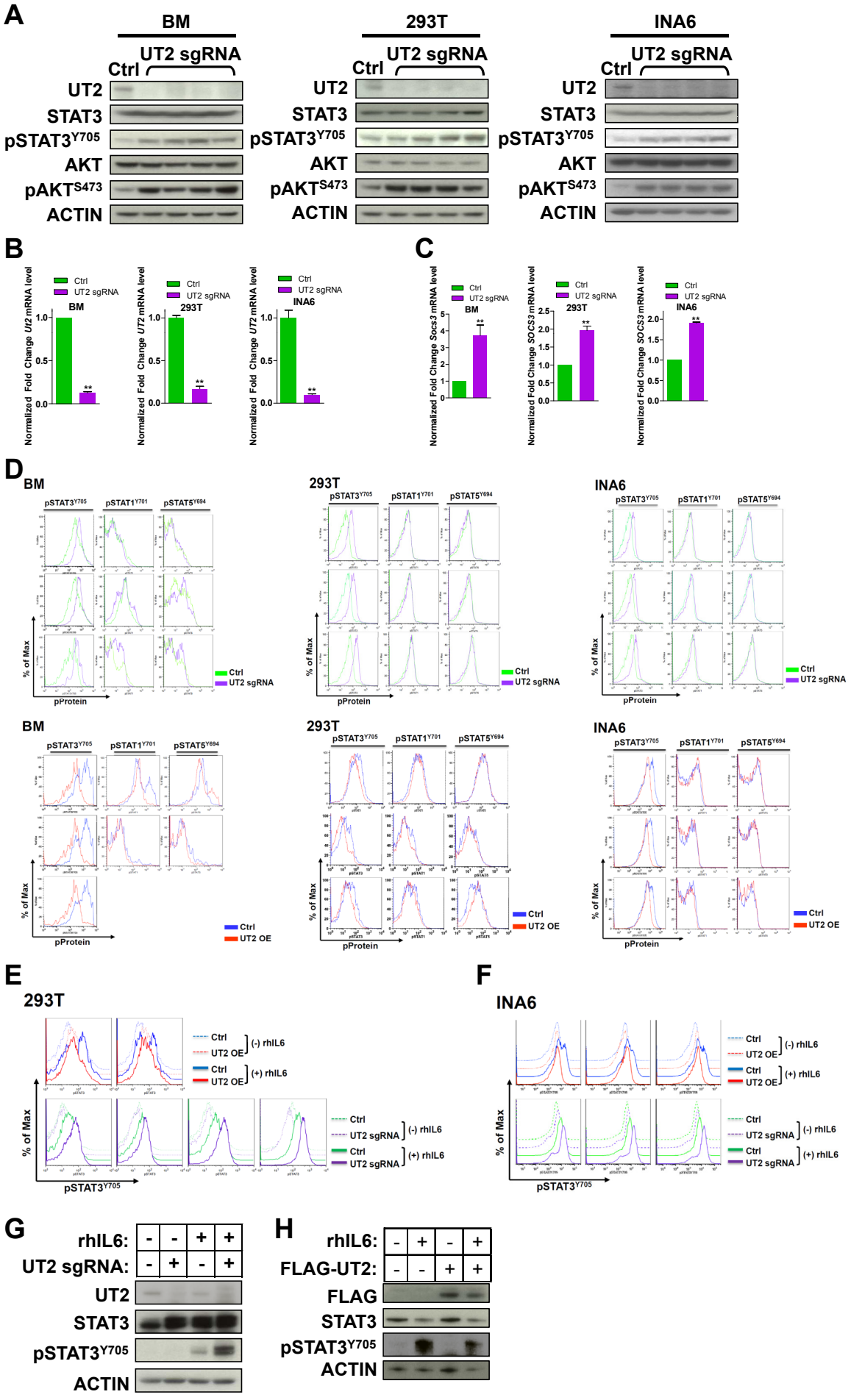


Supplemental Figure 1

Supplemental Figure 1. Investigation of the function of UT2 using the CRISPR/Cas9 system.

