

Expanded View Figures

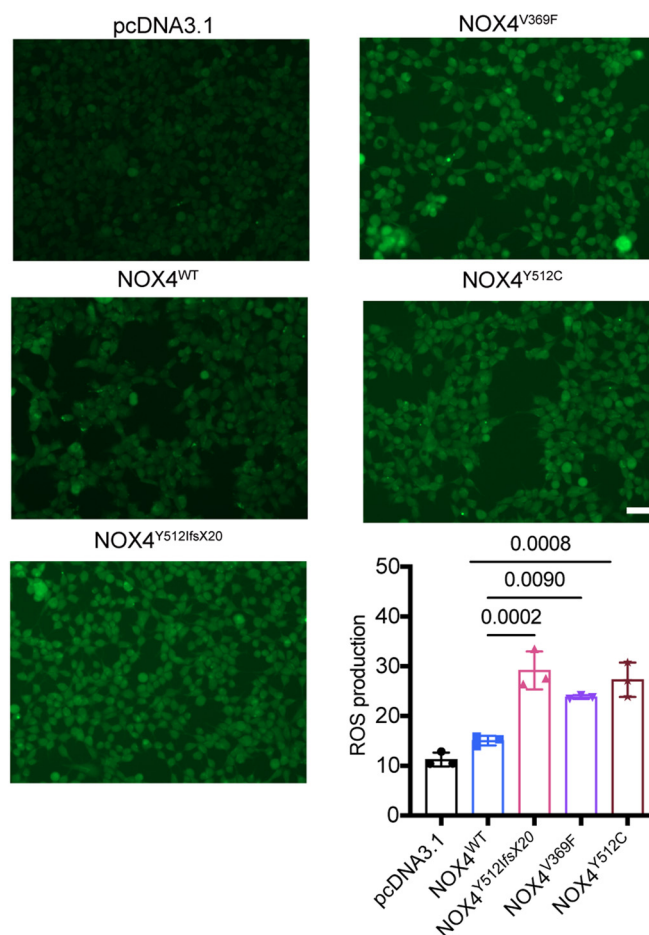


Figure EV1. Elevated ROS levels in HEK293 stable transfected cell lines expressing NOX4 variants.

HEK293 cells were subjected to 12 h of serum starvation after stably transfection with following plasmids: pcDNA3.1, NOX4^{wt}, NOX4^{Y512fsX20}, NOX4^{Y512C}, and NOX4^{V369F}. Fluorescence imaging was conducted following the incubation with 10 μ M DCFH-DA. Representative photomicrographs of the fluorescence are displayed and quantification of the mean fluorescence intensity was performed with ImageJ software. $N = 3$. Scale bars: 100 μ m. Data information: DCFH-DA 2',7'-dichlorofluorescein diacetate. Data presented as mean $\pm$ SD. $N =$ biological replicates. The P value was calculated by the ordinary one-way ANOVA multiple comparisons with Turkey correction of multiple hypothesis tests. Source data are available online for this figure.

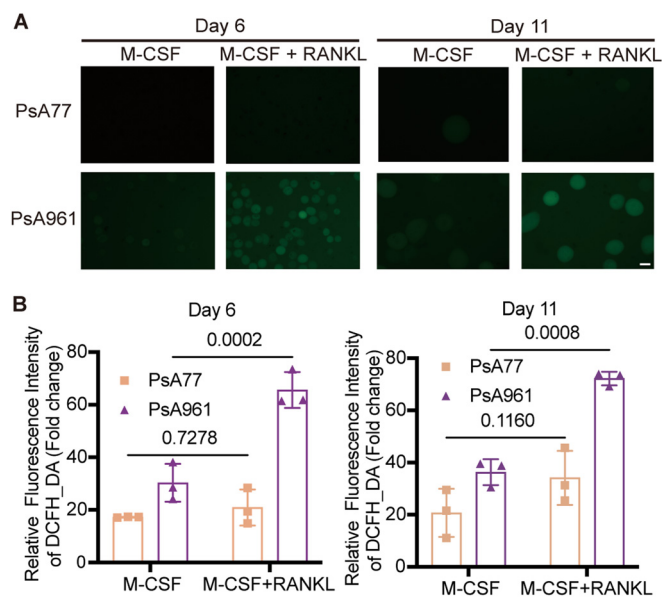


Figure EV2. Impact of ROS on osteoclasts differentiation from PsA961 (*NOX4*^{Y512C}).

