

## DIRECTOR'S NOTES

The CMBD will host a scientific symposium focused on bone biology and disease on Wednesday, April 14, 2004 in WPCC Room E, 12:30-5:30 p.m., followed by an external review of the Center. We have assembled the following outstanding panel of experts for this: John S. Adams, MD, University of California-Los Angeles, Ted S. Gross, PhD, University of Washington, Theresa A. Guise, MD, University of Virginia, Mark S. Nanes, MD, PhD, Emory University School of Medicine, and Nicola C. Partridge, PhD, UMDNJ Robert Wood Johnson School of Medicine. Julia B. Freeman, PhD, Centers Program Director for the NIH National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS) has also been invited.

The CMBD will fund two pilot and feasibility grants for up to \$33,000/year, renewable for one year. The general focus will be basic, clinical and translational research in bone biology and disease. Applications are due by February 6, 2004. Detailed information can be found on the CMBD web page (<http://cmbd.path.uab.edu>).

I am delighted that Huw F. Thomas, PhD, BDS, has accepted the position of Dean, School of Dentistry effective January 1, 2004. He has a distinguished career in developmental biology, pediatric dentistry and infant oral health research. The CMBD looks forward to continuing a mutually productive relationship in the metabolic bone disease area with the School of Dentistry.

Discussed below is an overview of the effects of microgravity on bone which is a newly funded program in the CMBD.

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## EFFECTS OF MICROGRAVITY ON BONE

Skeletal abnormalities including osteopenia, decreased bone formation, mineralization and reduced bone strength are serious debilitating consequences of spaceflight. Bone loss under conditions of low mechanical stress is not surprising since gravity and mechanical stress play a major role in the early development and maintenance of the skeletal system. Morphological changes observed in the bones of elderly osteoporotic and bed-ridden patients dramatically resemble those observed in astronauts after space flight. Understanding the mechanisms responsible for microgravity-induced bone loss is critical for developing effective countermeasures and provides useful models for developing anabolic treatments for bone loss in conditions such as age- and disuse-related osteoporosis.

Mechanisms producing microgravity-induced bone loss remain unclear. One factor many studies agree on is that altered osteoblast function and development play an important role in microgravity-induced bone loss.

The development of procedures to culture cells *in vitro* while modeling microgravity has expanded the possibilities of identifying important factors that regulate their proliferation, differentiation and function. Human mesenchymal stem cells (hMSC) are multipotent bone marrow cells that have the potential to differentiate to different lineages, including bone, cartilage, fat, muscle and marrow stroma. Under osteogenic conditions, the isolated hMSC form aggregates or nodules and differentiate into osteoblasts.

The tool we are using for modeling microgravity is a recently developed system by NASA which is a cell culture device that simulates several aspects of microgravity. The system developed, known as the Rotary Cell Culture System (RCCS), creates an optimized suspension culture. We have found that seven days of modeled microgravity is sufficient to totally suppress the differentiation of mesenchymal stem cells into osteoblasts. Our data indicate that PPAR $\gamma$  is an important factor in the hMSC response to modeled microgravity. This provides evidence that a reciprocal relationship exists between osteoblast and adipocyte differentiation which has important implications for understanding the molecular basis for osteopenia in numerous conditions.

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## **MISSION OF THE CMBD**

The mission of this Center is establishment of an infrastructure and provision of resources that support, catalyze and integrate basic research, clinical and outcomes/health services research, clinical activities and patient and physician education.