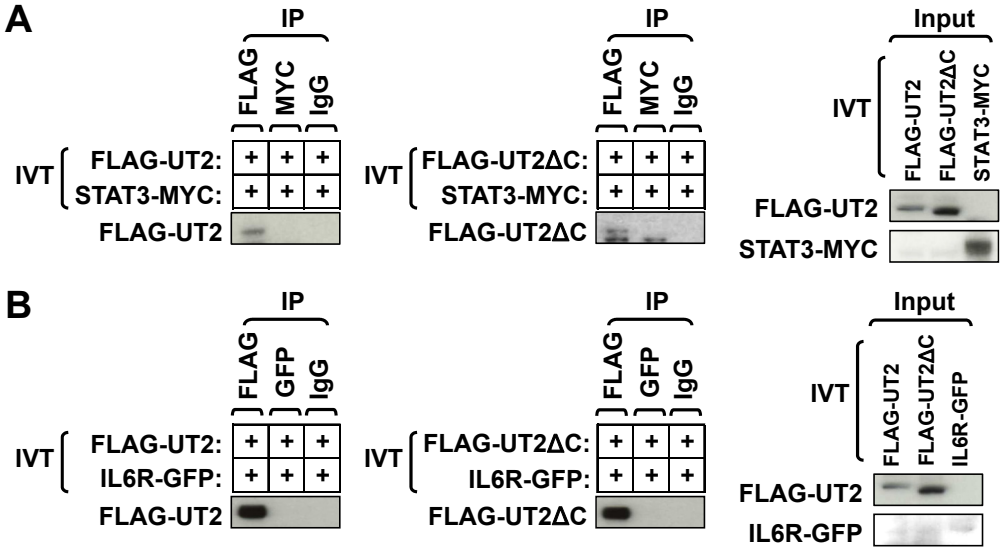
(A) sgRNA-depleted for UT2 primary hematopoietic BM, HEK293T and INA6 cells show a decrease in UT2 protein levels.

(B and C) qRT-PCR analysis analyses of *UT2* expression **(B)** and *SOCS3* expression **(C)** from sgRNA-depleted for UT2 primary hematopoietic BM, HEK293T and INA6 cells (n = 3 experiments; two-tailed, unpaired t-test). **p < 0.01.

(D) Flow cytometry was performed on sgRNA-depleted for UT2 (top panel) or overexpressing UT2 (bottom panel) primary hematopoietic BM (left panel), HEK293T (middle panel) and INA6 (right panel) cells and these were then processed for flow cytometry (n = 2-3 experiments).

(E and F) Flow cytometry was performed on sgRNA-depleted for UT2 (top panel) or overexpressing UT2 (bottom panel) HEK293T **(E)** and INA6 **(F)** cells were starved for 24 hr, and then restimulated with IL6 (20 ng/ml) for 30 min prior to fix and these were then processed for flow cytometry (n = 2-4 experiments).

