

Figure S1. Overall survival analysis. (A) The univariate Cox regression analysis between FHL2, ACP5, FOSL1, CSF1R, TNFRSF11B and OS in the TARGET dataset (osteosarcoma gene chip array data, n=89). (B) Survival rate of CSF1R between the high- and low-expression groups from TARGET dataset (osteosarcoma gene chip array data, n=89). (C) AUC time-dependent ROC curves for CSF1R in the TARGET dataset (osteosarcoma gene chip array data, n=89). (D) The univariate Cox regression analysis between FHL2, ACP5, FOSL1, CSF1R, TNFRSF11B and OS in the TARGET dataset (RNA-seq data in osteosarcoma, n=98). (E) Survival rate of CSF1R between the high- and low-expression groups in the TARGET dataset (RNA-seq data in osteosarcoma, n=98). (F) AUC time-dependent ROC curves for CSF1R in the TARGET dataset (RNA-seq data in osteosarcoma, n=98). (G) Survival rate of TNFRSF11B between the high- and low-expression groups in TARGET dataset (RNA-seq data in osteosarcoma, n=98). (H) AUC time-dependent ROC curves for TNFRSF11B in the TARGET dataset (RNA-seq data in osteosarcoma, n=98). CSF1R, colony-stimulating factor-1 receptor; FHL2, four and a half LIM domains 2; ACP5, acid phosphatase 5, tartrate resistant; FOSL1, FOS-like 1, AP-1 transcription factor subunit; TNFRSF11B, TNF receptor superfamily member 11b; AUC, area under the curve; ROC, receiver operating characteristic; RNA-seq, Ribonucleic Acid-sequencing; OS, overall survival; HR, hazard ratio; CI, confidence interval.

