Nanosystems ERC for Directed Multiscale Assembly of Cellular Metamaterials with Nanoscale Precision (CELL-MET)

Boston University (lead institution)

Using Nanotechnology to build cardiac tissues with increasing levels of functionality and complexity, with applications ranging from drug testing to creating implantable patches that can repair damaged heart tissue

CELL-MET

A National Science Foundation Engineering Research Center since 2017

Partner Institutions:

- University of Michigan
- Florida International University

Heart disease is the number one cause of death in the US and a leading cause worldwide, but current medicine cannot regenerate diseased human heart tissue. Today, there is no cure for a heart attack. The vision of CELL-MET is to change this. CELL-MET will develop tissue-engineering principles to create scalable, low-cost technologies for growing clinically significant cardiac tissues from cell-level building blocks. The research will adapt and advance novel nanomanufacturing techniques to integrate a variety of functional biological structures and elements into flexible polymer scaffolds that support and guide heart cells. Our goal is to create cardiac patches that will someday allow for the repair of hearts damaged by a heart attack or other diseases.

In addition to their potential for repairing damaged hearts, artificial cardiac tissues will be used to test the effects of heart drugs or other drugs more realistically and efficiently than is currently possible.

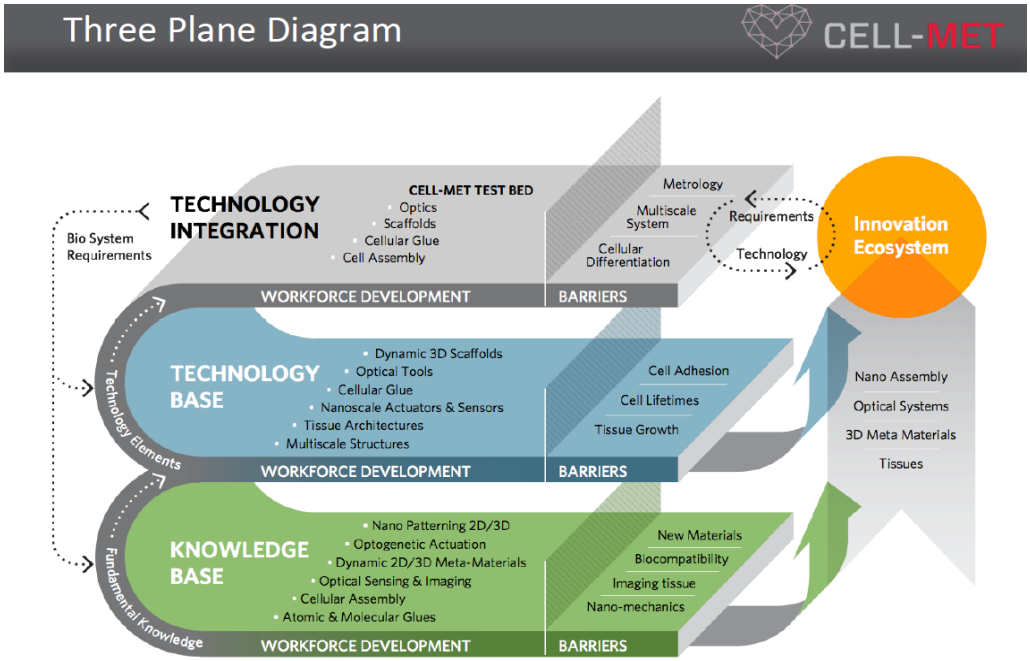
Broader impacts will include kindergarten-to-postdoc education and training programs that will produce a diverse, well-trained, world-aware workforce to support the new, billion-dollar industries enabled by CELL-MET research. Industrial partners will work with CELL-MET to create these new industries, developing the business opportunities generated by the research breakthroughs.

