SUPPLEMENTARY MATERIALS

1

2 **Table S1** List of primers used for qRT-PCR

Gene names	Primer	Sequence
Mouse *Neu1*	Forward	5'-CGAATTGTCCTCCGCAGCTA-3'
Mouse *Neu1*	Reversed	5'-TCCGCCATGAGGTACCATTG-3'
Mouse *Acp5*	Forward	5'-AGACGAGGTTACGCTGTGC-3'
Mouse *Acp5*	Reversed	5'-TCGGGGACAATTCGGTAAACT-3'
Mouse *Ctsk*	Forward	5'- GCGGCATTACCAACAT -3'
Mouse *Ctsk*	Reversed	5'- CTGGAAGCACCAACGA -3'
Mouse *Nfatc1*	Forward	5'-GAGGAGTTGGCTCAGTG-3'
Mouse *Nfatc1*	Reversed	5'-TAGCGTTCCGTTCGTT-3'
Mouse *OCstamp*	Forward	5'- TTATGTGTTTCCACGAAGCCCTA -3'
Mouse *OCstamp*	Reversed	5'- ACAGAAGAGAGCAGGGCAACG -3'
Mouse *Pdgfb*	Forward	5'-CATCCGCTCCTTTGATGATCTT -3'
Mouse *Pdgfb*	Reversed	5'-GTGCTCGGGTCATGTTCAAGT -3'
Mouse *St3gal1*	Forward	5'- TCCAACACGGGAGTACCCA -3'
Mouse *St3gal1*	Reversed	5'- GCTGGTCGAACCAATATGATACC -3'
Mouse *St6gal1*	Forward	5'-CTCCTGTTTGCCATCATCTGC -3'
Mouse *St6gal1*	Reversed	5'-GGGTCTTGTTTGCTGTTTGAGA -3'
Mouse *Gapdh*	Forward	5'- AACGTCGGAACGATAGCA -3'
Mouse *Gapdh*	Reversed	5'- CTTAAGGCTAGTTAGGCCC -3'

