

Figure S1: BinGO graph of biological function enrichment analysis using Cytoscape tool. Yellow nodes indicate significant values after FDR adjustment  $p < 0.05$ . Genes with at least two carriers of a rare variant were considered in the analysis (132 genes).

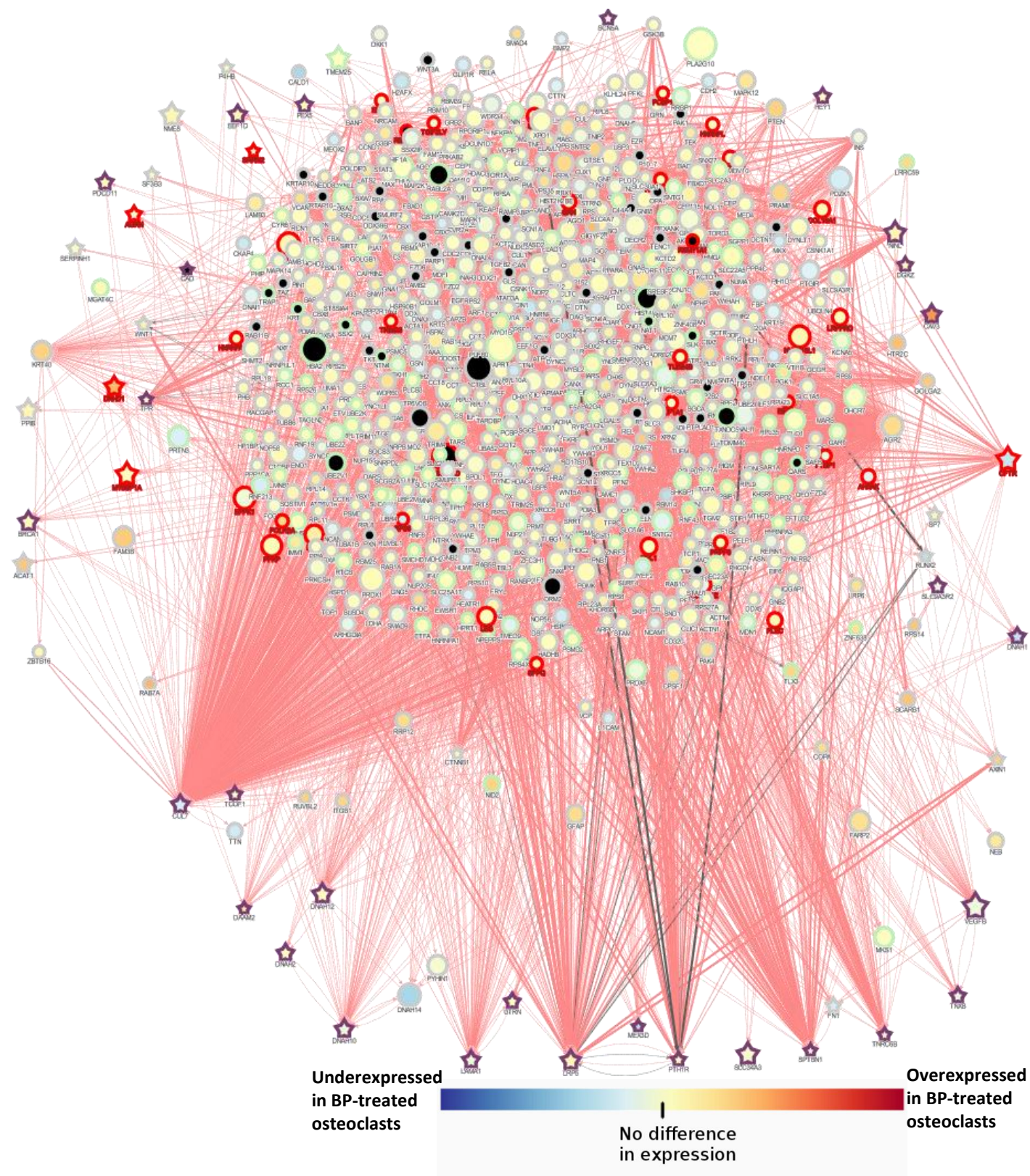


Figure S2: Network analysis of bone-related genes mutated in at least 2 AFF patients using the AFFNET tool. All possible interactions among candidate genes were displayed. The purple star indicates a candidate gene. The red border tags those genes with z-score outside of the threshold according to constraints obtained in gnomAD. Node color represents their expression depending on the expression data obtained in the GSE63009: Osteoclastic precursor cells treated or not with bisphosphonates (alendronate or risedronate) during their differentiation into mature osteoclasts.



