

DIRECTOR'S NOTES

The Bone and Joint Institute at the new UAB Highlands campus is in the planning stages for both service and research. We view this as a critical aspect of the integration of bone and joint research with the delivery of comprehensive first rate clinical service. This program may represent a prototype for new initiatives in bench to bedside to population research at UAB. Currently the Departments of Biomedical Engineering, Medicine, Pathology, Physical Medicine and Rehabilitation, and Physiology and Biophysics are participating in the planning. We welcome others to this forum.

Also, I am happy to announce that the CMBD received funding for its NIH P30 Research Core Center grant (one of five in the country) for the next five years (June 1, 2006 – May 31, 2011) including four cores and three pilot and feasibility projects.

The CMBD and the Osteoporosis Prevention and Treatment Clinic have jointly funded a new clinical/translational pilot and feasibility project. The awardee is Majd Zayzafoon, M.D., Ph.D., Assistant Professor, Department of Pathology and the title of his project is Alpha-CaMKII: A New Marker and Novel Target for Treating Osteosarcoma.

Below is an overview regarding bioreactor development for tissue engineering written by Timothy M. Wick, Ph.D., Professor and Chair, Department of Biomedical Engineering.

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BIOREACTOR DEVELOPMENT FOR TISSUE ENGINEERING

Tissue engineering involves the use of living cells and a biological biomimetic matrix to grow a three-dimensional living tissue equivalent that when implanted, restores the metabolic and mechanical functions of the diseased or damaged native tissue. Native tissues are complex three-dimensional structures that perform multiple metabolic and mechanical functions. Cells produce and maintain a complex extracellular matrix that is critical to tissue function *in vivo*. Proper tissue function *in vivo* requires replication of tissue microenvironment and differentiated function prior to implantation. Strategies using either differentiated cells (such as chondrocytes, osteocytes, neurons, smooth muscle cells, etc.) or undifferentiated cells (such as mesenchymal stem cells) are effective for development of orthopaedic, cardiovascular, dental, or neural tissues and secretory organs. Similarly both native matrix materials (collagen, fibronectin, etc.) and synthetic degradable matrices are suitable scaffolds to guide tissue growth and differentiation.

Bioreactors are engineered tissue culture vessels that guide cell growth and differentiation in porous three-dimensional scaffolds under controlled conditions. Bioreactors are useful for fundamental studies to develop quantitative relationships between bioreactor environment and tissue growth. Both biochemical factors and mechanical loading regulate cell proliferation, matrix deposition and tissue maturation. At UAB, we develop bioreactors that deliver well-defined spatial and temporal nutrient transport and mechanical loading to promote cell proliferation and matrix deposition to produce functional tissues for implantation. Tissue composition and microenvironment can be made spatially distinct by controlling mechanical loading or nutrient transport throughout the tissue to create tissue with heterogeneous architecture and function that mimics native tissue. We use bioreactors to study cell-cell and cell-matrix interactions in 3-D culture to identify conditions that promote development of tissue with microenvironment and mechanical properties suitable for human implantation. Our studies use cartilage and vascular constructs as model tissues. We have identified roles for matrix composition, mechanical loading, oxygen tension, steroid hormones and specific nutrients in regulating cell growth and tissue differentiation. Engineered tissues are evaluated by histomorphometry, biomechanical testing and *in vivo* implantation to identify bioreactor conditions that produce functional tissue.

A challenge for tissue engineering is development of viable preservation methods to ensure long-term off-the-shelf availability of tissue constructs. Cryopreservation, using cryoprotectants and subzero temperatures to halt metabolic activity until the tissue is rewarmed, can increase tissue shelf life to maintain product inventory to meet patient demand. By controlling cryoprotectant loading in mature tissues, bioreactors can facilitate tissue preservation for long-term storage of tissues prior to implantation. Recent collaborations allow us to develop bioreactors that integrate tissue production and preservation in a well-controlled, sterile bioprocess that can be scaled to meet patient demand.

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