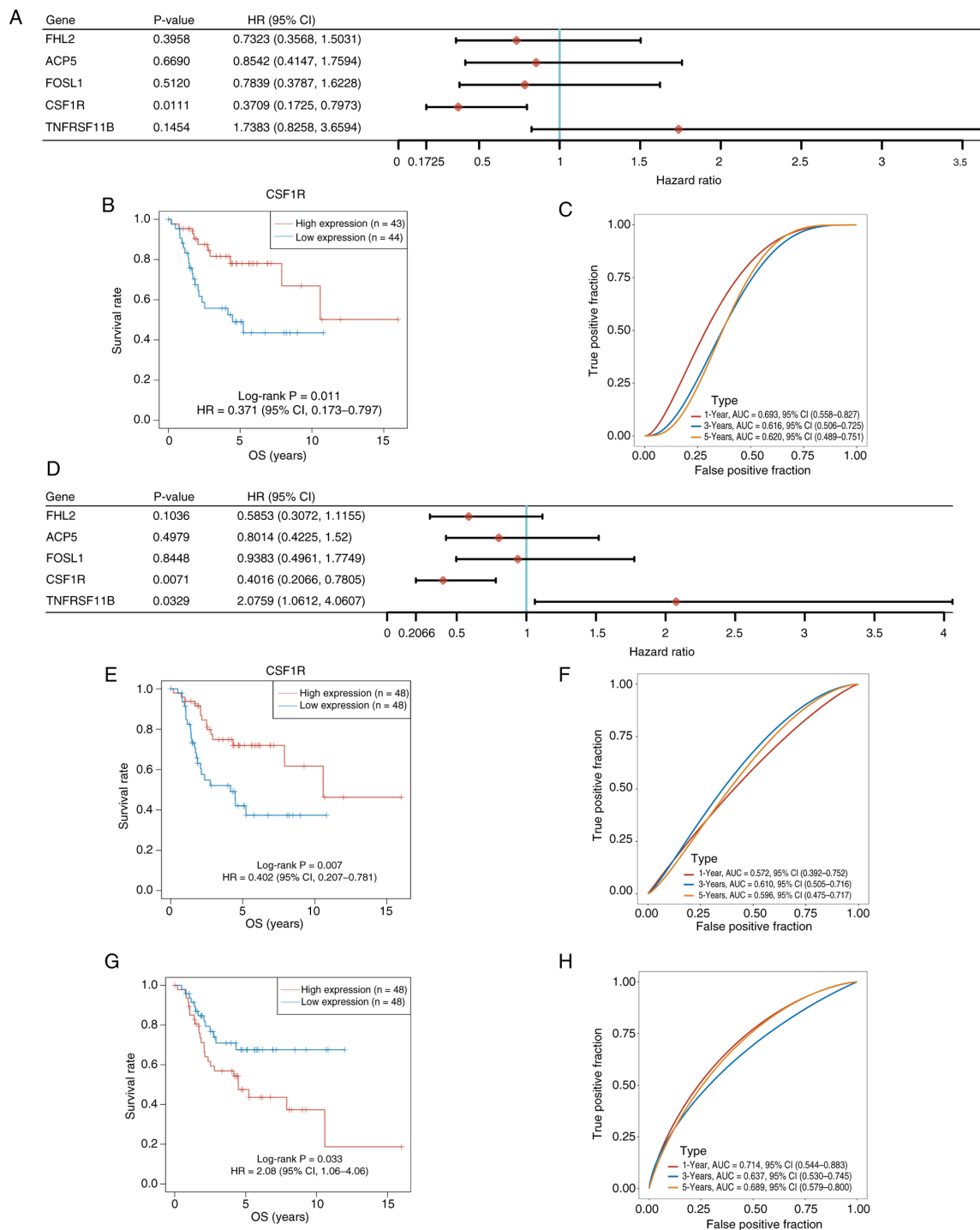


Figure S2. Comprehensive analysis of CSF1R in pan-cancer. (A) The expression of CSF1R across a pan-cancer dataset was explored from TCGA/GTEX database via the GEPIA2 portal (red, downregulated; green, upregulated). (B) The expression distribution of CSF1R across pan-cancer cell lines from the CCLE database. (C) Spearman's correlation analysis of TMB and CSF1R gene expression across a pan-cancer dataset from TCGA database. (D) Spearman's correlation analysis of MSI and CSF1R gene expression across a pan-cancer dataset from TCGA database. CCLE, cancer cell line encyclopedia; CSF1R, colony-stimulating factor-1 receptor; TCGA, The Cancer Genome Atlas; GTEX, Genotype-Tissue Expression; MSI, microsatellite instability; TMB, tumor mutational burden.

