

Center for Biomedical Engineering

Executive Summary

The mission of the Center for Biomedical Engineering (CBE) is to combine engineering with molecular, cellular, and systems biology to develop new approaches to biomedical technology with applications to medicine and biotechnology. CBE continues to play a lead role in the evolution of MIT's activities in cell and 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. To maintain intellectual leadership during a 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 has identified and focused on a set of core research thrusts. It has also continued to develop and improve its core research facilities and its connections to industry. 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.

Core Facilities

One of the critically important missions of CBE is to maintain and expand a set of central core research facilities. These are made available campus-wide to faculty, staff, and students at no or minimal cost, and are particularly relevant for CBE's major research thrust areas. Three new instruments have been brought online and expanded this past year, and are now being widely used. An Applied Biosystems 7900HT Fast Real-Time PCR System (a 384-well plate quantitative polymerase chain reaction instrument) and associated peripherals are now being used by faculty in many departments at MIT as well as by investigators at Harvard Medical School. This instrument is particularly useful for systems-level genomics applications. A new NanoDrop ND-1000 UV-Vis Spectrophotometer to measure RNA quality is now online and has proved extremely useful in assessing samples prior to amplification using the AB 7900HT qPCR instrument described above. In addition, a new Alpha Innotech gel imager has been added for quantitative analysis of electrophoresis gels. All these instruments are located in the third floor laboratories of CBE in NE47 (500 Technology Square). CBE also continues to maintain its multiphoton microscopy instrument, the Cressington Freeze-Fracture/Deep Etch , to prepare specimens for follow-on electron microscopy, and the Biacore 2000 surface plasmon resonance instrument to quantify binding reaction constants between molecules and between molecules and surfaces. Finally, CBE also continues to run a large cell, tissue, and organ culture facility including four six-foot biosafety cabinets and eight incubators. These are available Institute-wide to faculty and students 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.

Major Research Areas

CBE continues to focus on a set of core research thrusts:

- Cell and tissue engineering
- Molecular-cell interactions
- Mechanobiology (effects of physical forces on cell and tissue regulation)
- Molecular and cellular biomechanics and biophysics

Basic research programs in these areas are being applied to problems in cardiovascular and musculoskeletal physiology, pathology, tissue regeneration and repair, and drug discovery. CBE maintains a broad funding base with support from the US Department of Health and Human Services (65%), industry (20%), and a variety of other public and private sponsors. While the federal (National Institutes of Health) 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

CBE researchers have continued a multidisciplinary, inter-institutional collaboration on the use of novel self-assembling peptide scaffolds for tissue engineering of cartilage, bone, liver, nerve, and heart tissue. This research is supported in part by a Bioengineering Research Partnership (BRP) Grant from the National Institute of Biomedical Imaging and Bioengineering (NIH/NIBIB), which is now in its third year. The partnership includes CBE investigators in biophysics, bioengineering, cell biology, molecular biology, physiology, chemistry, and imaging, and specialists in electrical engineering, mechanical engineering, chemical engineering, chemistry, and biological and clinical science.

CBE investigators have reported important new discoveries stemming from this program. Unique peptide sequences have been found to stimulate cell differentiation, proliferation, and migration, which have been optimized for new bone production. Peptides have been engineered to contain novel recombinant fusion proteins and growth factors, which have been successfully synthesized. Microfluidic systems have been developed to study the formation of capillary networks under the influence of various growth factors, interstitial flow, and different peptide scaffold materials. This has enabled CBE investigators to show that vascular networks are promoted in peptide gels of low modulus, and by vascular endothelial growth factor (VEGF) and interstitial flow normal to the cell monolayer. In cartilage tissue engineering applications, adult equine marrow-derived stem cells have been found to be capable of differentiating into cartilage-like cells that can synthesize cartilage-specific aggrecan molecules. These aggrecans provide compressive stiffness to the neo-tissue constructs. This important result shows direct evidence of stem cell differentiation to the chondrocyte phenotype in specific peptide scaffolds. For liver tissue engineering, investigators were able to maintain functional rat hepatocytes *in vitro* by developing a self-assembling peptide sandwich culture technique. Phenotypic and signaling responses of primary rat hepatocytes to tethered epidermal growth factor (EGF) were also demonstrated.

The ability to carry out appropriate animal studies is critically important to tissue engineering research. CBE's BRP partnership is now working with investigators at the Brigham and Women's Hospital, Boston, to study the injection of cell-free peptides, peptides having tethered growth factors, and cell-seeded peptide scaffolds for myocardial tissue engineering. In addition, a multi-institutional collaboration with Colorado State University's Clinical Sciences Department and Equine Orthopaedic Research Center has initiated rabbit and equine studies for cartilage repair. The equine knee joint model is particularly well suited for the study of osteoarthritis and cartilage resurfacing.

UROP Activities and Industry Connections

CBE continues to connect outstanding undergraduate students in several departments at MIT to cancer research laboratories at the Beth Israel Deaconess Medical Center, Boston. This is a long-standing partnership in which CBE provides logistical and administrative support. CBE's interactions with industry include a new initiative with Texas Instruments (TI) in the context of a day-long symposium at MIT focused on applications in medical electronics. Ten TI research laboratory personnel and business leaders were introduced to the research of a dozen MIT faculty members in six different departments and programs. The TI lead investigator will be on campus this coming fall term to attempt to broaden and solidify this interaction. CBE continues its interactions with 3-D Matrix (scaffold), Olympus Biomaterial Corporation (bone tissue engineering), Menicon Co. Ltd., and Mitsubishi Corporation (tissue engineering). In addition, research grants and partnerships with Centocor (Johnson & Johnson) and Pfizer Inc. continue to focus on cartilage degradation in osteoarthritis and rheumatoid arthritis.

Administrative Updates

We are extremely glad to welcome the new director of the Administrative Services Organization (ASO), Su Chung, who will be continuing ASO's outstanding leadership in assuring that CBE can continue its ability to serve the MIT biomedical engineering research community.

Alan J. Grodzinsky

Director

Professor of Mechanical, Electrical, and Biological Engineering

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