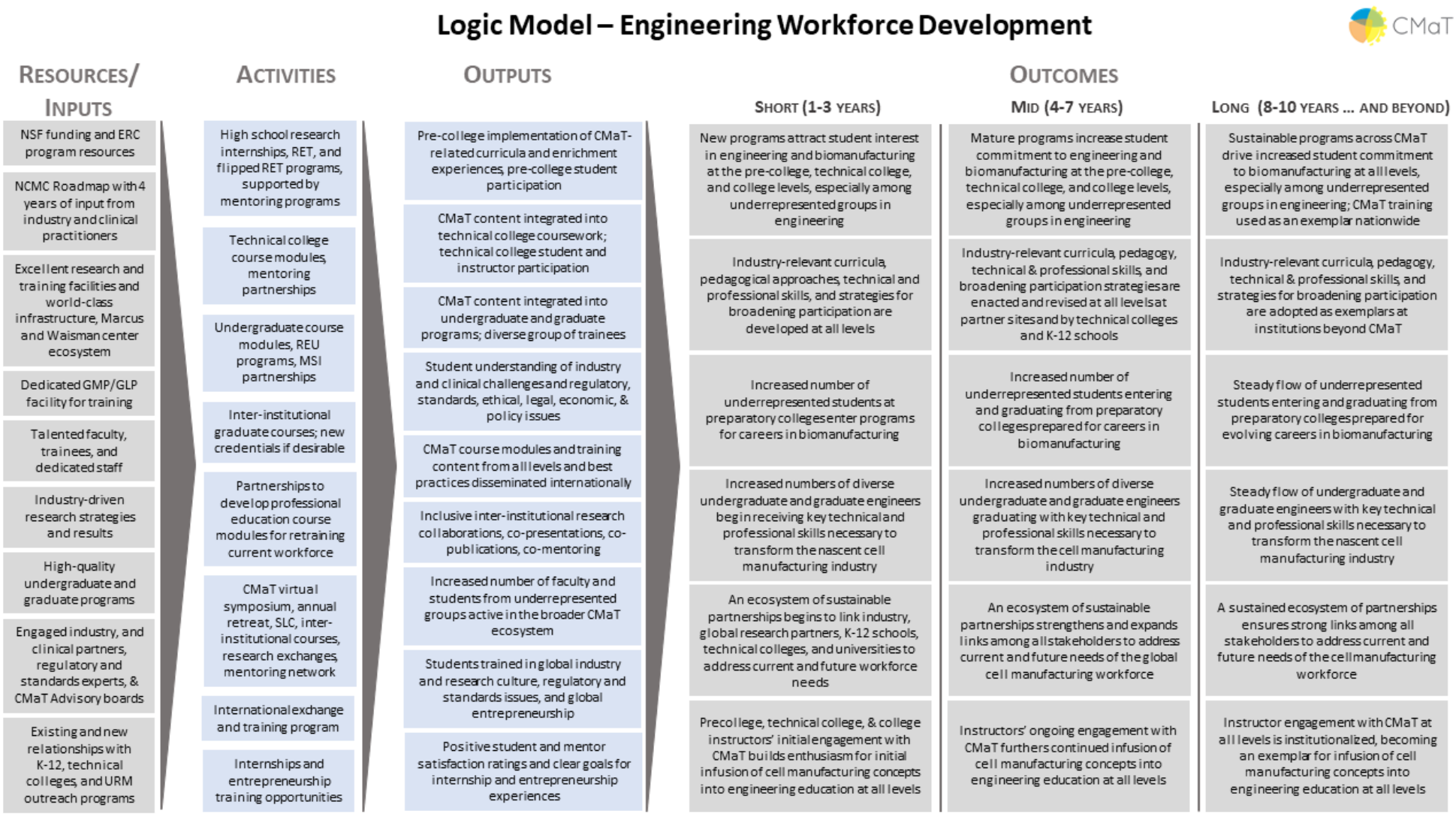


FIGURE 10. Engineering Workforce Development Logic Model



Assessment Plan

CMaT will employ a robust, independent evaluation – designed and led by GT's Center for Education Integrating Science, Mathematics and Computing (CEISMC) – to provide both formative and summative assessments. Each dimension will be assessed using SMART goals developed by CEISMC and refined through discussions with CMaT's Executive Committee and Advisory Boards.