3
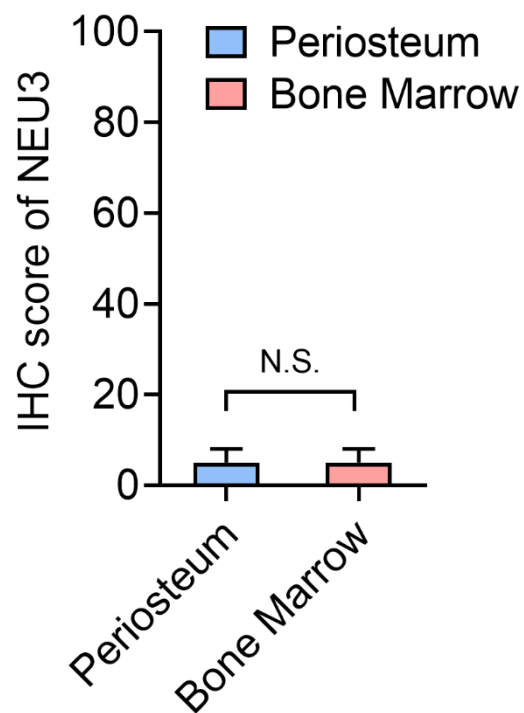
1   **Figure S1**

2
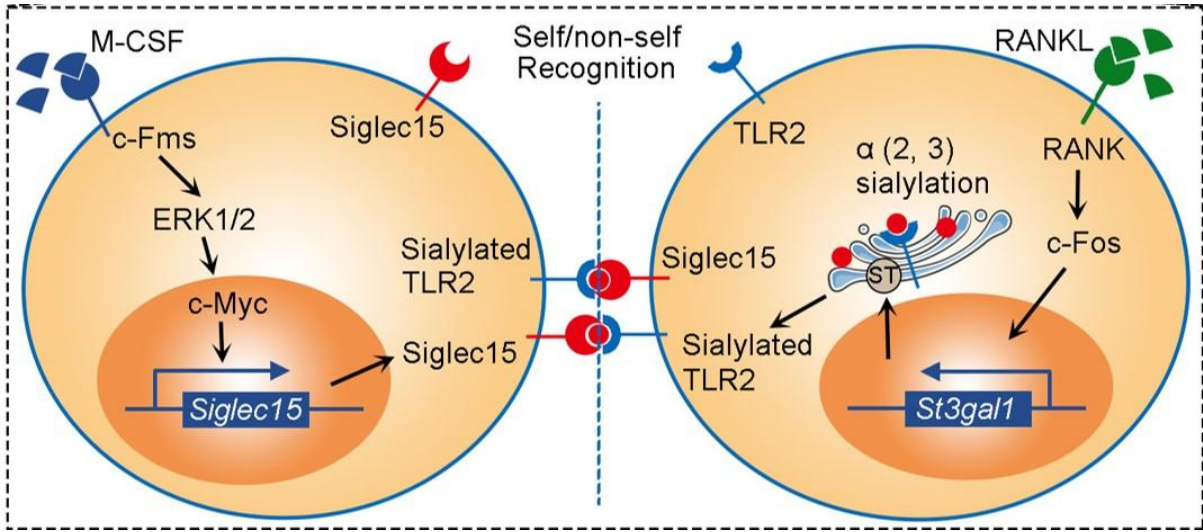3   **Figure S1.** NEU3 IHC score of periosteum and bone marrow; n=3;
4

1 **Figure S2**

3 **Figure S2.** Schematic of Siglec15 mediating osteoclast recognition and fusion by binding to
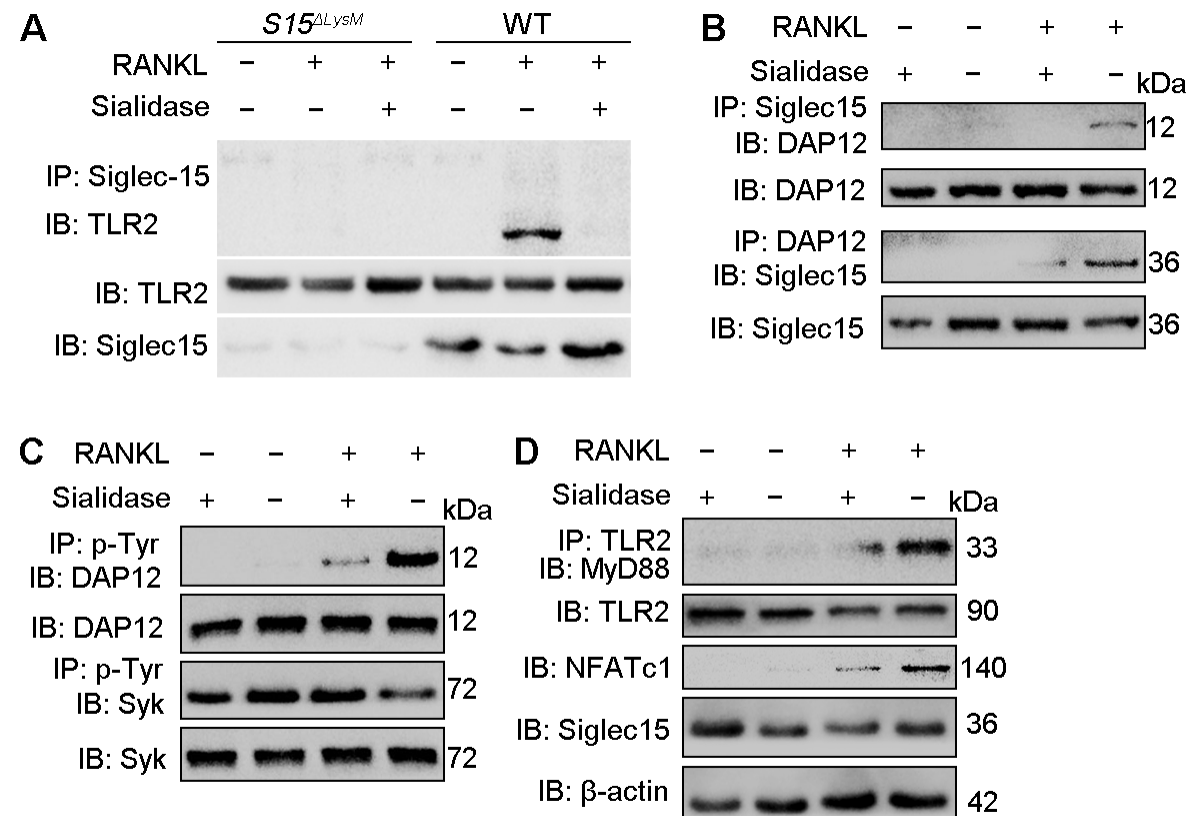
4 α-2,3 sialylated TLR2.