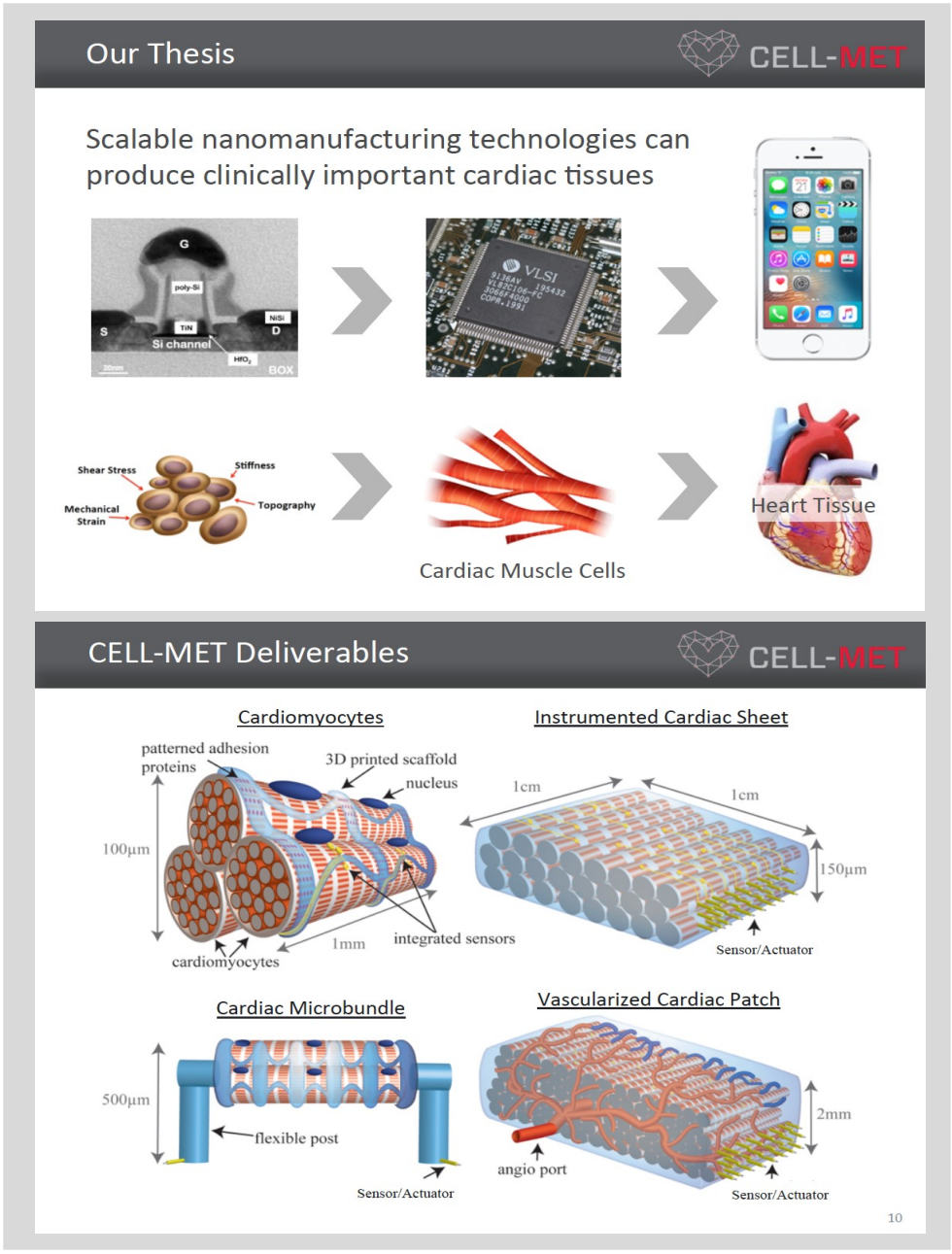
Research

CELL-MET aims to create functional, clinically significant heart tissue in the laboratory by controlling the structure across different length scales. From sizes smaller than a micron up to the 10-micron scale of cells, CELL-MET will align heart muscle cells (cardiomyocytes) and connect them to one another via special cellular structures, enabling them to contract in synchrony. At the multicellular scale, it will monitor and control chemical signaling both among these cells and between them and supporting cells. At the scale of tissue constructs, CELL-MET will create highly structured networks of blood vessels lined with epithelial cells, which are needed for any thick tissue to be useful. The Center's ten-year vision encompasses the incorporation of endocardial cells that help define the large-scale structure and electrophysiological function of the heart, as well as the valves that ensure unidirectional blood flow.