As an example, for EWD, the evaluation will use an educative, value-engaged approach defining high-quality STEM programs as those effectively incorporating cutting-edge scientific content, strong instructional pedagogy and sensitivity to culture, diversity, and equity issues. The evaluation will assess CMaT's workforce development plan on four key dimensions: Implementation: Are EWD activities being implemented as planned? If not, how will they be addressed? Effectiveness: Are EWD components operating effectively across all partners (e.g. cell manufacturing courses, graduate certificate programs, undergraduate modules, research exchanges, REUs, entrepreneurship and industry integration programs, pre-college and RET programs, EXCEL integration, and the technical colleges alliance)? How can these programs be improved? Impact: What outcomes are associated with participation at all levels (e.g. diversity, STEM interest, persistence, career and educational trajectory, awards, publications, professional networks, and satisfaction)? Sustainability: To what extent are EWD efforts becoming institutionalized at participating institutions? Assessment will include longitudinal tracking of CMaT participants with metrics tailored to participant level and designed to assess multiple relevant outcomes, including participant demographics and diversity, content knowledge, mentoring skills, publications and presentations, participant satisfaction, and career plans. Results will be reviewed frequently by CMaT's leadership team and Workforce Advisory Board and plans will be revised as appropriate.

A detailed initial assessment plan for each logic diagram (overall center-wide and EWD) is shown below, which will further evolve as CMaT matures.

Evaluation Plan: Engineering Research Center for Cell Manufacturing Technologies (CMaT) Center Level

Activities	Outputs	Outcomes	Evaluation Methods
Research Thrust 1: Comprehensive characterization; big data analytics, and predictive computational modeling	Robust analytic, computational and workflow tools for identifying CQAs and CPPS Identified CQAs and CPPS for specific test beds	• CMaT ecosystem enables innovations that result in publications, filed patents, and new industry collaborations • New research talent from associated fields begin working on areas supported by CMaT • Diverse perspectives, multi-disciplinary expertise and input from industry and clinicians synergize to enhance R&D activities • Industry and clinical input results in shortened technology/process development cycle, new research directions and projects • Leveraged funding from other sources • CMaT impacts establishment of	-Annual Faculty, Staff and Trainee Report: Aggregation of publications, presentations, patents, collaborations (summative) -Annual Social Network analysis of collaboration and interinstitutional connections (summative); -Focus groups with CMaT faculty, seed grant recipients, and CMaT affiliates to assess onboarding processes (formative); -Annual Climate Survey of all CMaT participants to assess multi-disciplinarity and impact of industry and clinical input (summative); -Annual focus groups with IPAB, SAB and CAB (formative); -IPAB, SAB and CAB evaluation of graduate student portfolios and annual reports (formative and summative); - Tracking studies of technology/process development cycle for selected projects (formative); -Annual Faculty, Staff, and Trainee Report: Aggregate of items on extent to which industry and clinical input influenced technology development, new research directions and projects;
Research Thrust 2: Invent and develop new technologies for monitoring cell quality and process parameters during manufacturing	New tools, methods and technologies for rapid, high throughput or real-time measurement of cell quality CQAs and CPPs across test beds		
Research Thrust 3: Systems optimization and process improvement; Supply chain and logistics	New technologies for scalable production and distribution		

Activities	Outputs	Outcomes	Evaluation Methods
		practices and standards internationally • CMaT faculty and trainees spin off new companies or license technologies to other companies • Engineered system to enable large scale, reproducible manufacturing of high quality cells disseminated to clinicians and industry	-Annual Faculty, Staff, and Trainee Report: Aggregate of funding leveraged by CMaT activities (summative); -Annual Faculty, Staff and Trainee Report: Aggregate of CMaT participants engaged in policy development and professional advocacy (summative); -Annual focus groups with IPAB, SAB and CAB (formative); -Annual Faculty, Staff and Trainee Report: Aggregate of # new companies formed; # of licenses to other companies (summative); -Annual focus groups with IPAB, SAB and CAB (formative);
Center-wide Diversity and Inclusion	Center-wide culture of inclusivity Best practices in diversity and inclusion across partners	• Participation of underrepresented groups in CMaT exceed institutional and national norms • Traditionally underrepresented groups are successful in CMaT programs • Faculty and trainees from underrepresented groups enter and	-% of underrepresented subgroups participating in CMaT at all levels (faculty, staff, pre-college, undergraduate, graduate, advisory) compared to institutional and national averages (formative and summative); -Annual Faculty, Staff and Trainee Report: Analysis of milestone accomplishment, time to degree, retention, publications, presentations and other outcomes for URM participants (formative and summative); -Annual Climate Survey of all CMaT participants to compare URM with majority ratings on dimensions of climate (summative); -Longitudinal follow-up of faculty and trainees to assess: postsecondary attainment and career trajectory over time (summative);