(A) Cells were cultured in the presence of M-CSF or M-CSF and RANKL. Visualization of ROS detected by DCFH-DA on Day 6 and Day 11, indicating a higher ROS effect in PsA961-differentiated osteoclasts. Scale bar: 100 μ m. (B) The relative fluorescence intensity of ROS was quantified by GraphPad Prism9.0.0. $N = 3$. Data information: DCFH-DA 2',7'-dichlorofluorescein diacetate. $N =$ biological replicates. For graph (B), error bars in figure represent mean $\pm$ SD (two-way ANOVA with Tukey's multiple comparisons tests). Source data are available online for this figure.

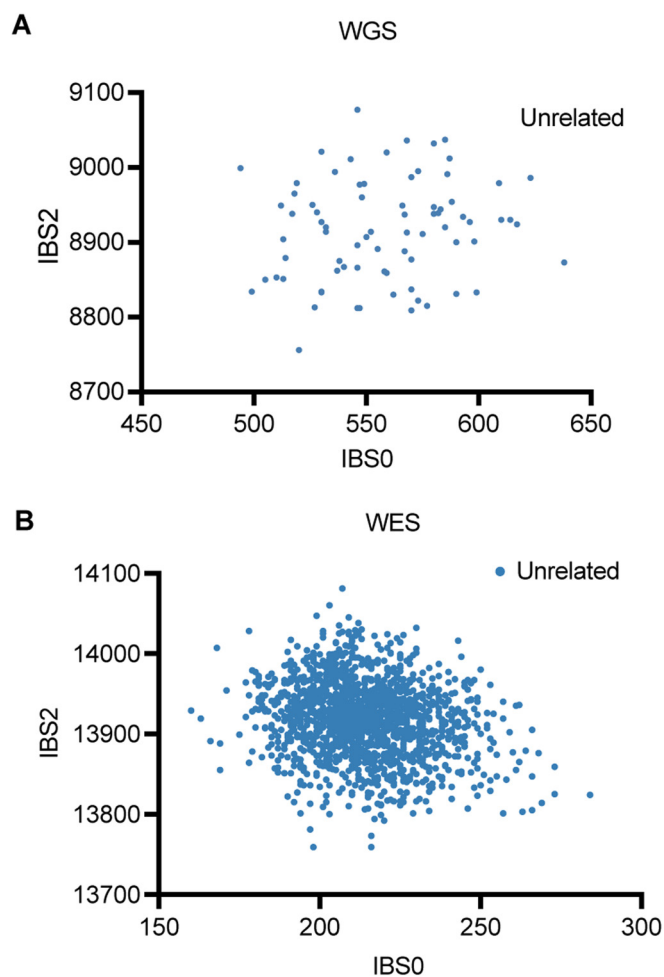


Figure EV3. Relatedness plot for WGS (A) and WES (B) samples.

(A) Relatedness plot for WGS samples. Six samples from the SweGene database (<https://swefreq.nbis.se/>) were added to the WGS analysis. Each dot represents a pair of samples. (B) Relatedness analysis of all WES samples. Data information: IBS0 is the number of sites where 1 sample is homozygous for the reference allele and the other is homozygous for the alternate allele. IBS2, is the count of sites where a pair of samples were both homozygous or both heterozygous. WGS Whole-Genome Sequencing, WES Whole-Exome Sequencing. Source data are available online for this figure.