

David Scadden, MD, Director of the Center of Regenerative Medicine, MGH spoke on “The Microenvironment Governing of Stem Cells”. The overall goal of the center is to develop cell and tissue-based therapies using stem cells. Such therapies may include sensing and imaging technologies as well as the development of tissue-engineered materials. Stem cells are of intense interest because of their capability of differentiating into multiple cell types and of self renewal. The three types of stem cells, totipotent, pluripotent and multipotent, represent different stages in development. Totipotent stem cells form after the division of a fertilized egg and can develop into a complete organism. Pluripotent cells have the potential to develop into a large number of cell types. Multipotent stem cells can become one of several cells types within a given organ; it now appears possible that they may be obtained from adult as well as fetal tissue. Stem cells are regulated by their interaction with the microenvironment. Niche components within the microenvironment are being studied to understand this interaction. Specifically, hematopoiesis within the bone marrow is of interest, with the osteoblasts forming a critical portion of the microenvironment. A question yet to be answered is how the stem cell-microenvironment interaction occurs in vivo.

Tejal Desai, PhD, Boston University discussed “Multifunctional Microdevices for Intelligent Drug Delivery: Pores, Particles, and More”. Microfabrication techniques are being applied to create medical and biological devices that interface with cells and cell receptors in order to allow drug delivery with greater safety, efficacy and drug stability than is possible with conventional delivery of therapy. Both oral and implanted systems are being investigated. A top-down approach, which starts with a large structure which is then patterned, is used to control the shape, size and surface properties of the resulting smaller asymmetric 3-D structures. In the case of conventional oral drug delivery, major issues include getting the drug from the GI tract to the site of interest, achieving both chemical and metabolic stability and having adequate solubility. The strategy being followed is to localize the drug using devices that can be targeted; surface-bound lectins are being used to guide device delivery. Devices carrying up to four drug-filled reservoirs have been fabricated. Conventional implantable drug-delivery devices suffer from a “burst” effect, characterized by high initial-dose delivery. To overcome this problem microdevices using nanopore membranes have been fabricated; the 11-50 nm pores of these devices are uniform in size and allow constrained diffusion, which is characterized by linear delivery versus time curves. Control of the pore size makes it possible to keep delivered-drug concentrations within the therapeutic window, avoiding over and under dosing. By using size-selective pores (< 15 nm) the entry of antibodies which may interact with the drug can be minimized. Animal experiments studying this approach for insulin delivery have been initiated.