Activities	Outputs	Outcomes	Evaluation Methods
		remain in career fields supported by CMaT • CMaT best practices for diversity and inclusion become exemplars for other programs	- Annual Faculty, Staff and Trainee Report: Analysis of publications and presentations relating to CMaT best practices (formative);
Engineering Workforce Development	Inclusive pre-college and technical college programs, enrichment and teacher experience programs	• New CMaT courses, modules and outreach developed across all levels • Increased interest and enrollment in biomanufacturing courses at all levels • CMaT best practices for pre-college engagement become exemplars for other programs	-Annual Faculty, Staff and Trainee Report: Analysis of courses, modules and outreach developed and offered by partner institutions (summative); -Demographic surveys of all students enrolled in biomanufacturing courses at all levels over time (summative); -Annual Faculty, Staff and Trainee Report: Analysis of publications and presentations relating to CMaT best practices (formative);
	Inclusive, industry driven UG, graduate and certificate programs	• Industry need-based training becomes a part of CMaT culture • Industry relevant biomanufacturing training becomes part of engineering curricula nation-wide • CMaT trainees begin impacting industry through cross-	-Annual focus groups with IPAB, SAB and CAB (formative); -Environmental scan of national reports on engineering education (summative); -Longitudinal follow-up of faculty and trainees to assess: publications, patents, licenses, policy and

Activities	Outputs	Outcomes	Evaluation Methods
		disciplinary expertise, policy and regulatory awareness and diversity • CMaT best practices for workforce development become exemplars for other programs	regulatory changes and other industry impacts (summative); - Annual Faculty, Staff and Trainee Report: Analysis of publications and presentations relating to CMaT best practices (formative);
	Strong international programs at faculty, graduate and undergraduate levels	• CMaT recognized as a global leader in cell manufacturing development and training • More globally engaged, holistic researchers • CMaT best practices for international programs become exemplars for other programs	-Centralized collection of citation rates for all CMaT publications (summative); - Annual Faculty, Staff and Trainee Report: Analysis of advisory board membership, invited addresses, awards (summative); - Annual Faculty, Staff and Trainee Report: Analysis of publications and presentations relating to international collaboration (summative); - Annual Faculty, Staff and Trainee Report: Analysis of publications and presentations relating to CMaT best practices (formative);
Innovation Ecosystem	Partnerships to guide research strategies, innovation, workforce development entrepreneurship, and knowledge transfer	• Faculty and trainees engage in more industry relevant research • CMaT best practices for industry and clinical partnerships	-Annual focus groups with IPAB, SAB and CAB (formative); - Annual Faculty, Staff and Trainee Report: Analysis of publications and presentations relating to CMaT best practices (formative);

Activities	Outputs	Outcomes	Evaluation Methods
		become exemplars for other programs • Significant activities and outcomes are sustained post-NSF funding	
	Diverse portfolio of highly engaged member companies and clinical partners, and other entities	• Sustainable ecosystem that links industry, global institutions, k-12 schools, technical colleges, universities and government agencies to address current and future needs of the cell manufacturing workforce	-Annual social network analysis of inputs, collaboration, inter-institutional connections; baseline and trends over time (formative and summative)

Evaluation Plan: Engineering Research Center for Cell Manufacturing Technologies (CMaT) Engineering Workforce Development

Activities	Outputs	Outcomes	Evaluation Methods
Pre-college: High school research internships; RET and flipped RET programs; mentoring programs	Pre-college implementation of CMaT-related curricula and enrichment experiences in high schools	• # of classrooms implementing CMaT modules (across partners and by other K-12 schools)	-Fidelity checklists completed by all RET and REM teachers documenting implementation of CMaT course modules (formative); -Tracking of other K-12 adoptees through professional development survey (summative); -Pre and post implementation surveys of teacher satisfaction and assessment of student outcomes

