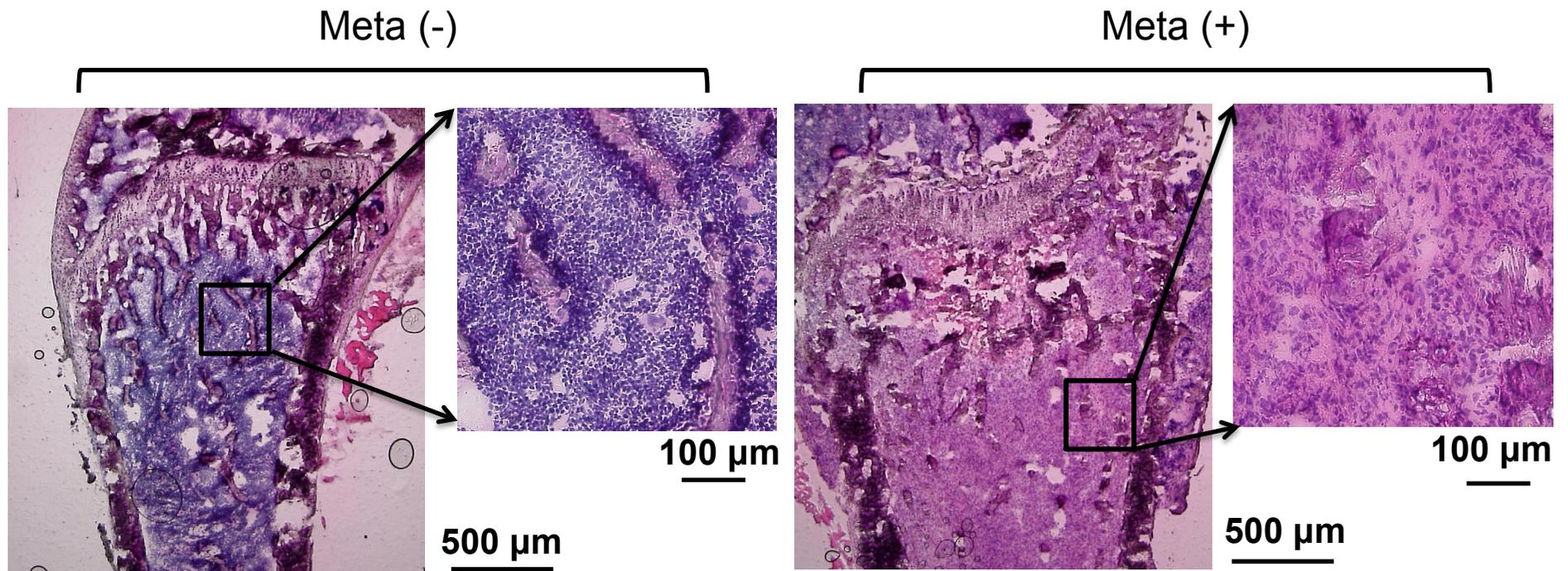
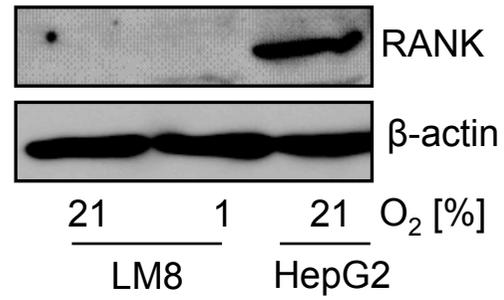


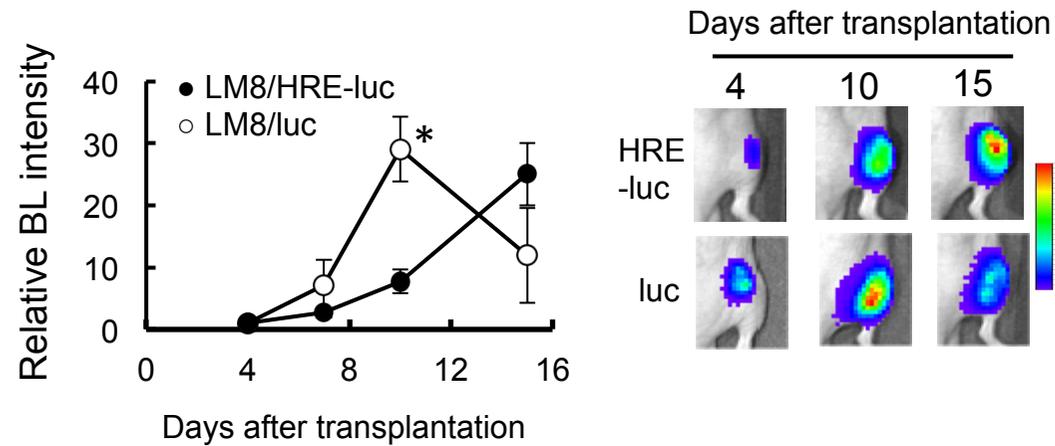
Supplementary Figure 1. Coronal images of the entire body image shown in Figure 1d. Coronal images are cross sections indicated by corresponding arrows 1 - 3 in the transverse image.



