Bone Tissue Engineering

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The field of bone tissue engineering has been at the forefront of research and product development in the fields of stem cell biology, tissue engineering and regenerative medicine. Osteoblasts are the building blocks of bone in appendicular, craniofacial and axial skeletons. The differentiation of osteoblasts from stem cells is one of the first cell lineages that were identified from mesenchymal, umbilical cord blood and embryonic stem cells. In comparison with a number of other systems whereby the differentiation of stem cells or progenitor cells into tissue-forming cells is being explored, osteogenic differentiation from several types of stem cells is a conventional practice in many laboratories. An exciting array of native and synthetic polymers have been ingeniously designed and fabricated, sometimes with features at the nanoscopic, microscopic and anatomic scales, to provide biomimetic and bioactive surfaces and framework for bone tissue engineering. A number of widely used assays are available to qualitatively and quantitatively assess the outcome of bone regeneration including genetic, molecular, biochemical, structural and mechanical tests. The powerful combination of stem cell biology with multiscale engineering tools has advanced the field of bone tissue engineering to an unprecedented level with widespread in vivo applications for the healing of craniofacial bony defects, segmental bony defects and spinal fusion applications. Bone fracture, non-union, segmental defects, craniofacial defects, arthritis, injuries, and spinal defects represent considerable challenges and economic burden not only in the United States and industrialized countries, but also developing countries. With these multiple fronts of previously built momentum in R&D, the field of bone tissue engineering is poised to further identify areas of true clinical needs and market opportunities, and to further engage biologists, engineers, clinicians and entrepreneurs towards further alignment of research effort between in vitro and in vivo experiments. A number of potentially important areas, which are by no means exclusive, are examined. The combined delivery of bone tissue engineering by both mesenchymal stem cells (MSC) and hematopoietic stem cells (HSC) demonstrates an enhancement of vascularized osteogenesis and needs to be further explored. Developmentally, osteogenesis fails to occur until and unless vascularization arrives. MSC and HSC can be isolated from bone marrow via a single aspiration procedure and can be autologous from the patient. Vascularization appears to be a key factor in bone tissue engineering, especially for large and critical size defects. The value of allogeneic cells has been demonstrated in bone tissue engineering and needs to be further explored. Allogeneic cells are advantageous in being formulated as an off-the-shelf product. A potential caution is the need of immunosuppressant for the use of allogeneic cells in bony defects resulting from cancer. Engineered scaffold is likely more critical for bone tissue engineering than other systems such as cell delivery without scaffolds. In bone tissue engineering, engineered scaffolds not only serve as structural conduits for bone regeneration, but also mechanical support for loading bearing. Mechanical stress plays critical roles in bone growth, remodeling and also bone regeneration. An example is provided to illustrate that mechanical stress at 1 Hz for 12 hrs in vitro in organ culture induces the secondary ossification center in postnatal chondroepiphysis (Sundaramurthy and Mao 2006 J Orthop Res 24:229-241). How mechanical stress is introduced in the process of bone tissue engineering represents an active area of research with optimal parameters to be determined. **Together, bone tissue engineering represents multiple opportunities for the engagement of biologists, engineers, clinicians and entrepreneurs. Due to the availability of several key technical approaches such as**

the understanding of osteoblast differentiation, scaffold sophistication and the abundance of in vivo studies and clinical trials, the field of bone tissue engineering represents more near-term opportunities for R&D. Supported by NIH Grants DE13964 and EB02332.