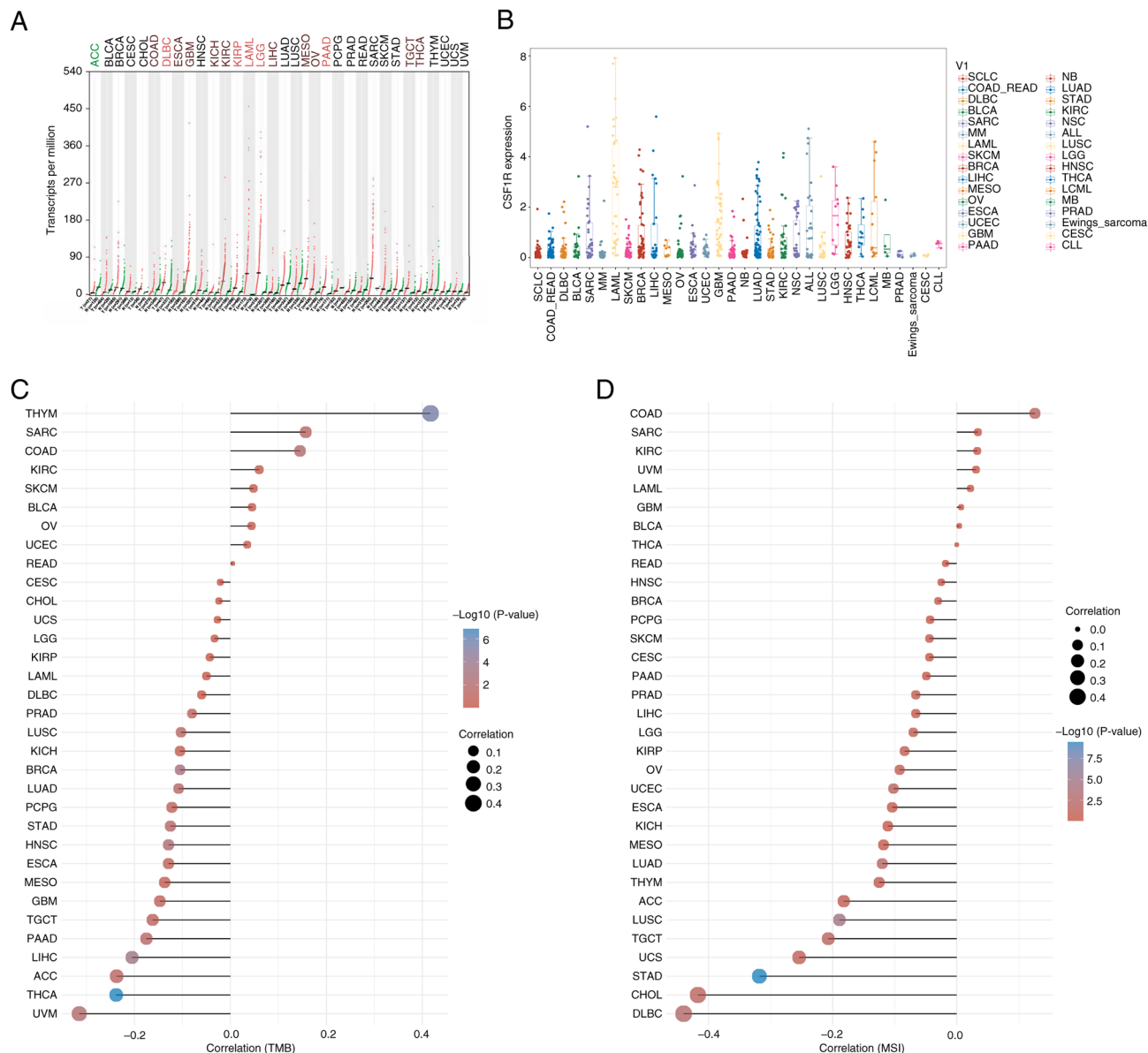


Figure S3. CSF1R's clinical and immunological significance. (A) Forest plot showing CSF1R as a prognostic factor across a pan-cancer dataset. (B) Immune checkpoint sensitivity analysis of CSF1R (blue, positive correlation; red, negative correlation). (C) Pan-cancer correlation analysis between CSF1R and immune cells performed using TCGA database via the CIBERSORT algorithm. CSF1R, colony-stimulating factor-1 receptor; TCGA, The Cancer Genome Atlas; HR, hazard ratio; CI, confidence interval.

