Center For Biomedical Engineering

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 plays a lead role in MIT's activities in tissue engineering and therapeutic approaches for applications in the repair of musculoskeletal and cardiovascular tissues. Recent initiatives have focused on the delivery of drugs to stop the progression of osteoarthritis associated with traumatic joint injuries. Ongoing collaborations with Harvard Medical School (HMS), Boston University Medical School (BUMS), Boston Children's Hospital (BCH), and Massachusetts General Hospital (MGH) have led to the formation of a center for translational research in osteoarthritis and the initiation of a four-way human clinical research study of femoroacetabular impingement. In addition, fundamental discoveries in microparticle- and nanoparticle-based drug delivery approaches by CBE faculty and students have enabled new approaches to the treatment of joint disease.

CBE continues to identify new opportunities and connections with industry that are aligned with its set of core research thrusts. The Center also maintains a well-used base of core research facilities that are provided at minimal user cost to the MIT community.

On July 1, 2012, CBE transitioned from an interdepartmental center reporting to the vice president for research to a center reporting to the Biological Engineering Department.

Major Research Areas

CBE's core faculty members represent a variety of academic units, primarily within the School of Engineering, but with collaborating faculty from Harvard Medical School; Colorado State University Medical School; Harvard School of Dental Medicine; Boston University Medical School and Department of Rheumatology; Lund University Department of Clinical Sciences, Malmö, Sweden; and the Laboratory for Molecular Biomechanics and Clinic for Orthopaedic and Trauma Surgery, Tübingen, Germany. These faculty members participate in multi-investigator programs focusing on CBE's primary research areas:

- cell and tissue engineering
- biomaterials and hydrogel scaffolds for regenerative medicine and drug delivery
- membrane protein structural biology, design, and fabrication
- mechanobiology and the underlying cellular mechanisms by which traumatic injuries cause degenerative diseases in connective tissues

Together, these research thrusts have direct applications to musculoskeletal and cardiovascular pathophysiology, tissue regeneration and repair, drug discovery, environmental and biohazard sensors based on membrane proteins, and nanobiotechnology. CBE faculty members participate in many interdepartmental programs as well as collaborative interactions with other universities and industry research laboratories.

Major Research Initiatives

CBE researchers have joined forces with experts from Boston University Medical School (Rheumatology), Boston Children's Hospital, and Massachusetts General Hospital to initiate a collaboration and clinical trial on the pathobiology and pathomechanics underlying the syndrome of femoroacetabular impingement (FAI). FAI is a hip problem that is highly prevalent among young active individuals caused by a deformity of the hip joint (in particular, a misshaped 'ball' of the ball-and-socket hip joint). This problem often leads to hip dysfunction and osteoarthritis. The Boston University Rheumatology team includes experts in the epidemiology of osteoarthritis and in gait analysis and rehabilitation. The MGH team includes experts in dual fluoroscopic and magnetic resonance imaging, used to measure motion of the joint and deformation of the hip cartilage in real time. The Boston Children's hospital team sees these patients in the clinic and has experience in the surgical procedures used to ameliorate the pain and dysfunction of the hip. MIT CBE researchers will be able to study the molecular biochemistry and molecular biochemistry of samples of tissues and synovial fluid that may be obtained from surgical procedures pending approval of the four-way Institutional Review Board (already approved in three of the four institutions). It is hoped that identification of tissue biochemical changes and molecular biomarkers that result from mechanical impingement of the femur against the socket of the hip joint may lead to improved diagnostics and surgical approaches for this syndrome.

Another recent initiative has focused on treatment of patients who suffer from traumatic knee injury, an event with very high risk for developing osteoarthritis. About 27 million Americans suffer from osteoarthritis, and it has been estimated that 12% of these cases result from a traumatic joint injury, such as a rupture of the anterior cruciate ligament or a tearing of the meniscus. Invariably, these injuries cause a slow but steady degradation of the knee articular cartilage, with a high rate of progression to osteoarthritis. This problem exists worldwide. CBE researchers are now collaborating with the Center for Advanced Orthopaedic Studies at Beth Israel Deaconess Medical Center (BIDMC) and HMS to study the mechanisms underlying cartilage degradation after such injuries and to initiate a clinical trial of Food and Drug Administration–approved therapeutics that may delay or even prevent the initiation of arthritis. BIDMC Center for Biomedical Engineering researchers have found that a glucocorticoid drug (dexamethasone) currently used to treat inflammatory diseases can also prevent cartilage deterioration from occurring, using an in vitro model of joint injury. The hope is that if such a drug is used very soon after injury, osteoarthritic processes may be completely halted. In essence, this would be repurposing an existing drug, as dexamethasone is already approved for human use.

