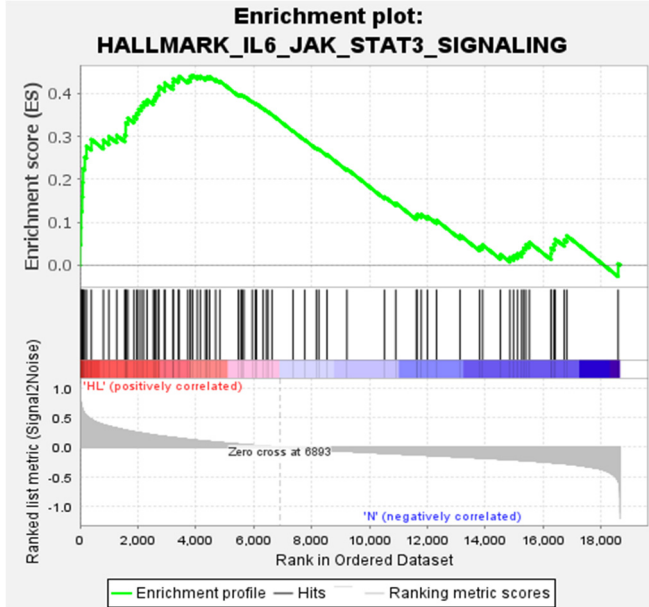
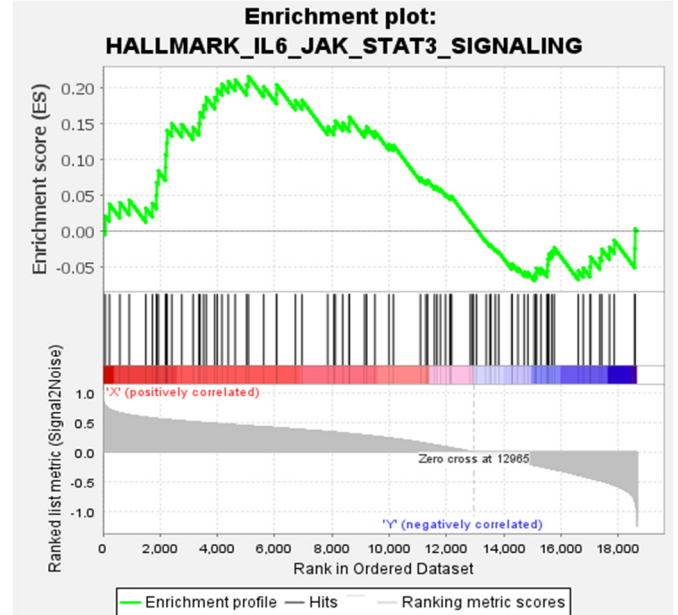