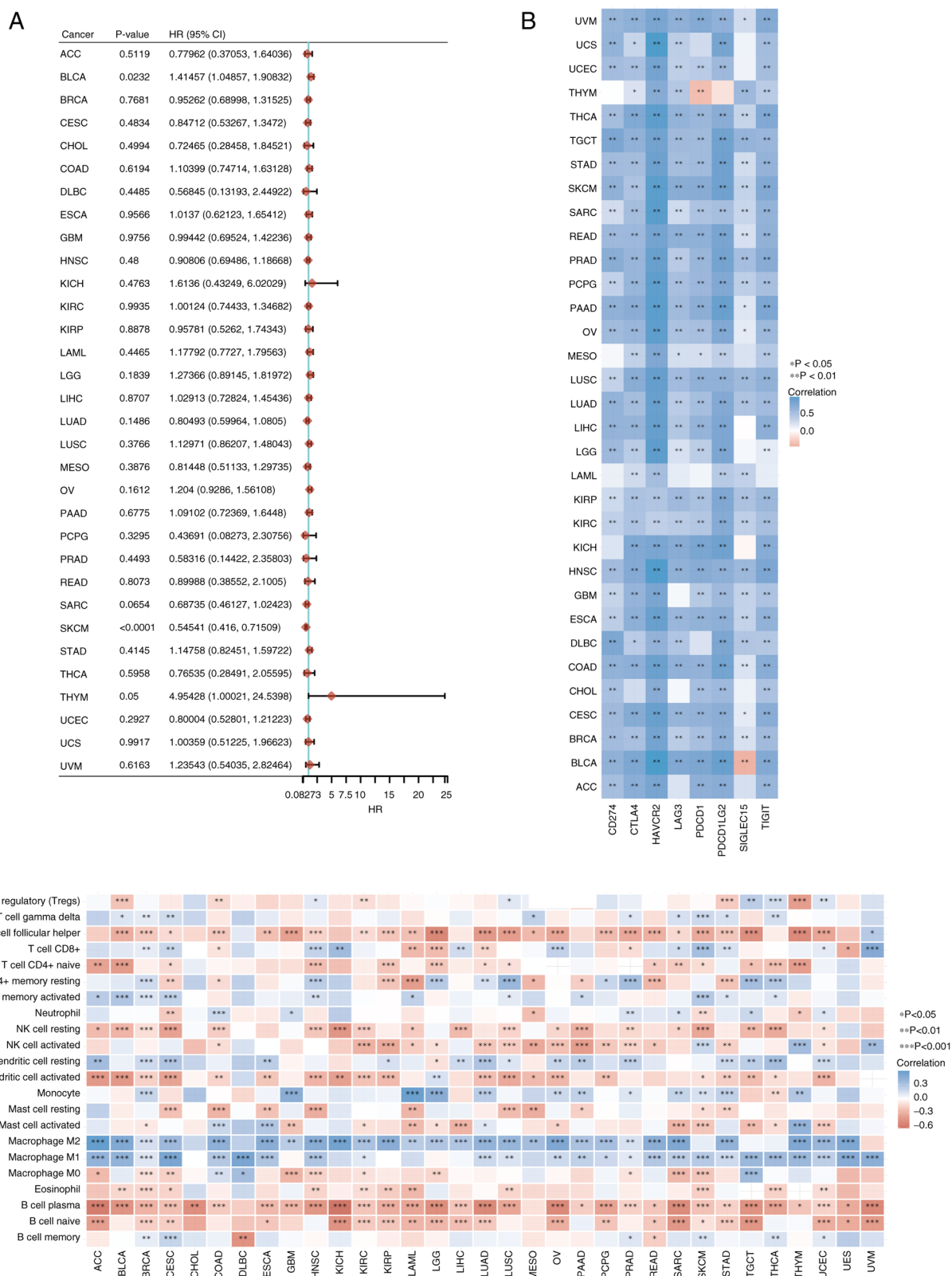


Figure S4. Binding interaction of sotuletinib (green sticks) with a colony-stimulating factor-1 receptor protein structure via molecular docking analysis.

