

Center for Biomedical Engineering

Executive Summary

The mission of the Center for Biomedical Engineering (CBE) is to combine engineering with molecular and cellular biology to develop new approaches to biomedical technology with applications to medicine and biology. CBE has played a lead role in the evolution of MIT's activities in tissue engineering. In addition, fundamental discoveries in cellular and molecular mechanics and mechanobiology by CBE faculty and students have enabled critical advances for applications in musculoskeletal and cardiovascular tissue repair and regeneration. New initiatives have focused on the structure and function of biomembrane proteins for applications in sensors. We are witnessing fundamental changes in MIT's approach to bioengineering research and education. To maintain intellectual leadership during this period of rapid evolution in bioengineering, nationwide, and during times of economic uncertainty, innovative approaches are needed to stimulate fundamental research and to facilitate timely translation of new discoveries into the biomedical industrial and health care sectors. With these goals in mind, CBE continues to identify new opportunities aligned with its set of core research thrusts. The Center also continues to improve and maintain its core research facilities and its connections with industry. Taken together, our aim is to pursue multidisciplinary biomedical research and create an outstanding training environment for a new generation of students/leaders in biomedical and biological engineering.

Major Research Areas

CBE's core faculty members represent a variety of academic units, primarily within the School of Engineering, but with substantial participation from School of Science faculty and collaborating faculty from the medical schools of Harvard and Colorado State University (CSU). These faculty participate in multi-investigator programs focusing on CBE's long-standing research areas: (1) cell and tissue engineering, (2) molecular-cell and cell-cell interactions, and (3) mechanobiology (effects of physical forces on cell and tissue regulation). A newly emerging high-impact area is, (4) biomembrane proteins: production and structure. Together, these research thrusts have direct applications to cardiovascular and musculoskeletal physiology, pathology, tissue regeneration and repair, sensors based on biomembrane proteins, and drug discovery. CBE maintains a broad funding base with support from the US Department of Health and Human Services (50%), industry (15%), the Department of Defense (30%), and a variety of other public and private sponsors. While the Health and Human Services funding climate for biomedical research has recently become more challenging, CBE has continued to provide facilities and leadership to maintain and broaden its base. CBE faculty members participate in interdepartmental programs as well as collaborative interactions with other universities and industry research laboratories.

Major Research Initiatives

Recent advances by CBE researchers have emerged from interdepartmental, multidisciplinary collaborative studies on stem cells for tissue engineering applications (myocardium, cartilage, and liver), microfluidics for investigation of capillary formation,

cellular mechanotransduction in musculoskeletal tissues, and cell-cell and cell-matrix interactions involved in angiogenesis in tumor growth. In addition, molecular and cellular nanomechanics continues to be a focal point for structure-function studies involving intracellular as well as extracellular matrix macromolecules. These focus areas continue as major initiatives over the next three to five years, coupled to ongoing and newly funded grants from the National Science Foundation (NSF), the National Institutes of Health (NIH), and industry.

A multi-group collaboration involves the use of self-assembling peptide scaffolds for tissue engineering of cartilage, bone, liver, nerve, and heart tissue, which is the basis of a large ongoing Bioengineering Research Partnership (BRP) Grant from NIH. This work is related in part to our industry connections with 3-D Matrix, Inc. (scaffold), Olympus (bone tissue engineering), and our work with Centocor (Johnson & Johnson) on cartilage degradation in osteoarthritis and the need for regenerative technologies. These activities also involve expertise in the biophysics and rheology of biomolecular networks. In addition, computational modeling and simulations at the level of molecular dynamics are essential. A rapidly expanding activity funded by an NIH-BRP grant is the use of mesenchymal stem cells for a variety of tissue engineering applications. Animal studies (rabbit and rat) have expanded from initial studies of toxicity to current studies of efficacy. These studies focus on the use of stem cells encapsulated within these novel scaffolds, and involve our collaborators in the Clinical Sciences Department of CSU. In addition, CSU researchers are planning equine knee joint studies for cartilage repair, a particularly well-suited animal model for the study of degenerative joint disease.

The recent discovery of a fusion protein consisting of a growth factor (insulin-like growth factor-1, or IGF-1) with a heparin-binding domain has led to new contacts with industry. This new growth factor construct can bind to a negatively charged extracellular matrix within tissues, which thereby constitutes a long-lasting delivery approach. IPSEN has primary intellectual properties rights to use of IGF-1, and ongoing negotiations between IPSEN and our collaborating CBE faculty at Brigham and Women's Hospital focus on expanded research and potential trials using this protein drug. This and related proteins are of interest as combination therapies with cytokine blockers for rheumatoid and osteoarthritis.

An exciting new research area involving the structure and function of biomembrane proteins has just received significant funding from the Defense Advanced Research Projects Agency, with applications focusing on biosensors that utilize natural membrane proteins. This project is based on the recent discoveries by CBE researchers concerning the production of properly folded, functional and stable olfactory receptor membrane proteins in large quantities and of sufficient variety. Additional critical discoveries focused on the development of mammalian cell bioreactors for high yield production of these proteins, and new technologies for the stabilization of these proteins outside of their natural cell environment, using lipid-like surfactants in conjunction with a class of designer, self-assembling peptide nanofiber scaffolds.

A continuing grant from the NSF Office of Emerging Frontiers in Research and Innovation focuses on a model of angiogenesis using modern control theory principles.

This multi-investigator project is important both in terms of its immediate goals with respect to understanding in vitro angiogenesis, and in the broader context of vascular network growth in cancer, regenerative medicine, and developmental biology.

Core Facilities

One of the critically important missions of CBE is to maintain and expand a set of central core research facilities. These core facilities are made available to faculty, staff, and students, MIT-wide, at no or minimal cost, and are particularly relevant for CBE's major research areas, as described below. These facilities include an Applied Biosystems 7900HT fast real-time 384-well plate quantitative polymerase chain reaction (qPCR) instrument and associated peripherals, a NanoDrop ND-1000 Spectrophotometric Analyzer to measure RNA quality (which is useful in assessing samples prior to amplification using the AB 7900HT qPCR facility), an Alpha Innotech Gel Imaging Facility has been added for quantitative analysis of electrophoresis gels, a multiphoton microscopy facility, a Cressington Quick-Freeze Deep Etch facility to prepare specimens for follow-on electron microscopy, and a BiaCore 2000 surface plasmon resonance instrument to quantify binding reaction constants between molecules and between molecules and surfaces. CBE also continues to run a large cell, tissue, and organ culture facility, including four 6-foot biosafety cabinets and eight incubators. These are available to faculty and students MIT-wide who would otherwise not be able to explore new ventures in biomedical engineering involving living cells because of a lack of specialized facilities in their own laboratories (including an array of associated instruments and peripherals needed for maintaining and experimenting with living cells and tissues). All these instruments are located in the third-floor laboratories of CBE in NE47 (500 Technology Square).

UROP Activities

CBE continues to connect outstanding undergraduate students in several departments at MIT to laboratories at the Beth Israel Deaconess Medical Center, Boston, that conduct cancer-related research. This is a long-standing partnership in which CBE provides logistical and administrative support to ensure continued success of this interaction.

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More information about the Center for Biomedical Engineering can be found at <http://web.mit.edu/cbe/www/>