5

3 **Figure S3.** Sialic acid A-2,3 mediates the fusion of mononuclear osteoclasts.

4 (A) Immunoblotting (IB) for TLR2 in whole-cell lysates or protein complexes
5 immunoprecipitated (IP) with Siglec15 in Siglec15ΔLysM or Siglec15fl/fl (WT) BMMs
6 to test the effects of sialidase.

7 (B) IB for DAP12 in whole-cell lysates or protein complexes IP with Siglec15 and IB for
8 Siglec15 in whole-cell lysates or protein complexes IP with DAP12 in the indicated
9 groups.

10 (C) IB for DAP12 and Syk in whole-cell lysates or protein complexes IP with p-Tyr in the
11 indicated groups.

12 (D) IB for MyD88 in protein complexes IP with TLR2 in the indicated groups. IB for TLR2,
13 NFATc1, and Siglec15 in whole-cell lysates.

14
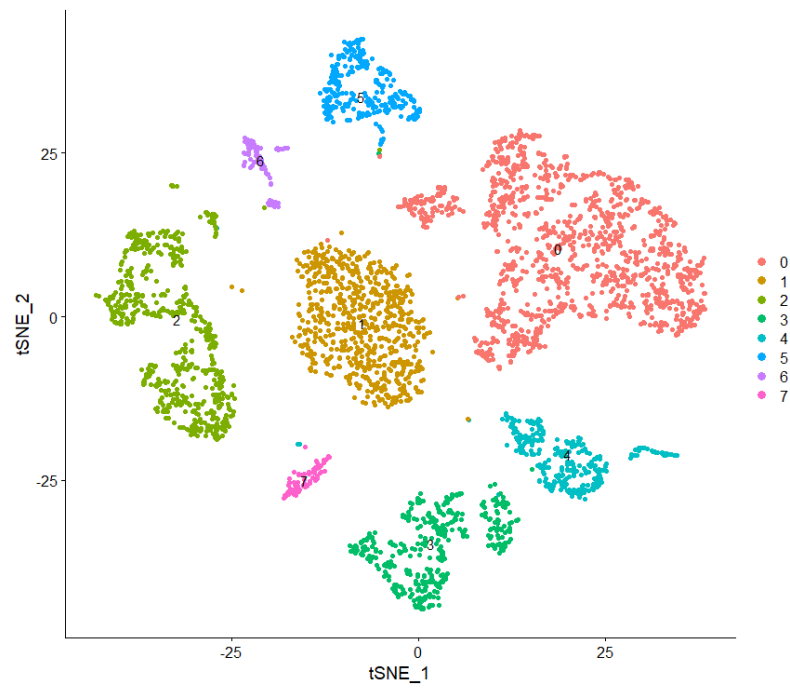
1 **Figure S4**

2

3 **Figure S4.** Clusters of cells that has passed through a reduced-dimension cluster
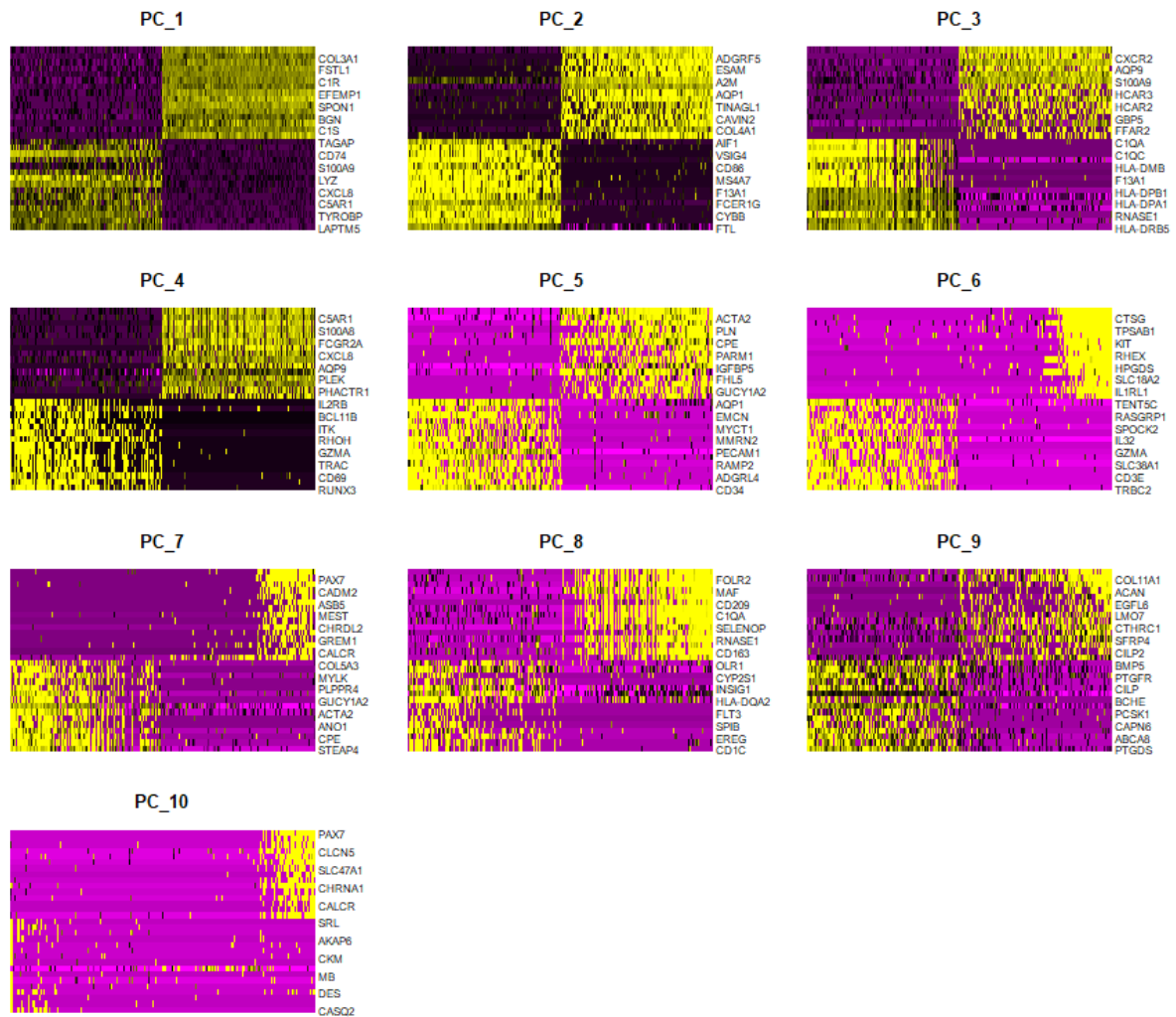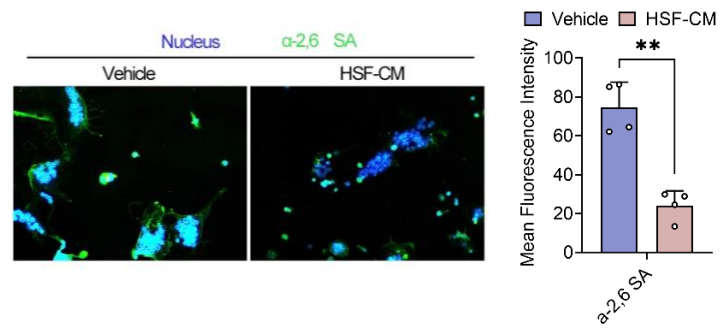
4

Figure S5

Figure S5. Differentially expressed genes (DEGs) of each cluster were identified with the Wilcoxon rank-sum test.