Activities	Outputs	Outcomes	Evaluation Methods
		• Teacher satisfaction with CMaT pre-college materials • Increased student interest in bioengineering and cell manufacturing across subgroups (e.g. gender, race, SES)	associated with CMaT course modules (formative/summative); -Demographic surveys of pre-college students who participate in CMaT related curricula (summative); -Pre and Post Student Interest surveys, disaggregated by gender, race, SES and fidelity of implementation (formative/summative); -Pre and Post student focus groups collecting formative data to improve modules and summative data on impact. (formative/summative)
	Diverse pre-college student participation in CMaT research	• # and diversity of pre-college students participating in CMaT research across partners, by subgroups • Student and mentor satisfaction with CMaT research experiences • Increased student interest in and knowledge of bioengineering and cell manufacturing research across subgroups (e.g. gender, race, SES)	-Demographic surveys of pre-college students who participate in CMaT research (summative); - Student and mentor exit surveys and focus groups collecting formative data to improve research experiences and summative data on impact (formative/summative) -Pre and Post Student Interest and Skills surveys, disaggregated by gender, race, SES and fidelity of implementation (summative); -Mentor evaluation of student technical, communication and leadership skills (summative); -Longitudinal follow-up of pre-college participants to assess: future course-taking; post-secondary participation, major, research engagement (summative)
Technical College: Technical college course modules, mentoring partnerships, internships	CMaT content integrated into technical college coursework	• # of technical college courses integrating CMaT content, pedagogy, etc.	-Annual checklist completed by all technical college instructors documenting integration of CMaT content, pedagogical approaches; development of new courses; new certificates/degrees (summative);

Activities	Outputs	Outcomes	Evaluation Methods
		• Adoption of CMaT course content and programming by other technical colleges • Increased student interest in bioengineering and cell manufacturing across subgroups (e.g. gender, race, SES)	-Pre and post implementation surveys of teacher satisfaction and assessment of student outcomes associated with CMaT content integration (summative); -Demographic surveys of technical college students who participate in CMaT related courses (summative); -Pre and Post Student Interest and Skills surveys, disaggregated by gender, race, SES and fidelity of implementation (summative); -Pre and Post student focus groups collecting formative data to improve modules and summative data on impact (formative/summative).
	Diverse technical college student and instructor participation in CMaT research	• # and diversity of technical college students participating in CMaT research (REM, internships) across partners • Student and mentor satisfaction with CMaT research experiences • Increased numbers of diverse students from two-year technical colleges prepared for careers in manufacturing	-Demographic surveys of pre-college students who participate in CMaT research (summative); - Student and mentor exit surveys and focus groups collecting formative data to improve research experiences and summative data on impact (formative/summative); -Pre and Post Student Interest and Skills surveys, disaggregated by gender, race, SES and fidelity of implementation (summative); -Mentor capstone evaluation of student technical, communication and leadership skills (summative); -Longitudinal follow-up of pre-college participants to assess: future course-taking; internships; time to degree, retention; initial employment (summative) -IPAB ratings of student research presentations (formative/summative)
Undergraduate: Undergraduate course	CMaT content integrated into undergraduate	• # of undergraduate courses integrating	-Annual checklist completed by all undergraduate instructors documenting integration of CMaT content,

Activities	Outputs	Outcomes	Evaluation Methods
modules; REU programs, MSI partnerships	program at partner institutions	CMaT content, pedagogy, etc. across partner institutions • Adoption of CMaT course content and programming by other institutions. • Increased student interest in bioengineering and cell manufacturing across subgroups (e.g. gender, race, SES)	pedagogical approaches; development of new courses; new certificates/degrees (summative); - Tracking of other undergraduate adoptees through website analytics and tracking survey (summative); - Student and mentor exit surveys and focus groups collecting formative data to improve new course experiences and summative data on impact (formative/summative). -Pre and Post Student Interest and Skills surveys, disaggregated by gender, race, SES and fidelity of implementation (summative);
	Diverse undergraduates engaged in CMaT research across partner institutions	• Increased numbers of diverse undergraduate engineers with key technical and professional skills necessary to transform the cell manufacturing industry	-Mentor capstone evaluation of student technical, communication and leadership skills (summative); -Longitudinal follow-up of undergraduate participants to assess: future course-taking; internships; time to degree, retention; initial employment (summative); -IPAB, SAB and CAB ratings of student research presentations (formative and summative)
Graduate: Interinstitutional graduate courses, new credentials	Graduate student understanding of industry and clinical challenges	• Graduate student research, education and public engagement addresses pressing industry and clinical challenges	-IPAB, SAB and CAB evaluation of projects and graduate student activities and annual reports. (formative and summative)