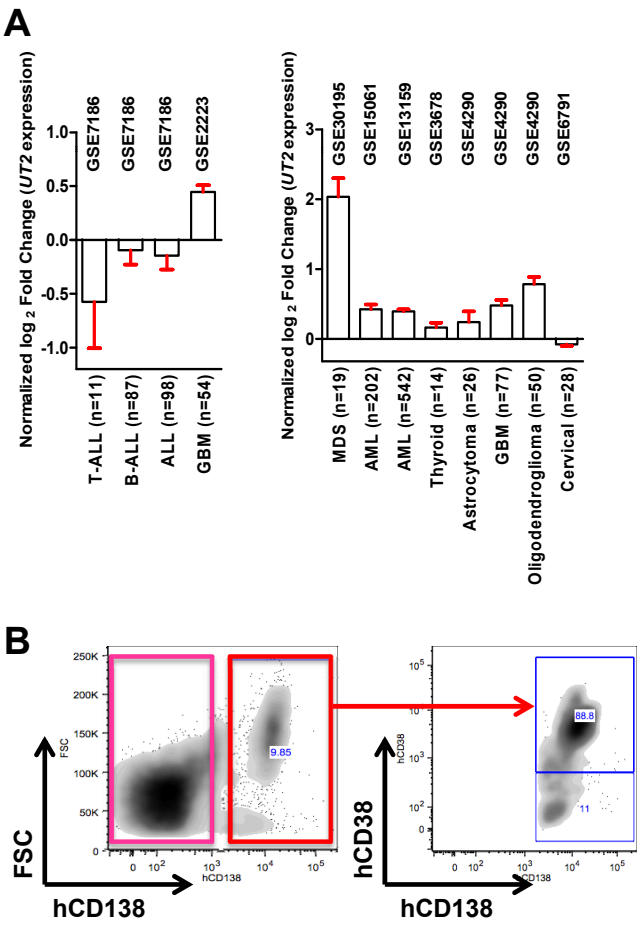
(G and H) sgRNA-depleted for UT2 **(G)** or overexpressing UT2 **(H)** HEK293T cells were starved for 24 hr, and then restimulated with IL6 (20 ng/ml) for 30 min prior to lysis, and analyzed by western blotting.



Supplemental Figure 2

Supplemental Figure 2. UT2 does not directly bind STAT3 or IL6R.

In vitro translated either FLAG-UT2 full length or FLAG-UT2ΔC mutant proteins were subjected to IP using the indicated antibodies in the presence of *In vitro* translated STAT3 proteins **(A)** and IL6R proteins **(B)**.