1 **Figure S6**

2

3 **Figure S6.** Immunofluorescence staining showed the inhibitory effect of fibroblast conditioned

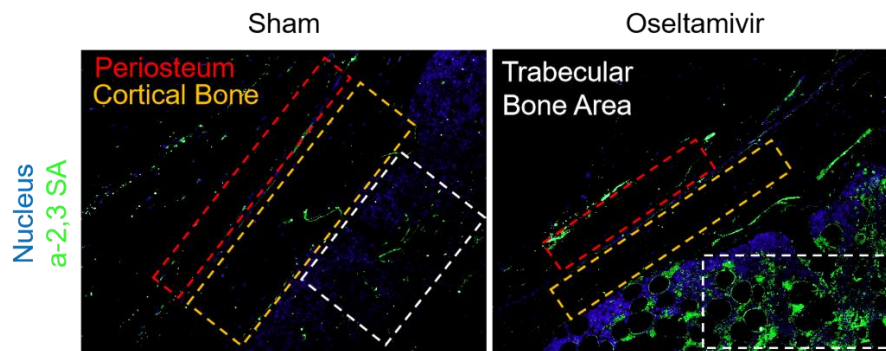4 medium on the sialylation of osteoclasts (a-2,6 SA).

1 **Figure S7**

3 **Figure S7.** Oseltamivir effectively inhibits NEU1 activity and increases sialic acid levels in
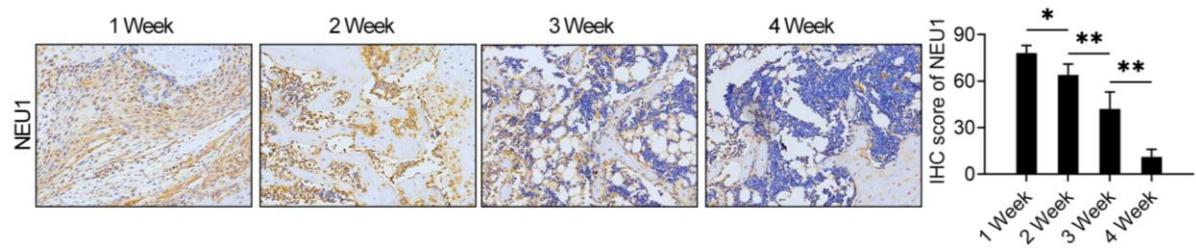4 bone tissue

1 **Figure S8**

2

3 **Figure S8.** Expression level of NEU1 in callus at different stages of fracture healing.
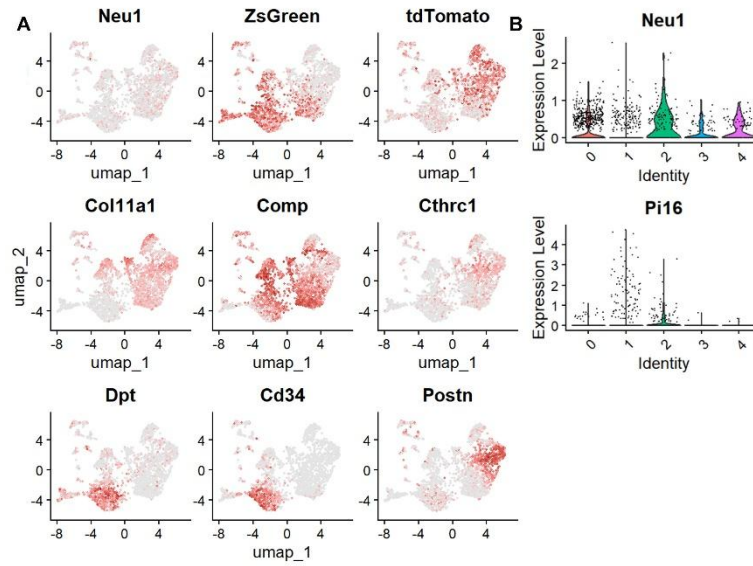4

