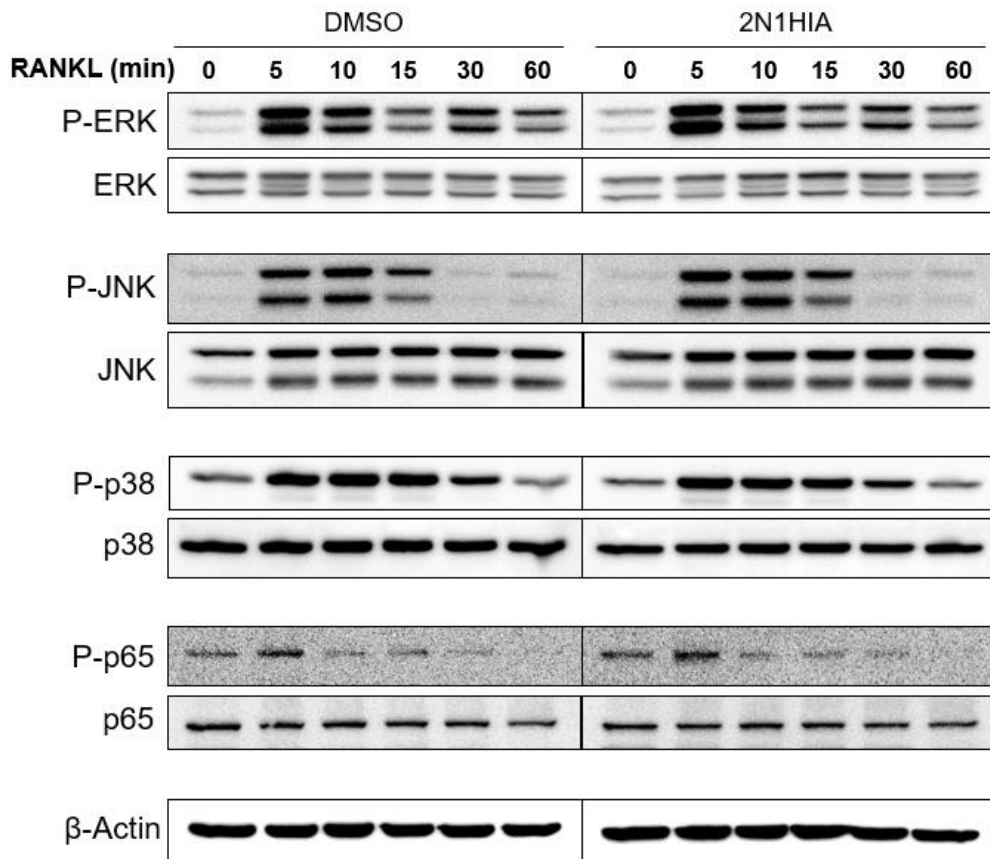
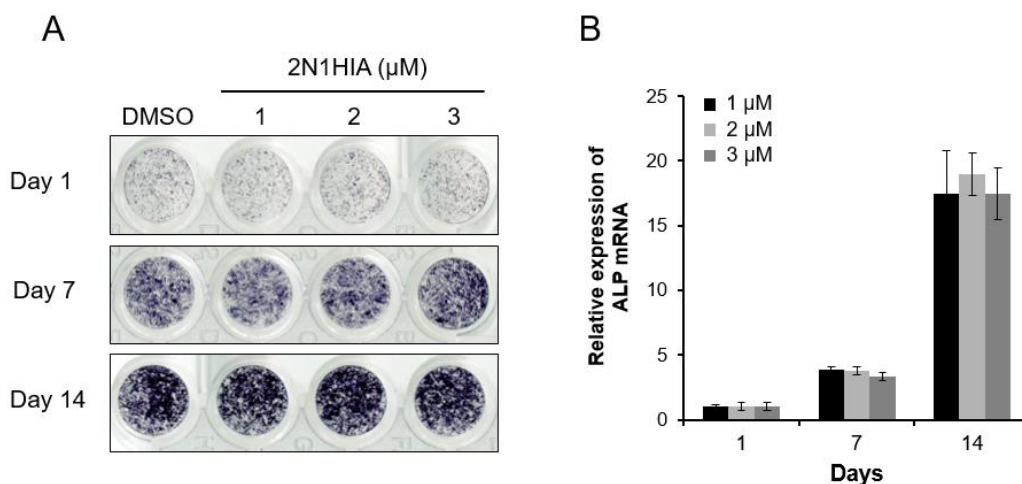


**Figure S1.** Cell viability and cell proliferation were measured using the MTT (A) and BrdU (B) assays, respectively. Data are presented as mean  $\pm$  SD from three independent experiments; \*  $p < 0.05$ , \*\*  $p < 0.01$  (comparison to the control 100%).