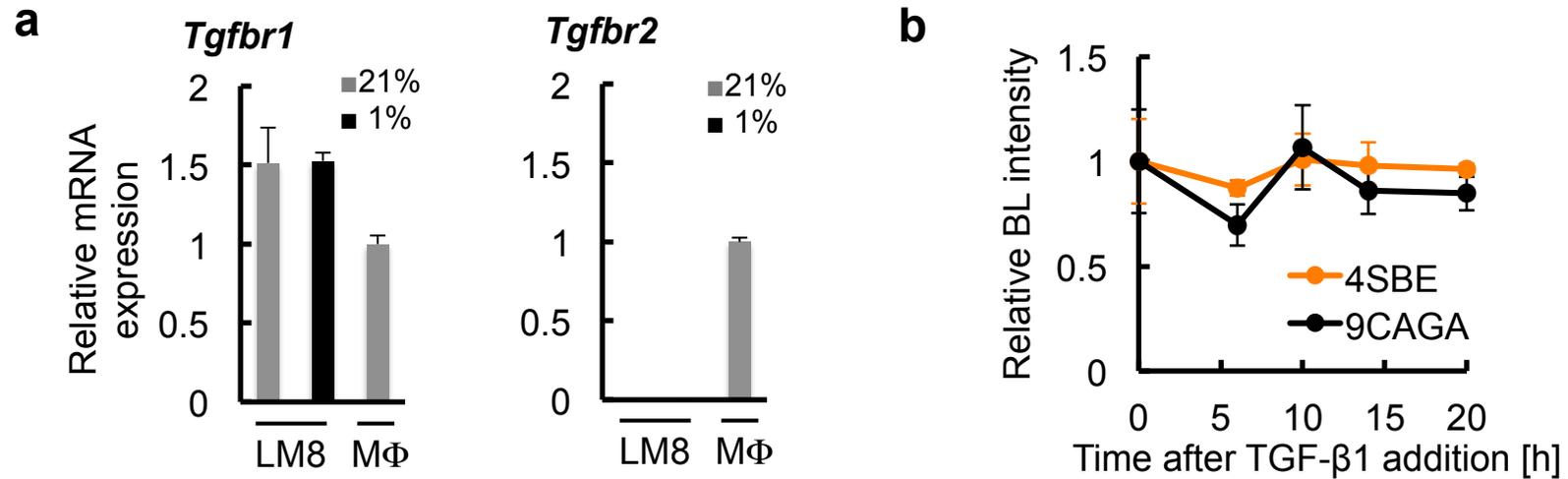
Supplementary Figure 2. Histology analysis of LM8 osteoblastic bone metastasis. HE staining was performed using metastasis free (Meta-) and bone metastatic (Meta+) serial cross sections shown in Fig.1 (e).



Supplementary Figure 3. Protein level of RANK in LM8. Human liver cancer HepG2 cultured under 21% O₂ was used as a control.



Supplementary Figure 4. Quantitative analysis of HIF activity in subcutaneous tumors. Relative luciferase activity in subcutaneous tumors of LM8/HRE-luc or LM8/luc was measured at indicated time after transplantation. Representative images of LM8/HRE-luc and LM8/luc were shown. $n = 8$ for LM8/HRE-luc, $n = 5$ for LM8/luc, $*p < 0.01$.



Supplementary Figure 5. Analysis of TGF- β /Smad signaling in LM8. **(a)** Relative mRNA levels of *Tgfb1* and *Tgfb2* in LM8 cultured under 21% and 1% O₂. Mouse primary macrophage (M Φ) cultured under 21% O₂ was used as a control. **(b)** Response of TGF- β /Smad pathway in LM8 treated with TGF- β (10 ng/mL). TGF- β /Smad pathway activation was assessed by using indicated TGF- β responsive luciferase reporters.