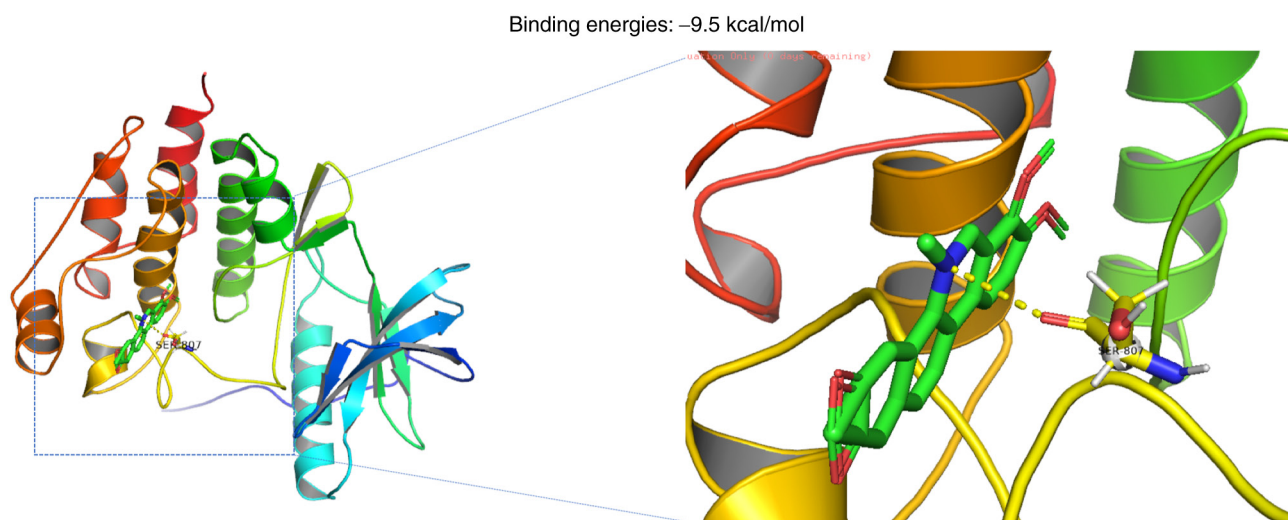


Figure S5. Molecular dynamics simulation studies. (A) RMSD curves of sotuletinib with CSF1R protein. (B) RMSF curves of sotuletinib with the CSF1R protein. (C) Rg analysis of sotuletinib with the CSF1R protein. (D) H-bond number of sotuletinib with the CSF1R protein. (E) Amino acid energy analysis of sotuletinib with the CSF1R protein. (F) Key amino acid energy analysis of sotuletinib with the CSF1R protein. CSF1R, colony-stimulating factor-1 receptor; MM/PBSA, molecular mechanics Poisson-Boltzmann surface area; RMSD, root mean square deviation; Rg, radius of gyration; RMSF, root mean square fluctuation; SASA, solvent-accessible surface area.

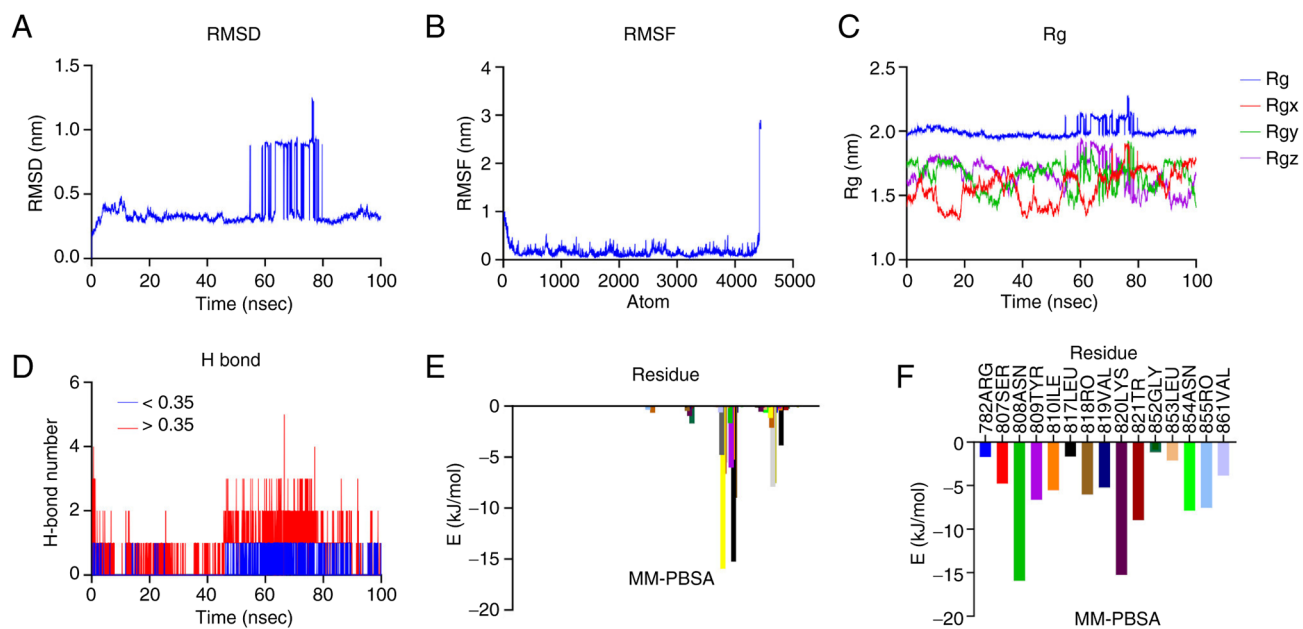


Figure S6. Binding interaction of linarin and saikosaponin c with CSF1R. (A) Binding interaction of linarin (green sticks) with a CSF1R protein structure via molecular docking analysis. (B) Binding interaction of saikosaponin c (green sticks) with a CSF1R protein structure via molecular docking analysis. CSF1R, colony-stimulating factor-1 receptor.

