ABSTRACT

Background: microRNAs (miRNAs) play important roles in diverse biological processes including tumor progression and metastasis. Previously we discovered that miR-125b were selectively accumulated in bone matrix with matrix vesicles budding from osteoblasts. Since miR-125b inhibited osteoclast formation by targeting *Prdm1*, a transcriptional repressor, transgenic (Tg) mice overexpressing miR-125b under the control of the human osteocalcin promoter exhibited high bone mass in parallel with a decrease in osteoclast numbers. As bone is the most common site of breast cancer metastasis, we hypothesized that miR-125b accumulated in bone matrix may suppress osteolytic bone metastasis.

Methods and Results: Murine mammary carcinoma PY8119 cells were tagged with luciferase and then injected into wild-type (WT) and Tg mice via caudal artery. In vivo imaging showed that signals in hind limbs were markedly diminished in Tg mice. Micro CT revealed that bone parameters in Tg mice, such as trabecular bone volume, and cortical bone volume were less than those in Tg mice. Concomitantly, metastatic lesions in hindlimb bones were reduced in Tg mice with decreased numbers of osteoclasts.

Conclusion: These results suggest that miR-125b embedded in bone matrix may suppress osteolytic metastasis through the suppression of osteoclastogenesis. An additional mechanism for miR-125b-dependent inhibition of bone metastasis is currently under investigation.

Keywords: miR-125b, Matrix vesicle, Osteolysis, Breast cancer, Bone metastasis