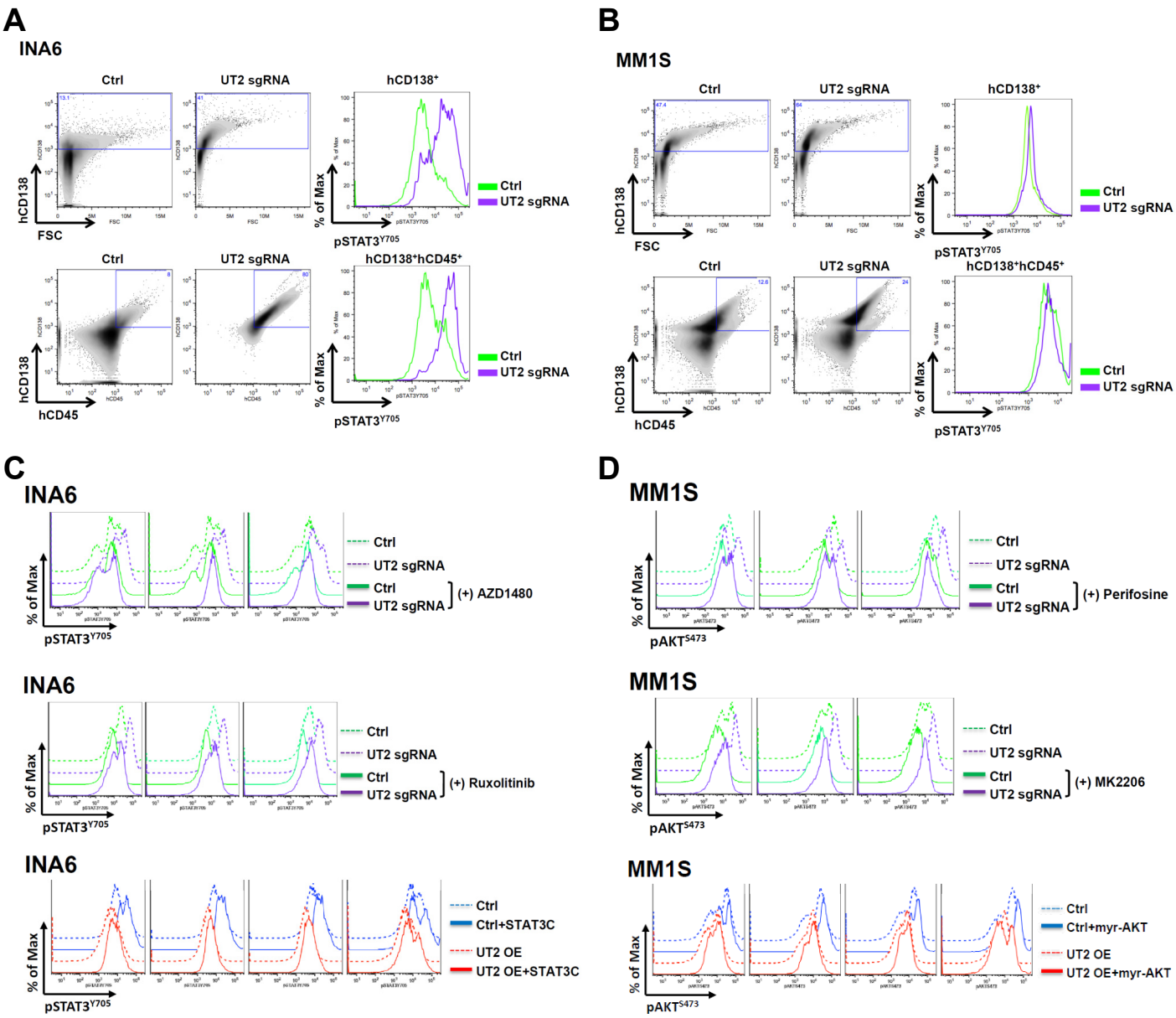


Supplemental Figure 3

Supplemental Figure 3. *UT2* expression in human hematological malignancies.

(A) UT2 expression from human patients (ALL in GSE7186 data (n=98), ref. (50), GBM in GSE2223 (n=54) and GSE4290 data (n=153), ref. (47, 49), MDS in GSE30195 data (n=19), ref. (54), AML in GSE15061 (n=202) and GSE13159 data (n=542), ref. (52, 53), Thyroid in GSE3678 data (n=14), ref. (48), Astrocyte in GSE4290 data (n=153), ref. (49), Oligodendroglioma in GSE4290 data (n=153), ref. (49)), Cervical in GSE6791 data (n=28), ref. (51)).

(B) Flow cytometry was performed from MM patients BM cells.



Supplemental Figure 4

Supplemental Figure 4. Role of UT2 in myeloma cells

(A) Flow cytometry analysis of $hCD138^+$ and $hCD138^+hCD45^+$ BM cells and phosphorylated STAT3 expression from recipient mice in **Figure 4A**. Animals were examined when moribund.

(B) Flow cytometry analysis of $hCD138^+$ and $hCD138^+hCD45^+$ BM cells and phosphorylated STAT3 expression from recipient mice in **Figure 4D**. Animals were examined when moribund.

(C) Flow cytometry was performed on sgRNA-depleted for UT2 INA6 cells with treatment of AZD1480 (top panel) or Ruxolitinib (middle panel), or overexpressing UT2 INA6 cells with STAT3C expression (bottom panel). sgRNA-depleted for UT2 INA6 cells were cultured with AZD1480 (10 μM, 6hr) or Ruxolitinib (10 μM, 2hr), respectively.

(D) Flow cytometry was performed on sgRNA-depleted for UT2 MM1S cells with treatment of Perifosine (top panel) or MK2206 (middle panel), or overexpressing UT2 MM1S cells with myristoylated AKT (myr-AKT) overexpression (bottom panel). sgRNA-depleted for UT2 MM1S cells were cultured with Perifosine (10 μM, 6hr) or MK2206 (10 μM, 2hr), respectively.