Activities	Outputs	Outcomes	Evaluation Methods
	Graduate student understanding of regulatory, ethical, legal, economic & policy issues	• Graduate student research, education and public engagement addresses pressing regulatory, ethical, legal, economic, and policy issues.	-IPAB, SAB and CAB evaluation of projects and graduate student activities and annual reports (formative and summative)
	New credentials, coursework and degree programs	• Increased numbers of diverse graduate engineers with key technical and professional skills necessary to transform the cell manufacturing industry	-Mentor capstone evaluation of student technical, communication and leadership skills (summative); -Longitudinal follow-up of graduate participants to assess: future course-taking; internships; time to degree, retention; initial employment (summative) -IPAB, SAB and CAB ratings of student research presentations (summative)
Cross-institutional collaboration: CMaT Virtual Symposium, SLC, interinstitutional courses, research exchanges, mentoring networks	Inter-institutional research collaborations, co-presentation, co-publication, co-mentoring	• Sustained ecosystem of research and education across K-12, technical college and university partners to address the current and future needs of cell-manufacturing industry	-Annual Social network analysis of inter-institutional connections; baseline and trends over time (formative and summative); -Biennial cell manufacturing workforce needs survey administered to industry and clinical partners (formative).
Industry Linkages: Internships and entrepreneurship opportunities	Robust array of internship and entrepreneurship opportunities available all all partner sites for students at technical college, undergraduate and graduate levels	• # and diversity of students participating in internships and entrepreneurship opportunities across partners	-Demographic surveys of pre-college students who participate in internships and entrepreneurship opportunities (summative);

Activities	Outputs	Outcomes	Evaluation Methods
		• Student and mentor satisfaction with industry experiences • Increased numbers of diverse students from technical colleges and universities prepared for careers in industry and entrepreneurship • Sustained ecosystem of research and education across K-12, technical college and university, clinical and industry partners to address the current and future needs of cell-manufacturing industry	- Student and mentor exit surveys and focus groups collecting formative data to improve internship experiences and summative data on impact (formative and summative); -Mentor capstone evaluation of student technical, communication and leadership skills (summative); -Longitudinal follow-up of internship participants to assess: future course-taking; research interests; time to degree, retention; initial employment (summative); -IPAB, SAB and CAB ratings of student internship activties (formative and summative); -Annual social network analysis of inter-institutional connections; baseline and trends over time (formative and summative); -Biennial cell manufacturing workforce needs survey administered to industry and clinical partners (formative)

Infrastructure and Management

CMaT management will be transparent; decisive; effective in achieving research, innovation, and workforce development visions; and adaptive to ensure timely and assessment-driven changes. In addition, CMaT management will ensure an ecosystem that facilitates regular exchange of ideas, allocation of needed resources, continuous refinement of strategies and goals, inclusive and nimble operation, and strong collaboration among partners.