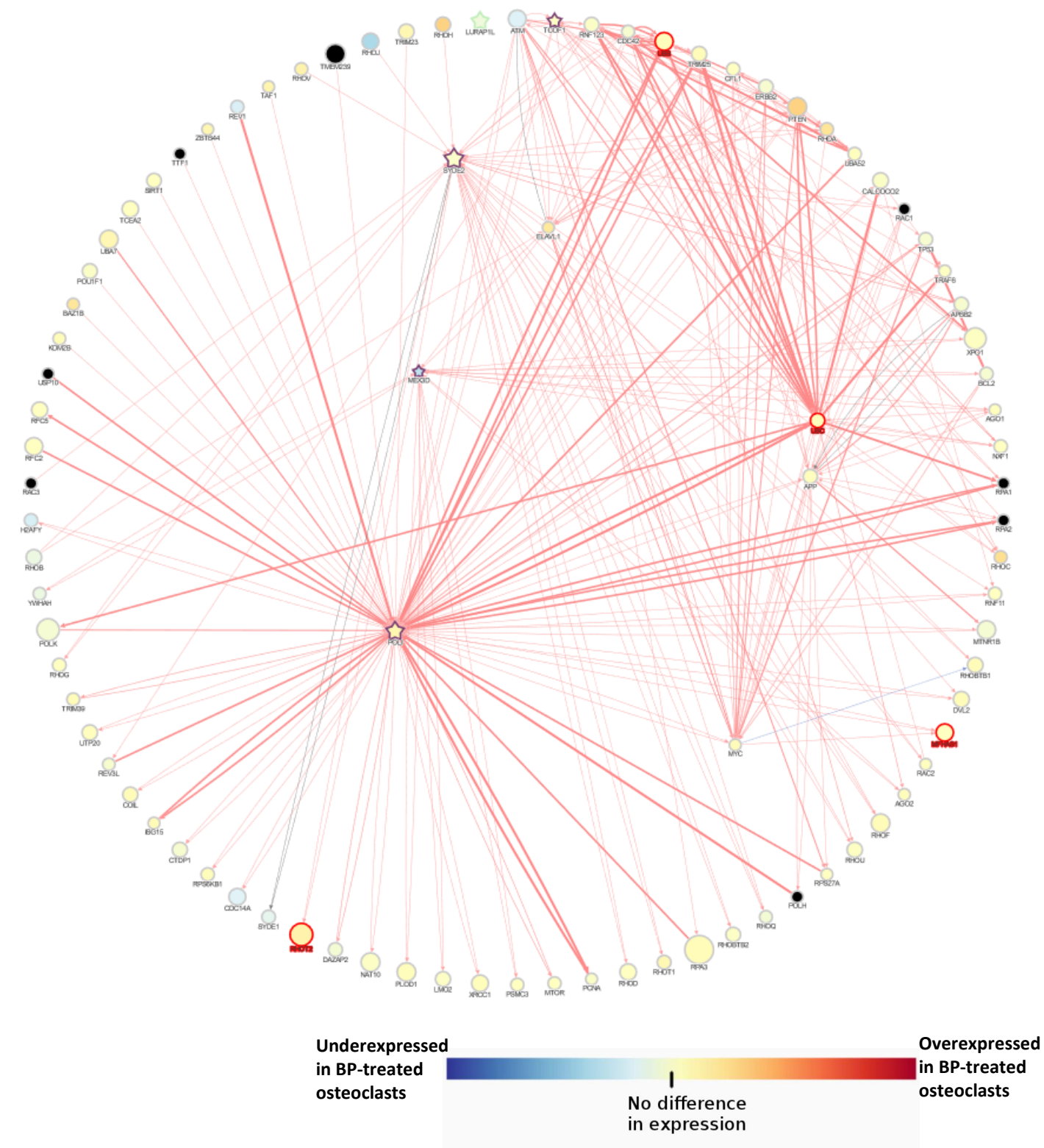


Figure S3: Network analysis of genes mutated either in AFF patients and in three sisters from a previous study<sup>12</sup> using the AFFNET tool. All possible interactions among candidate genes were displayed. The purple star indicates a candidate gene. Green star indicates candidate genes without other gene interaction. The red border tags those genes with z-score outside of the threshold according to constraints obtained in gnomAD. Node color represents their expression depending on the expression data obtained in the GSE63009: Osteoclastic precursor cells treated or not with bisphosphonates (alendronate or risedronate) during their differentiation into mature osteoclasts.