

Supplementary Figures and Legends

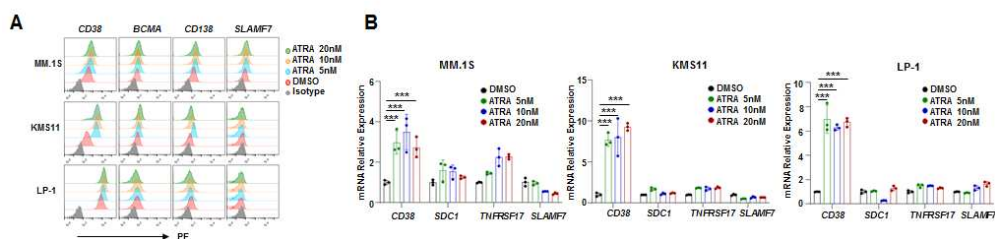


Fig. S1 ATRA induced CD38 upregulation on MM cells.

(A) Flow cytometry histograms representing cell surface expression of CD38, BCMA, CD138 and SLAMF7 on MM.1S, KMS11 and LP-1 MM cells before and after 5nM, 10nM and 20nM ATRA treatment for 24h. (B) qPCR shows *CD38*, *SDC1*, *TNFRSF17* and *SLAMF7* expression in MM.1S, KMS11 and LP-1 MM cells treated with increasing concentrations of ATRA for 24 h. All data represent results from at least three independent experiments, Two-sided *P*-values were determined by Student's *t* test; mean \pm s.d.

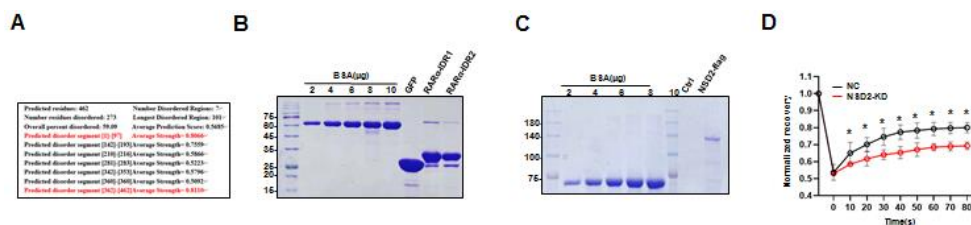


Fig. S2 NSD2 enhances RAR α liquid-liquid phase separation in MM cells

(A) Prediction of intrinsically disordered regions (IDRs) sites (red font) of RAR α protein using PONDR algorithms. (B) The purified GFP-fusion RAR α -IDR proteins detected by Coomassie brilliant blue staining. (C) The purified NSD2 protein detected by Coomassie brilliant blue staining. (D) Kinetic recovery times of bleached GFP-fusion RAR α droplet foci in HEK293T co-transfected with sgRNA (NSD2 KD) by 488 nm laser ($n=3$ biologically independent experiments).

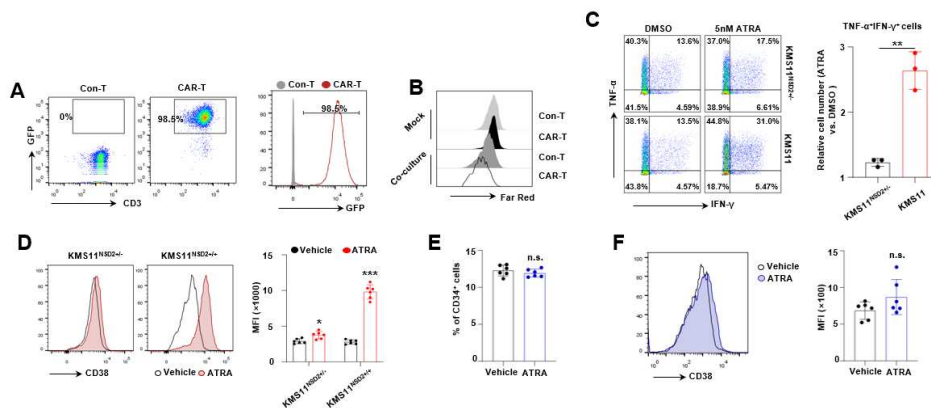


Fig. S3 ATRA improves response to CD38 CAR-T in NSD2^{high} MM cells

(A) Purified CD38 CAR-T cells by Fluorescence Activating Cell Sorting (FACS), and flow cytometry detected CAR-T purity. (B) Con-T and CAR-T cells stained with Far Red and co-cultured in the presence or absence of MM cells after 24h. (C) Flow cytometry histograms representing cell expression of IFN- γ and TNF- α in CAR-T cells which co-culture with KMS11^{NSD2+/+} or KMS11^{NSD2-/-} after ATRA treatment. (D) Flow cytometry histograms representing cell surface expression of CD38 on MM cells after ATRA injection. (E) Frequency of CD34⁺ cells in BM cells. (F) Flow cytometry histograms representing cell surface expression of CD38 on CD34⁺ cells after CAR-T and ATRA treatment. *P* values were determined by Pearson Coefficient and Log-ranks test. **P* < 0.05, ***P* < 0.01, ****P* < 0.001. Two-sided *P* values were determined by Student's *t* test. Data indicate the mean \pm SD.