1　**Figure S9**

2

3　**Figure S9.** (A) Feature Plot shows the distribution characteristics of marker genes in various cell
4　subpopulations. Among these, the original authors consider *ZsGreen+, Dpt+, Cd34+*, and *Pi16* as
5　markers for the periosteal fibrous layer, while *tdTomato+* and *Postn+* are markers for the periosteal
6　cambium layer. (B) Violin plots show that there is expression consistency between the high-expression
7　subpopulations of *Neu1* and *Pi16* (the fibroblast marker gene identified by the original authors).
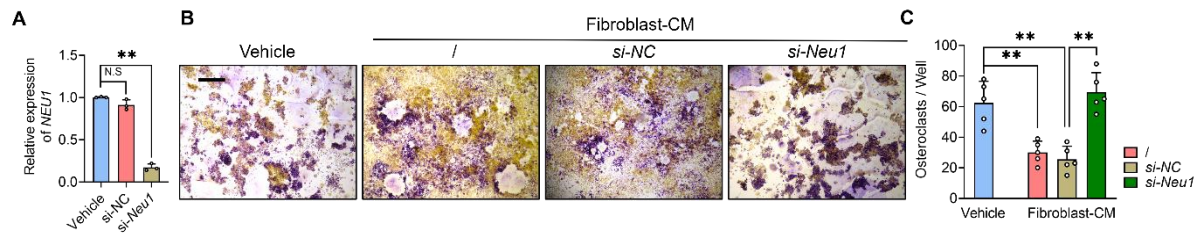8

Figure S10

Figure S10. (A) Relative expression of *NEU1* mRNA in fibroblasts treated with vehicle, control siRNA (*si-NC*), or Neu1-targeting siRNA (*si-Neu1*), normalized to *Gapdh*, n = 3; (B) Representative TRAP staining images of osteoclasts cultured in conditioned medium produced by fibroblasts treated with vehicle, *si-NC*, or *si-Neu1*, scale bar = 200 um; (C) Quantification of osteoclasts per well in different treatment group, n = 5;
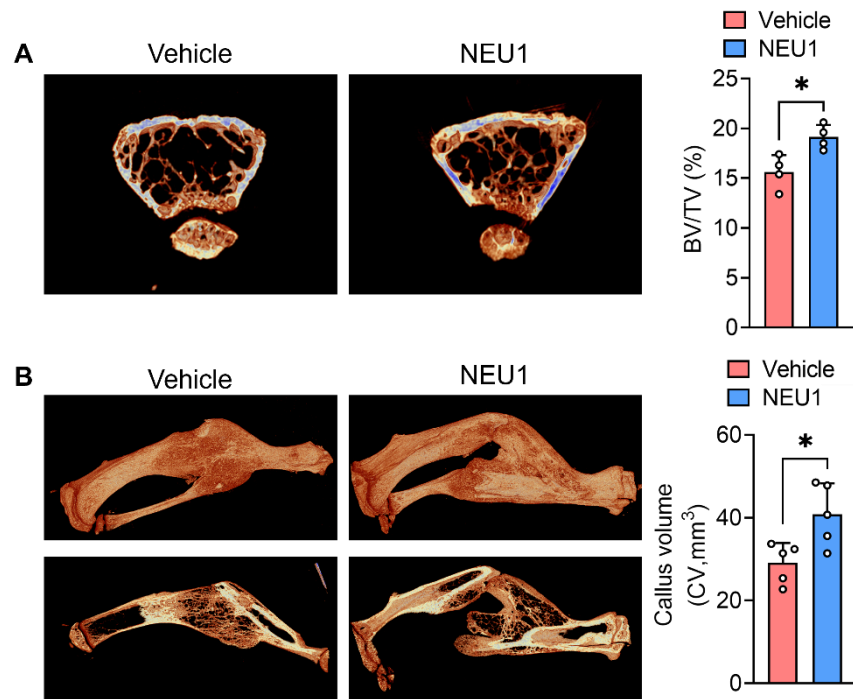
1 **Figure S11**

2

3 **Figure S11.** (A) Representative micro-CT images show cortical and trabecular bone of OVX model
4 mice after treatment with vehicle or NEU1 homologous protein for 4 weeks; BV/TV (Bone bone volume
5 fraction) analysis of trabeculae bone in both groups, n = 4. (B) Representative micro-CT images
6 showing callus of fracture mice after treatment with vehicle or recombinant NEU1 for 4 weeks,
7 quantification of CV (callus volume) from each group, n = 5;

8