## Supplementary materials

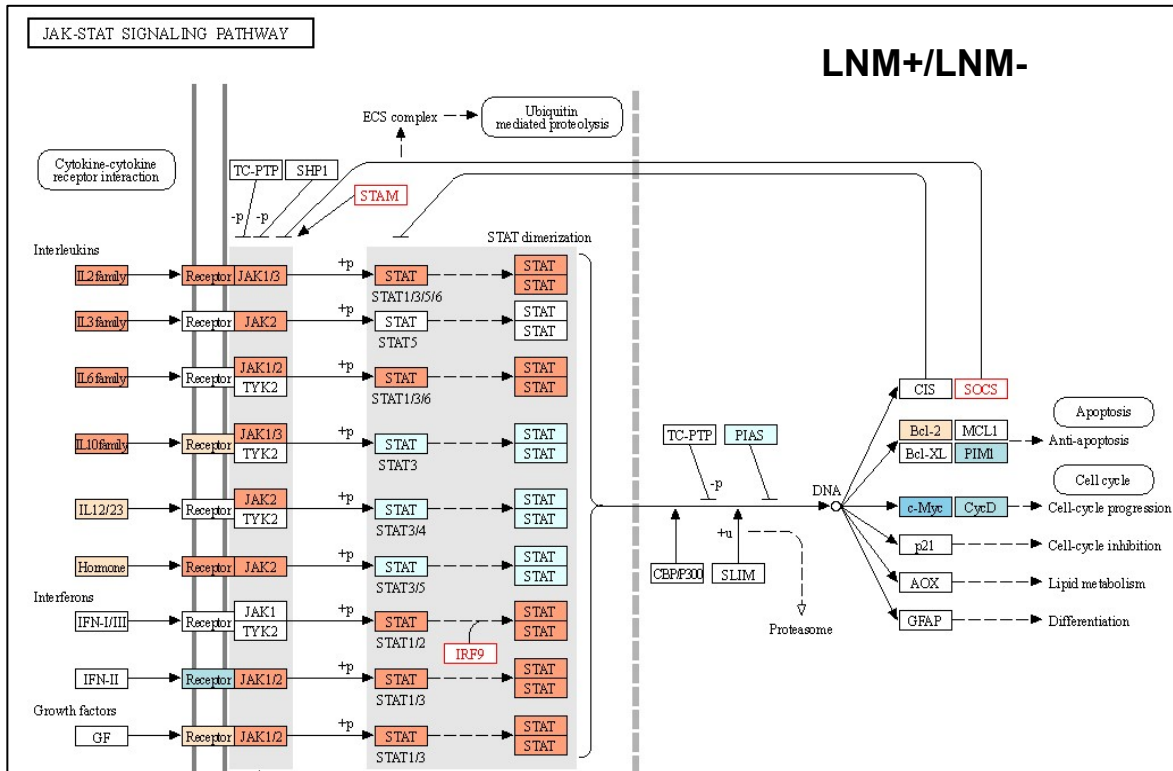
# A



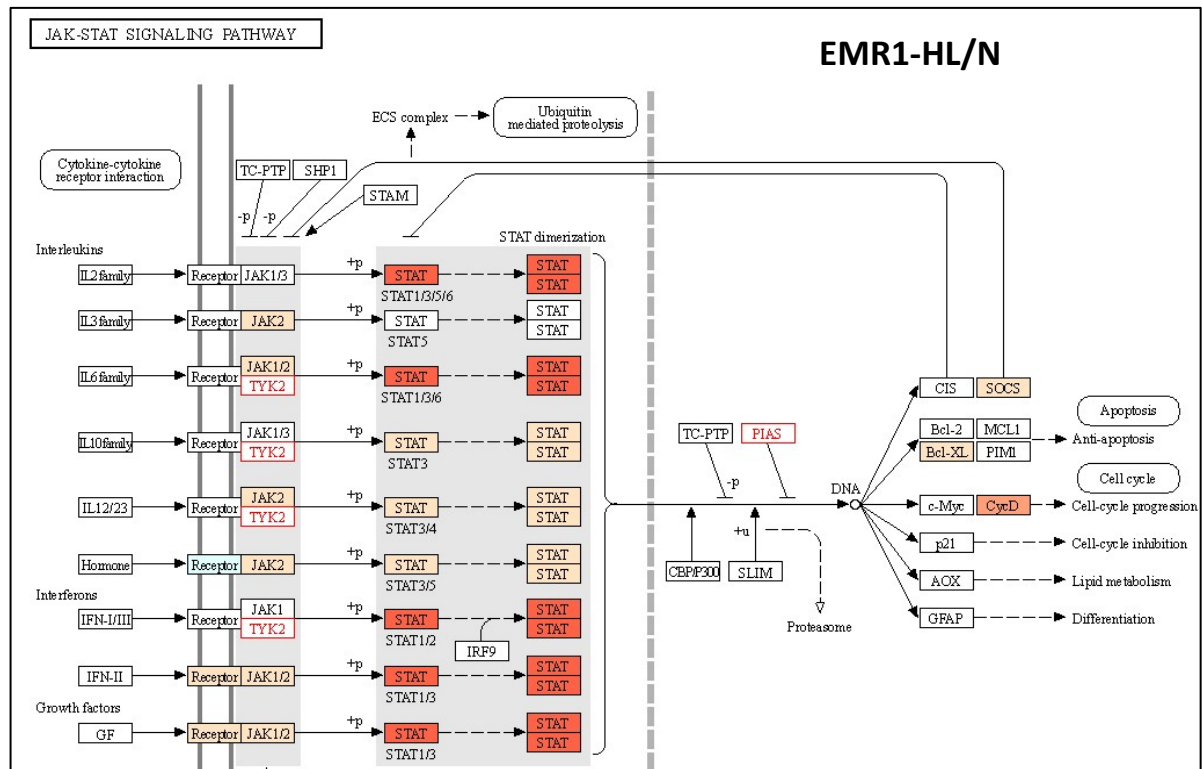
# B



C

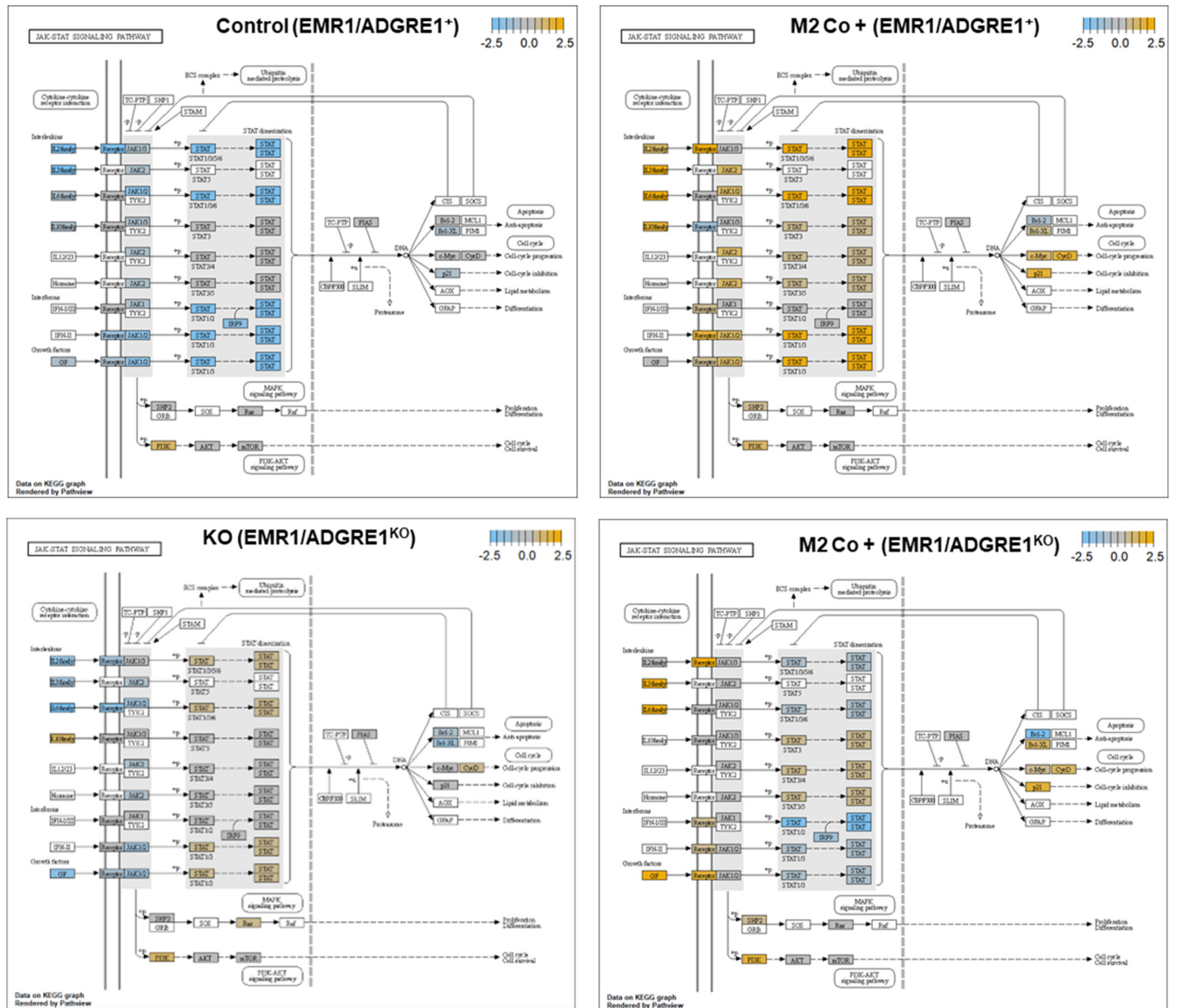


D

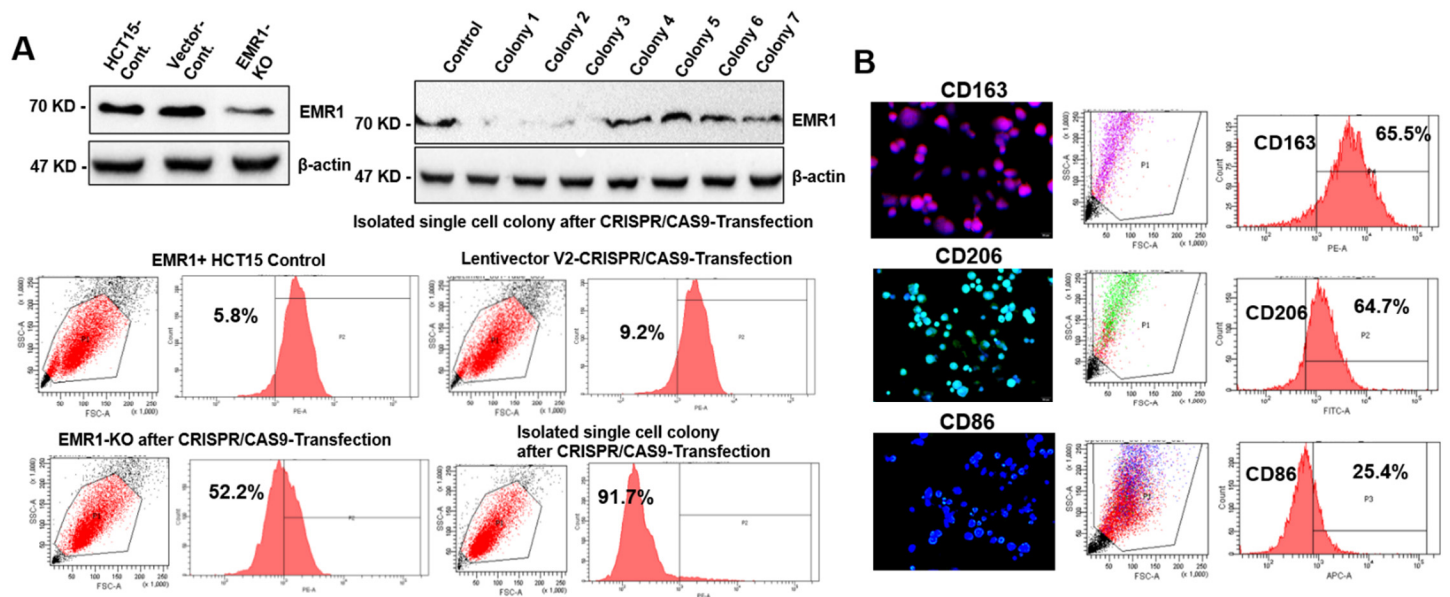


**Supplementary Figure S1. Spatial transcriptomic analysis of CC according to EMR1 expression and LNM. A, B.** GSEA enrichment plots showing JAK-STAT signaling pathway was enriched in the LNM+ vs LNM- group as well as EMR1-HL vs EMR1-N group. **C, D.** Map of the KEGG pathway “JAK-STAT SIGNALING PATHWAY” displaying genes with differentially expressed mRNA fragments in the LNM+ vs LNM- group as well as EMR1-HL vs EMR1-N group. The red color indicates upregulated and the blue color indicates downregulated mRNA. Here, X=LNM+, Y= LNM-. **Abbreviations:** LNM, lymph node metastasis; L=Low, H= High, N=Negative