Since severe joint injuries are more common in younger people, who are likelier to participate in sports and military service, this approach may greatly decrease the risk of progression to osteoarthritis that is known to exist with or without such reconstructive surgery. Animal studies are being planned to test this approach in vivo and to determine how many joint treatments may be necessary to maintain the protective effect. If those animal studies yield positive results, the findings could be rapidly translated to human treatments. Discussions are now underway with a surgical team from MGH to delineate the steps needed to initiate a clinical trial for injuries common to the wrist.

CBE investigators received a new National Institutes of Health grant to study the use of self-assembling peptide hydrogel scaffolds for the tissue engineering of cartilage repair. These studies focus on the basic mechanisms by which such scaffolds can initiate and accelerate the conversion of autologous bone marrow stem cells into cartilage-like cells, a process called chondrogenesis. In order to do this, researchers will design and functionalize the peptides with matrix molecules and growth factors specialized for chondrogenesis and for initiating a process to integrate the "neo-cartilage" tissue with existing surrounding tissue in the joint surface. These specially designed peptide scaffolds will then be used in two sets of animal studies, one in rabbits and one in horses, both in collaboration with the Equine Orthopaedics Laboratory of Colorado State University. This equine study is important since the FDA now essentially requires that any potential tissue engineering product for the repair of cartilage defects be tested in a horse model involving challenging, long-term loading of the joints typically for a period of a year.

In addition, studies to design and develop novel microparticle- and nanoparticle-based drug delivery systems are now under way. These systems involve the delivery of combination therapeutics, including anabolic factors (e.g., growth factors) to promote growth of new tissue, along with anti-catabolic drugs to separately block tissue degradation.

One such anabolic factor is a modified version of insulin-like growth factor-1 (IGF-1), which stimulates tissue growth and cell biosynthesis of tissue extracellular matrix. The use of IGF-1 for musculoskeletal connective tissue repair is a particularly important application. However, this is not a practical therapy when the growth factor is delivered systemically, due to rapid release of the drug from the body and potential side effects in non-targeted tissues. Therefore, CBE members in collaboration with scientists and clinicians at the Brigham and Women's Hospital (BWH), Boston, have been studying the use of a modified IGF-1, formed by adding a heparin-binding domain to give the fusion protein HB-IGF-1. This fusion protein is bioactive in that it stimulates sustained extracellular matrix synthesis in tissues having a matrix containing a high negative charge density, such as cartilage and the meniscus. Recent animal studies at BWH showed that intra-articular injection of HB-IGF-1 into rat knee joints resulted in sustained retention and bioactivity for up to eight days. While electrostatic interactions help to augment partitioning of this positively charged drug into tissues with a high negative charge, such proteins would rapidly diffuse out of the tissue unless they could specifically and reversibly bind to sites near the tissue cells. Such binding enables local depot delivery of the drug. This discovery suggests that modification of growth factors with heparin-binding domains may be a new strategy for sustained and specific local delivery to a range of musculoskeletal and cardiovascular tissues.

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 all across the Institute at no or minimal user cost and are particularly relevant for CBE's major research thrust areas.

These facilities include the widely used Applied Biosystems 7900HT fast real-time 384-well plate quantitative polymerase chain reaction instrument and associated peripherals, an Alpha Innotech Gel Imaging Facility 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. The labs also include an array of associated instruments and peripherals needed for maintaining and experimenting with living cells and tissues. These are available to all MIT 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. All these instruments are located in the third-floor laboratories of CBE in NE47 (500 Technology Square).

Undergraduate Research Opportunities Program Activities

CBE continues to connect outstanding undergraduate students in several departments at MIT to laboratories associated with CBE and various Boston-area hospitals. 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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