CELL-MET

CELL-MET brings together a diverse, world-class team from Boston University, the University of Michigan, Florida International University, Harvard, Columbia, Argonne National Lab, EPFL (Switzerland), and Centro Atomico-Bariloche (Argentina). Team members are experts in semiconductors, photonics, nanotechnology, optical systems, organic molecules, cardiac biology, and cellular assembly. CELL-MET is uniquely positioned to harness the capabilities and synergies among these disciplines. CELL-MET plans to combine novel techniques for patterning molecules on the scale of 50 nm or less





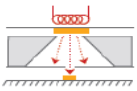
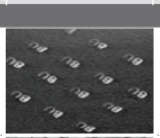
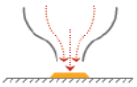
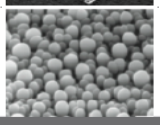
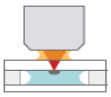
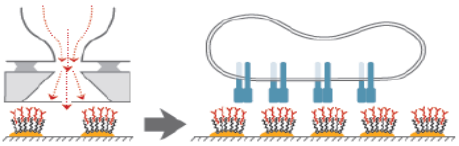
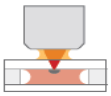
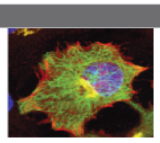
with nanometer-scale 3D-printed scaffolds. 3D nanoprinting technologies will produce scaffolds that Atomic Calligraphy and Organic Vapor Jet Printing will write upon to create the focal adhesion points, the places that attach the cells. Advanced tissue engineering techniques will populate these nanostructures with cardiomyocytes and other cardiac cell types to produce the living tissues.

Education

Our five-year plan includes opportunities to impact all learners. In addition to fundamental scientific breakthroughs and understanding in nanopatterning, nanomechanics, biomicroscopy and advanced cell engineering, CELL-MET will cultivate the scientific interests of a K-12 audience through museum (K-6) and urban school (7-12) outreach programs and will train a diverse workforce through undergraduate, graduate, and postdoctoral programs. Targeting skills development at all levels of education from K-12 through PhD and postdoctoral training programs will sustain interest, create a sense of belonging, build

Technology Tasks and Flows Between TAs

CELL-MET

	TECHNIQUE	MATERIALS	STRUCTURES	FEATURE	PURPOSE	WHO
THRUST AREA 1						
Atomic Calligraphy		Au, Ag, Ni, Al, etc.		<50 nm	High resolution patterns of metal that template organic/cellular assembly	BU
OVJP		C60, fluorescent, Pc OTS, HMDS, PEGDA, dPMT, pluronic, thiols, other organics, linear & cyclic RGD		< 2 µm	Functional coatings to create attachment points for cells	UM
THRUST AREA 2						
Nanoscribe		PEG, PEO, PMMA, etc.		<1 µm	3D nanoscale structures to act as scaffolds for cells and sensors/actuators	BU FIU ANL UM
AC + OVJP +Scaffolds				< 50 nm	Patterned 3D structures with focal attachments that direct cell binding, motion and function	BU UM
THRUST AREA 3						
Tissue Assembly				< 50 nm	Complex surfaces and 3D scaffolds for cell binding/ proliferation-multiscale, hierarchical, dynamic, embedded sensing	BU Harvard Columbia
THRUST AREA 4						
Imaging & Actuation		fluorescent proteins, quantum dots		<1 µm	Deep 3D tissue imaging, fluorescent tagging, optogenetic actuation of tissue	BU FIU

curiosity, and increase the preparedness of students entering the job market. We will build upon the strengths of our existing research and education programs to develop a cohesive set of activities that are evaluated in regular data-driven improvement cycles.

