Breast Cancer Bone Metastasis by Tumor Secreted BMPS

Breast as well as other cancers, preferentially metastasize to the bone creating lesions that are often extremely painful and lead to fractures. Currently, there is limited treatment for bone metastases other than palliative. It is critical that we understand how breast cancer cells (BCCs) are able to promote colonization of and subsequent growth in the bone. This study will help identify therapeutically targetable interactions between the bone and BCCs.

Osteoclasts are required for normal bone development, repair and maintenance. Their primary function is to degrade bone in response to homeostatic or repair cues. Tumor cells may secrete factors that enhance osteoclast activity and maturation. We are just now beginning to appreciate that BMPs play a role in osteoclast activity (Pham et al., 2011, Jensen et al., 2010) independent of osteoblasts which are well known targets of BMP. Our preliminary data show that bonetropic BCCs downregulate BMP2 and upregulate BMP4 and BMP7. This switch may be the basis by which BCCs influence osteoclast activity.

To assess the ability of different BMP ligands to contribute to osteoclast differentiation, osteoclast precursors were isolated from C57/Bl6 mice, induced to differentiate with RANKL and treated with BMP2, BMP4, or BMP7. Cells were harvested and changes in osteoclast specific gene expression measured. The number of nuclei, size and activity were also measured. Our findings demonstrate that specific BMP ligands differentially affect both osteoclast differentiation and activity. Furthermore, those BMP ligands which are upregulated in many BCCs may play a significant role is osteoclastogenesis.