

## DIRECTOR'S NOTES

The School of Medicine is in the middle of developing a strategic plan for research. At the spring meeting of the CMBD Steering Committee, considerable discussion was focused on this issue. Certainly the joint Biomolecular Engineering and Regenerative Medicine Program (BERM) will be emphasized. Another area for discussion will be on the Bone Metastasis Program, directed by Dan R. Welch, PhD, interfacing with the Comprehensive Cancer Center (see below).

One of the major commitments of UAB to bone research includes the recruitment and promotion of key basic bone research faculty. Two new faculty members have been recruited by the School of Dentistry with a start date of June 1, 2005. Mary B. MacDougall, PhD, has been recruited to develop a basic craniofacial biology program and will be the new Associate Dean for Research and Director of the new Institute of Oral Health Research. Amjad Javed, PhD, has accepted a position as Assistant Professor, Department of Oral and Maxillofacial Surgery. His basic research program is focused on understanding molecular mechanisms involved in bone turnover and repair.

Discussed below is an overview of the new Bone Metastasis Program, jointly developed by the CMBD and the Comprehensive Cancer Center. Dan R. Welch, PhD, Leonard H. Robinson Professor of Pathology was recruited from Pennsylvania State School of Medicine to lead this program.

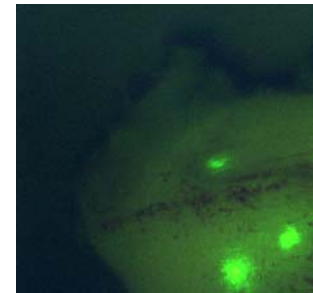
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## NEW MODELS HOLD PROMISE FOR BREAST CANCER RESEARCH

Bone is the most common site of breast cancer metastasis. These tumors are extremely painful and frequently result in compression fractures. Although recognized for more than a century, the mechanisms underlying predilection of breast carcinoma cells for bone remain ill-defined. One of the main drawbacks in studying this problem is the lack of models that allow the study of early steps in the metastatic colonization of bone. Historically, bone metastases have been studied using x-rays which require >50% of bone matrix to be lost before lesions are visible. Our laboratory has recently developed a model for studying early steps in bone metastasis using human breast carcinoma cell lines that constitutively express enhanced green fluorescent protein. After selecting for

the most highly fluorescent subpopulations, we can detect single cells within intact bones stripped of surrounding soft tissues. Following entry into the vasculature, cells take residence at the ends of bones and within 1 wk, begin to proliferate. Histomorphometry shows that osteoblast and osteoclast numbers changed minimally within the first two weeks of tumor cell colonization. But by four weeks both osteoblast and osteoclast numbers decreased significantly as the tumors got larger and while relative bone matrix area decreased. Concurrent *in vitro* experiments showed that tumor cells induced osteoblast apoptosis. While numerous studies have implicated tumor cell activation of osteoclast activity, these recent studies represent the first *in vivo* experiments showing that tumor cells negatively regulate osteoblasts. The observations provide a likely explanation for why bisphosphonate drugs, despite being effective inhibitors of bone resorption, do not ultimately lead to re-gaining of bone matrix.



Green fluorescent protein expressing MDA-MB-435 breast cancer cells were injected intracardially in 4-6 week old mice. Mice were necropsied and femurs were dissected at 1 week post-injection. Areas of green fluorescence were seen using a fluorescent stereomicroscope, and were indicative of tumor cells.

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