Education Program Goals

1. Create evidence-based education derived from CELL-MET research to broaden participation of underrepresented groups (URGs) in STEM disciplines and careers.

2. Create an inclusive training environment that supports and sustains URG interest to pursue STEM workforce careers.

Education Research Questions

1. What skill-based experiences are most influential in strengthening and maintaining students' interest in STEM disciplines and careers throughout their training?

2. What interventions positively influence university and precollege faculty confidence to deliver relevant STEM lessons based on CELL-MET?

3. How do collaborative relationships and programmatic supports influence students' sense of belonging and community to increase retention?

4. What drivers motivate URGs to pursue careers in an emerging sector of the workforce?

Innovation Ecosystem

CELL-MET's innovation ecosystem is focused on Technology Development, Workforce Development, Translational Research and Economic Development, Sustainability, and Dissemination for better healthcare outcomes. The success of the innovation ecosystem is dependent on the contribution and participation of industry at all levels of the value chain. Industry membership is open to all for-profit and non-profit corporations, foundations, government agencies, federally funded research and development corporations, and government-owned contractor-operated laboratories. The intention is to have membership at all levels of the value chain and to be inclusive of partners ranging from technology start-ups to large market-capitalization, multinational corporations. A tiered membership structure with aligned fee and benefits is in place to capture the commitment of larger companies while providing opportunities for small business enterprises. The CELL-MET membership structure will involve four classes of membership (Sustaining, Full, Associate, and Affiliate) with rights and privileges commensurate with the level of support. A sliding fee

schedule as well as Membership Benefits are outlined in the Membership Agreement and Bylaws. Sustaining membership has the highest annual fee and also the highest level of benefits and rights associated with membership. Sustaining members would typically be those companies with multiple business units benefiting from CELL-MET, having significant internal research efforts and a product vision that includes leadership in tissue engineering and related fields. Full members are likely small to mid-cap companies that see growth opportunities in this field. Associate membership will typically be for early stage venture-backed or grant-funded organizations; one-year complementary memberships will be granted at this level for companies based at the university's Business Innovation Center (BIC) or Incubators. Affiliate memberships will be reserved for organizations such as hospitals/clinicians, media companies, state economic development offices, or industry trade groups that can provide significant non-monetary support through clinical studies, regulatory and insurance consultancy, publicity, networking opportunities, and market insight.

Center Configuration, Leadership, Team Structure

CELL-MET's long-term vision and coordinated program relies upon interdisciplinary collaboration among faculty groups at three partner institutions (Boston University, University of Michigan, and Florida International University), two domestic affiliates (Columbia University and Harvard Medical School), and collaborators from Argonne National Laboratory, EPFL in Switzerland and Instituto Balsiero in Argentina. Center-wide activities are organized to foster research, innovation partnerships with industry and practitioners, a culture of inclusion and diversity for all aspects of the Center's operations, engineering workforce development to address education and assessment, and public outreach. The Administrative Component supports the Senior Leadership Team (SLT) in carrying out these essential elements and facilitates interactions among multiple boards and councils that provide expertise and perspectives that guide the Center. The NSF Cooperative Agreement, Center By-Laws (including IP policy), and Membership Agreement for industry and practitioners govern the Center's integrated activities.

CELL-MET is organized with a flat organizational structure, with 8 thrust areas, each reporting to the Director and Deputy Director. The Director and Deputy Director report to a Council of Deans and are advised by scientific and industrial advisory boards.

Facilities

Center Headquarters

Photonics 915 (CELL-MET)
8 Saint Mary's Street
Boston, MA 02215

www.sites.bu.edu/cell-met/

Center Director: David Bishop
(617) 990-4037 • djb1@bu.edu

Deputy Director: Christopher Chen
(617) 353-2805 • chencs@bu.edu

Admin Director: Robert Schaejbe
(617) 358-4257 • rschaejb@bu.edu