

Table S4: Summary of studies on impacts of hypoxia on osteoclast formation and activity *in vivo*

Study	Author	Type of Study & Sample	Hypoxic Conditions	Methods	Findings
1.	Durand et al. (2019)	<i>in vivo</i> ; 10-week-old male C57BL/6J mice	4 days of hypobaric hypoxia FiO ₂ = 10%	a. Osteoclast number/bone surface (Oc. N/ BS) was measured by bone static histomorphometry.	a. Hypoxia drastically increased Oc.N/ BS by 2 fold. b. Hypoxia did not affect bone volume (BV/TV)
2.	Takemori et al. (2018)	<i>in vivo</i> ; 5 w.o. female BALB/c mice in which cell line was intramedullary implanted into proximal epiphysis	CO ₂ hydrogel was applied at the tissue where the cells were implanted 4 weeks before.	a. Osteoclast number on CO ₂ treated tibiae was detected by tartate-resistant acid phosphatase (TRAP) staining. b. Micro-CT for bone volume	a. Transcutaneous application of CO ₂ hydrogel decreased TRAP-positive cells on treated tibiae.
3.	Wang et al. (2016)	<i>in vivo</i> ; Normal or ovariectomized (OVX) adult female Sprague Dawley rats of 12 weeks old	Intermittent hypobaric hypoxia was induced at 4 weeks after ovariectomy procedure. Hypoxic condition was performed using experimental high-altitude imitation: rats were housed in a chamber with reduced pressure equivalent to an altitude of 5000 m ($P_B=404$ mmHg; $P_{O_2}=84$ mmHg) for 4 h once daily for 14 consecutive days.	a. Serum level of C-telopeptide of collagen (CTX) as bone resorption marker was measured by ELISA. b. Osteoclasts in the femur were identified using TRAP staining.	a. Osteoclast number and serum CTX-I level were higher in OVX rats that were exposed to intermittent hypobaric hypoxia. b. No change in between normal rats under hypoxia or normoxia.
4.	Dalle Carbonare et al. (2015)	<i>in vivo</i> ; Humanized mouse model for sickle cell disease (SCD: $Hba^{tm1(HBA)Tow} Hbb^{tm2(HB G1,HBB^*)Tow}$ SS) and	Hypoxia/reoxygenation (H/R) stress: hypoxia (8% O ₂ for 10 h) followed by reoxygenation for 3 h	a. mRNA level of RANK in tibia bones was determined using RT-qPCR. b. Osteoclast number/tissue area (N.Oc/TA) and erosion surface/bone surface (ES/BS)	a. mRNA level of RANK in bone was higher in both healthy and SCD mice under H/R stress compared with normoxia. N.Oc/TA, ES/BS and serum CTX levels were higher only in SCD mice

		healthy control <i>(Hba^{tm1(HBA)Tow} Hbb^{tm3(H}</i> <i>BC1,HBB)Tow</i> AA) aged 16-18 weeks, male and female.		were measured by bone histomorphometry. c. Serum CTX-1 level was measured by ELISA.	under H/R stress.
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Note: Normoxia or reoxygenation: 20-21% O₂. Terms & Abbreviations: Oxygen (O₂), Quantitative reverse transcriptase polymerase chain reaction (RT-qPCR), messenger RNA (mRNA), Enzyme linked immunosorbent assay (ELISA), Number of osteoclasts over Total bone area (N.Oc/TA), Erosion surface over bone surface (ES/BS), Tartrate-resistant acid phosphatase (TRAP) & Carboxy-terminal cross-linked telopeptide of type 1 collagen (CTX-1).