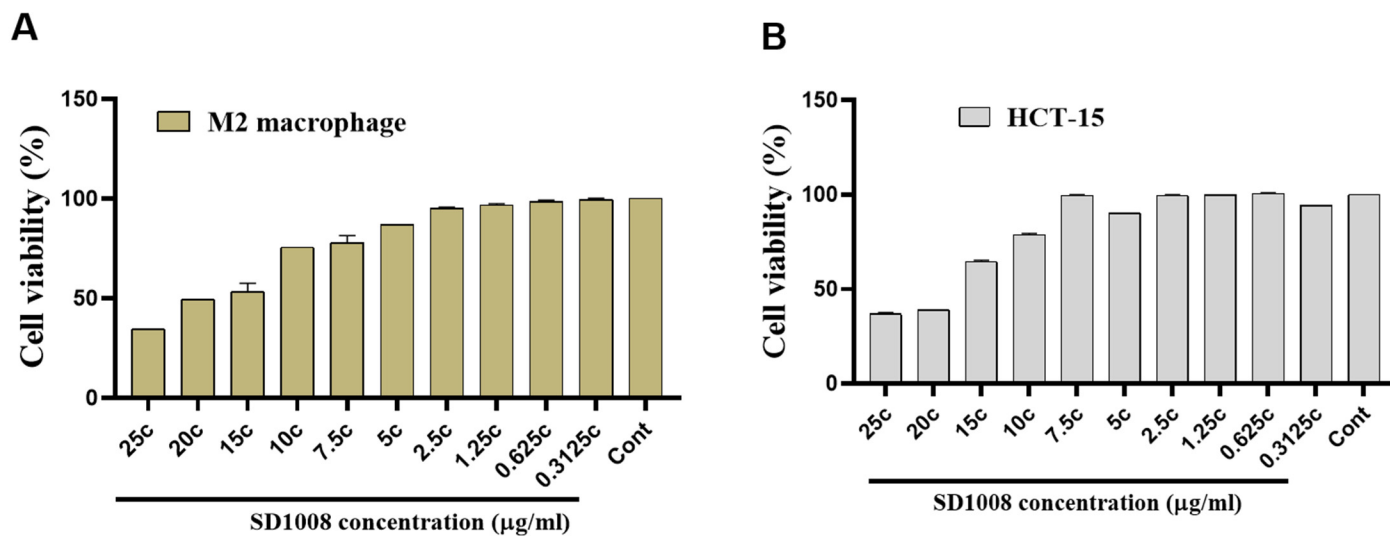
**A**



**Supplementary Figure S2. Molecular changes between EMR1<sup>+</sup> and EMR1<sup>KO</sup> CC cells after coculture with macrophages in vitro. A.** Map of the KEGG pathway “JAK-STAT SIGNALING PATHWAY” displaying genes with differentially expressed mRNA fragments. The yellow color indicates upregulated genes and the sky-blue color indicates downregulated genes.



**Supplementary Figure S3. EMR1 knockout and macrophage polarization validation results.** **A.** Validation of CRISPR/Cas9-mediated EMR1 knockout by western blot and flow cytometry analysis. **B.** Validation of THP1-derived macrophage polarization by immunofluorescence and flow cytometry analysis. Abbreviations: CRISPR/Cas9.



**Supplementary Figure S4.** Toxicity of JAK2/STAT3 inhibitor (SD1008) in macrophage and CC cells (HCT15). (A-B) The cells were treated with different concentrations of the SD1008 inhibitor for 48 h and toxicity was detected using a WST-1 reagent. Graphs represent data as means  $\pm$  SD.