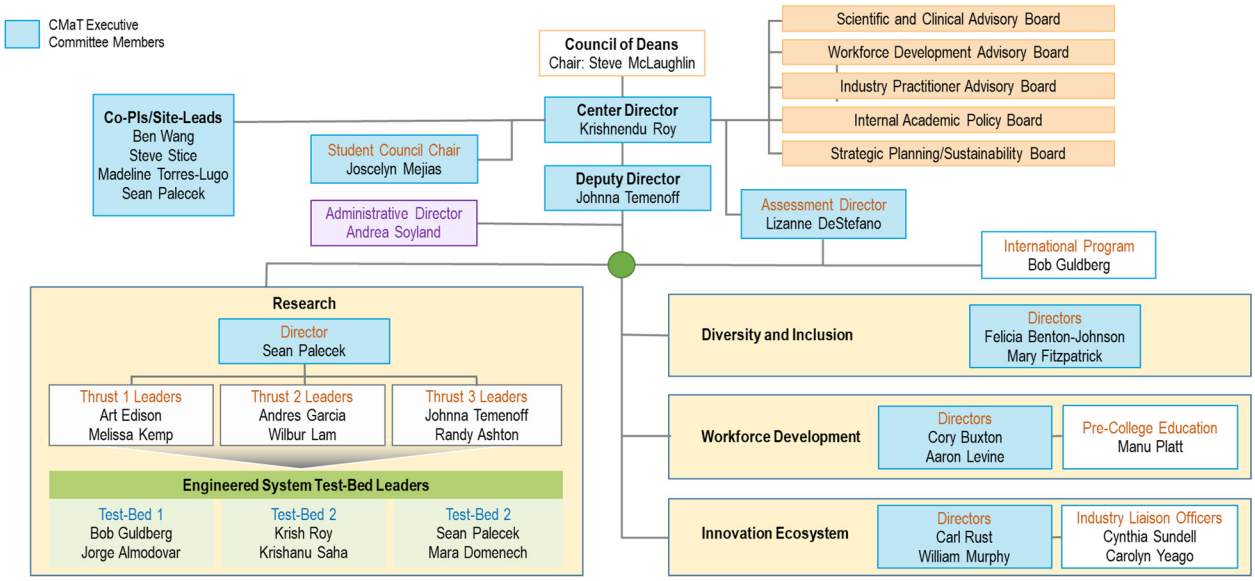
CMaT has a diverse group of leaders with deep experience and complementary, synergistic expertise. All positions in CMaT have been filled. The leadership group is show in **Figure 11** below.

FIGURE 11. CMaT Leadership

CMaT's organization chart is shown below in **Figure 12**. CMaT deeply believes in a mentorship-centered team-based leadership approach. All Thrusts and Test-Beds are led by a senior faculty member and a junior/mid-level faculty member, and all team leads, including those in EWD, Diversity-Inclusion, and Innovation Ecosystem, are researchers and practitioners in their respective fields.

The CMaT Executive Committee (EC) will include the Director, Deputy Director, and Associate Director for Research, Workforce Directors, Industry Liaison Director (Rust), Diversity Directors, and the Student Council Chair. CMaT keenly values student input, and hence has included the student council chair; however, it is anticipated that she or he will be recused when faculty, project issues, or sensitive personnel issues are discussed. The EC will meet monthly to assess all programs and recommend actions/corrections. It will seek advice from the Scientific and Clinical Advisory Board (SAB), the Industry/Practitioner Advisory Board (IPAB), and the Workforce Development Advisory Board (WDAB). A Research Oversight Committee (ROC) will be established with the Associate Director for Research and all Thrust and Test-Bed leaders and co-leaders, which will meet monthly before the EC meeting to assess continuing progress of projects.

FIGURE 12. CMaT Organization Chart



The SAB will consist of world-renowned scientists, engineers, and clinicians from all fields related to CMaT's research objectives, including GMP manufacturing facility directors, standards experts, and regulatory affairs experts. The goal is to ensure that engineering, science, clinical practice, standards development, and manufacturing expertise are well represented in the board. The NCMC and our roadmapping effort serves as the foundation of the IPAB, and many members have committed to CMaT membership. As CMaT matures, we will continue to add new industry membership and a Venture Advisory Board (VAB) and seek to have a balanced board with large as well as small and medium-sized enterprises and a mixture of therapy, tools, and supply chain companies. In addition, CMaT will actively seek representatives from the FDA, patient advocacy groups, and the reimbursement industry to join the IPAB. The WDAB will consist of renowned workforce, innovation, and entrepreneurship experts from around the country and administrators from partner K-12 and 2-year colleges that will advise CMaT on best practices, appropriate directions, and the optimal allocation of resources while also helping with continual assessment of workforce activities.

In addition to these advisory boards, CMaT is forming a Strategic Planning and Sustainability Board (SSB). This Board will include members who have deep experience in governing large, sustainable multi-disciplinary national centers and will be chaired by Prof. Robert Nerem, NAE, NAM, who served as the Director of the GTEC (Georgia Tech-Emory Tissue Engineering Center) ERC. The task of the SSB will be to advise CMaT's Director on sustainability, IPAB membership, global trends and partnerships, and international thought leadership. Continual assessment and quantitative feedback-based strategic realignment is key to CMaT's success. DeStefano, Director of Assessment, will meet with the EC every 6 months to provide assessment.

