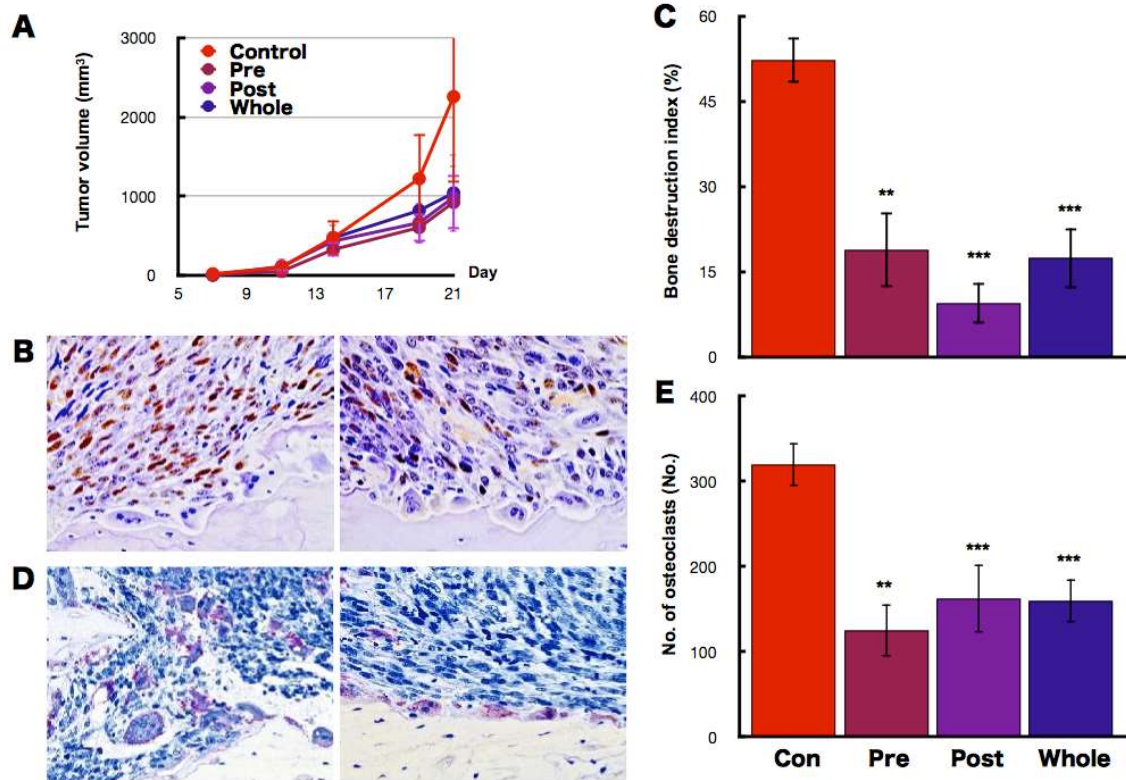


Supplement Figure S1. Effects of hOCIF on osteolysis in the tumor microenvironments **A:** Typical example of a defect in the cranial bone. The extent of bone destruction was determined using a 'bone destruction index', which is the ratio of the length of osteolysis to the length of the cranial bone. **B:** Quantitative analysis of the bone destruction index revealed that hOCIF significantly suppressed the degree of osteolysis. Numerous TRAP positive osteoclasts were observed in the control group (**C**), but only a few positive cells were observed in the hOCIF treatment group (**D**). Quantitative analysis revealed that hOCIF treatment significantly reduced the number of TRAP positive osteoclasts at the TB-interface (**E**). **, *** : $p < 0.01$, $p < 0.001$ vs. Control.



Supplement Figure S2: Preventive effects of hOCIF on bone-associated tumor growth, osteolysis, and activation of osteoclasts in the bone microenvironment. A: Tumor growth was suppressed to the same extent in the Pre, Post, and Whole groups. B: IHC study of PCNA in the control (left) and Pre groups (right). C: hOCIF treatment significantly suppressed the degree of osteolysis in the Pre, Post, and Whole groups. D: TRAP staining in the control (left) and Pre groups (right). E: hOCIF significantly suppressed osteoclast induction in the bone micro environment in all three treatment groups. **, *** : $p < 0.01$, $p < 0.001$ vs. Control.