**Figure S2.** Effects of 2N1HIA on RANKL-induced signals in BMMs. M-CSF treated BMMs were pre-treated with 1  $\mu\text{M}$  of 2N1HIA or control (DMSO) for 10 min and RANKL (50 ng/mL) was used to stimulate cells at the indicated times. Cells were analyzed via western blotting to detect anti-phospho-ERK, JNK, p38, and p65 signal proteins, as indicated.



**Figure S3.** Effects of 2N1HIA on BMP-induced osteoblast differentiation. (A) Calvarial osteoblasts were cultured for different periods of time and then stained for ALP. (B) At the indicated time points, ALP mRNA was analyzed using real-time PCR. The expression was normalized to glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and presented relative to day one.

**Table S1.** Compounds used in the study.

No.	Name	Molecular weight (kDa)	Catalog number
1	2-[3-(2-fluoro-4-methoxyphenyl)-6-oxo-1(6H)-pyridazinyl]-N1H-indol-5-ylacetamide	392.38	9309204
2	2-[3-(2-fluorophenyl)-6-oxo-1(6H)-pyridazinyl]-N-phenylacetamide	323.32	9288567
3	2-[3-(3-methoxyphenyl)-6-oxo-1(6H)-pyridazinyl]-N-phenylacetamide	335.36	9329589
4	N-(2-chlorophenyl)-2-(6-oxo-3-phenyl-1(6H)-pyridazinyl)acetamide	339.78	9328644
5	N-(2,4-difluorophenyl)-2-(6-oxo-3-phenyl-1(6H)-pyridazinyl)acetamide	341.31	9217398
6	N-(2-fluorophenyl)-2-[3-(2-fluorophenyl)-6-oxo-1(6H)-pyridazinyl]acetamide	341.31	9338014
7	N-1H-indol-5-yl-2-(6-oxo-3-phenyl-1(6H)-pyridazinyl)acetamide	344.37	9314216
8	N-1H-indol-6-yl-2-(6-oxo-3-phenyl-1(6H)-pyridazinyl)acetamide	344.37	9324040

	pyridazinyl)acetamide		
9	2-[2-(2,3-dihydro-1H-indol-1-yl)-1-methyl-2-oxoethyl]-6-phenyl-3(2H)-pyridazinone	345.39	9192738
10	4-[[6-oxo-3-phenyl-1(6H)-pyridazinyl)acetyl]amino}benzamide	348.36	9317292
11	N-1,3-benzodioxol-5-yl-2-(6-oxo-3-phenyl-1(6H)-pyridazinyl)acetamide	349.34	9233542

**Table S2.** Primers used in the study.

Gene	Primer sequence (5'→3')	
<i>Cathepsin K</i>	Forward	GGACGCAGCGATGCTAACTAA
	Reverse	CAGAGAGAAGGGAAGTAGAGTTGTCCT
<i>CD47</i>	Forward	TTTGGTCGGGCTGTGTCTCT
	Reverse	GCTATGATCCCCAACCTGAAA
<i>DC-STAMP</i>	Forward	CGCACGATGCTTCATTCTTC
	Reverse	CAGTGCCAGCCGCAATC
<i>GAPDH</i>	Forward	TGTGTCCGTCGTGGATCTGA
	Reverse	GATGCCTGCTTCACCACCTT
<i>MMP9</i>	Forward	CTGGACAGCCAGACACTAAAG
	Reverse	CTCGCGGCAAGTCTTCAGAG
<i>NFATc1</i>	Forward	ACCACCTTTCCGCAACCA
	Reverse	GGTACTGGCTTCTCTTCCGTTTC
<i>OC-STAMP</i>	Forward	ACTATGGCCACCCGGAAT
	Reverse	GGCCCAAGGGAGTCATGTG
<i>OSCAR</i>	Forward	TGGCGGTTTGCACTCTTCA
	Reverse	GGAAGAACTCAGCCAGCTCAA
<i>RANK</i>	Forward	CGACTGGTTCACTGCTCCTAATC
	Reverse	CTGTCGTTCTCCCCACTTC
<i>TRAF6</i>	Forward	TCGGACCCTGGAGGACAA
	Reverse	CCAAACTTGCCAATCTTCAA
<i>ALP</i>	Forward	AGTTCAGTGCAGTTCCAGACA
	Reverse	TGGCCTGGATCTCATCAGTATTT