Key Personnel in Innovation Ecosystem

Carl A. Rust (Director)

Carl A. Rust is Associate Vice President for International Initiatives and Principal Director in the Office of Industry Collaboration at GT where he is responsible for pursuing the university's international goals,

particularly those related to industry-university collaboration, entrepreneurship, commercialization, and economic development.

Between his tenure at both GT and the University of Maryland, Rust has accumulated over 24 years of experience in industry-university partnerships, technology transfer, new business development, commercialization, innovation-led economic development, and global collaboration. He pioneered novel collaboration models of embedding industry research, development, and innovation centers at universities. He has also forged new ways of effectively connecting university-based startup companies to larger well-established companies as potential customers, suppliers, partners, and investors.

His prior industrial experience includes serving as an engineering manager at Texas Instruments and co-founding four technology-based start-up companies. He serves as a consultant for the National Science Foundation and other organizations on industry-university collaboration, international partnerships, and innovation matters. He has a bachelor's degree in electrical engineering from The Citadel and has seventeen publications. Rust was a 2014 Fulbright award recipient to study the higher education and research system of France.

William Murphy, Ph.D. (Co-Director)

Bill Murphy, Ph.D., is the Harvey D. Spangler Professor of Biomedical Engineering, Professor of Orthopedics & Rehabilitation, Co-Director of the Stem Cell and Regenerative Medicine Center, and Director of the Human MAPs Center at the University of Wisconsin.

His research interests focus on creating new biomaterials inspired by the materials found in nature. Murphy's research group is using new biomaterials to understand stem cell behavior and to induce tissue regeneration. He has published more than 150 scientific manuscripts, filed over 40 patents, co-founded multiple venture-backed start-up companies, and received awards that include the National Science Foundation Career Award, the Wisconsin Vilas Associate Award, the Romnes Fellowship, and induction as a Fellow in the American Institute for Medical and Biological Engineering.

Cynthia Sundell, Ph.D. (ILO)

Cynthia Sundell, Ph.D., serves as the Senior Director for Life Science Industry Collaboration for GT in the Office of Industry Collaboration and the Parker H. Petit Institute for Bioengineering and Bioscience. In this role, Sundell works with industry partners to enable new medical innovation, sponsored research, technology commercialization, and creative scholarship.

Prior to coming to GT, Sundell spent 16 plus years as a life science executive in the United States and abroad designing and implementing corporate strategies in discovery research and clinical development. Sundell brings a strong knowledge of regulatory and commercial environments as well as extensive management experience, including leadership of global pharmaceutical development teams to her role at GT.

Sundell serves on the Boards of Georgia Bio and the Georgia BioEd Institute and is active in the Atlanta Chapter of Women in Bio. She received a B.A. from Rutgers University and a Ph.D. in Biology from the University of Pennsylvania.

Carolyn Yeago, Ph.D. (ILO)

Carolyn Yeago, Ph.D., is currently the Associate Director of the Marcus Center for Therapeutic Cell Characterization and Manufacturing (MC3M) at GT. She is responsible for overseeing research and development activities supported by the Marcus Center and leads a team of scientists to advance the clinical use and commercial production of therapeutic cells. MC3M research focuses on identifying critical quality attributes of therapeutic cells to enable the necessary development of sensors, in-line monitoring and testing, and final product validation testing to achieve large-scale manufacture of cells, including modified T-cells, mesenchymal stem cells, and induced pluripotent cells.

Yeago joined the Marcus Center after seven years with Halyard Health and Kimberly Clark Health Care where she directed research and evaluated technologies to inform new platform strategies. During her time with Halyard Health and Kimberly Clark Health Care, Yeago worked on the industry side of industry-university partnerships to advance research development, and she brings that passion for connecting related research and ensuring commercial relevance and translation to the Marcus Center and CMaT.

Yeago received her Ph.D. in Biomedical Engineering from the Georgia Institute of Technology and Emory University and her B.S. in Biomedical and Bioengineering from North Carolina State University.

Figure 13 shows the key roles of the Innovation Ecosystem leadership team.

FIGURE 13. Innovation Ecosystem Leadership