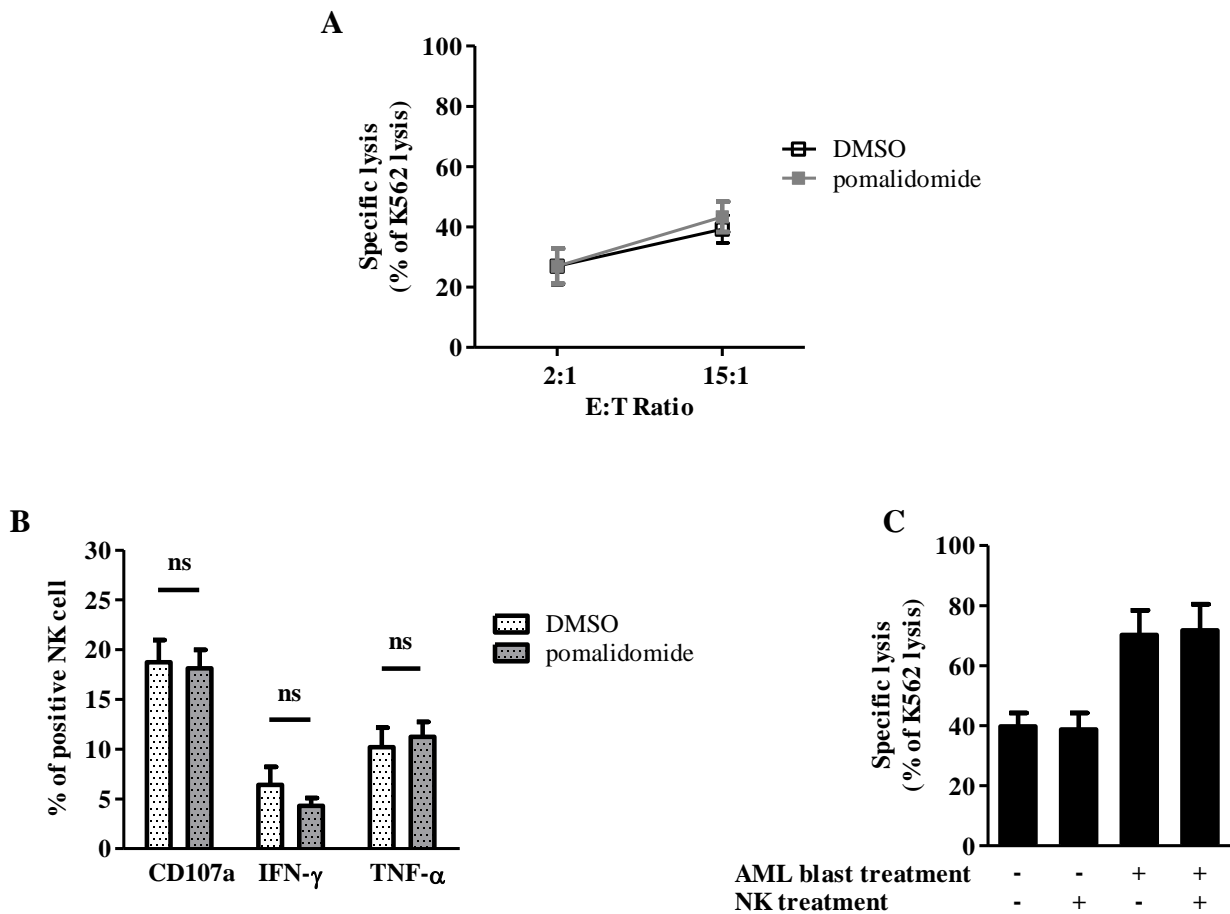
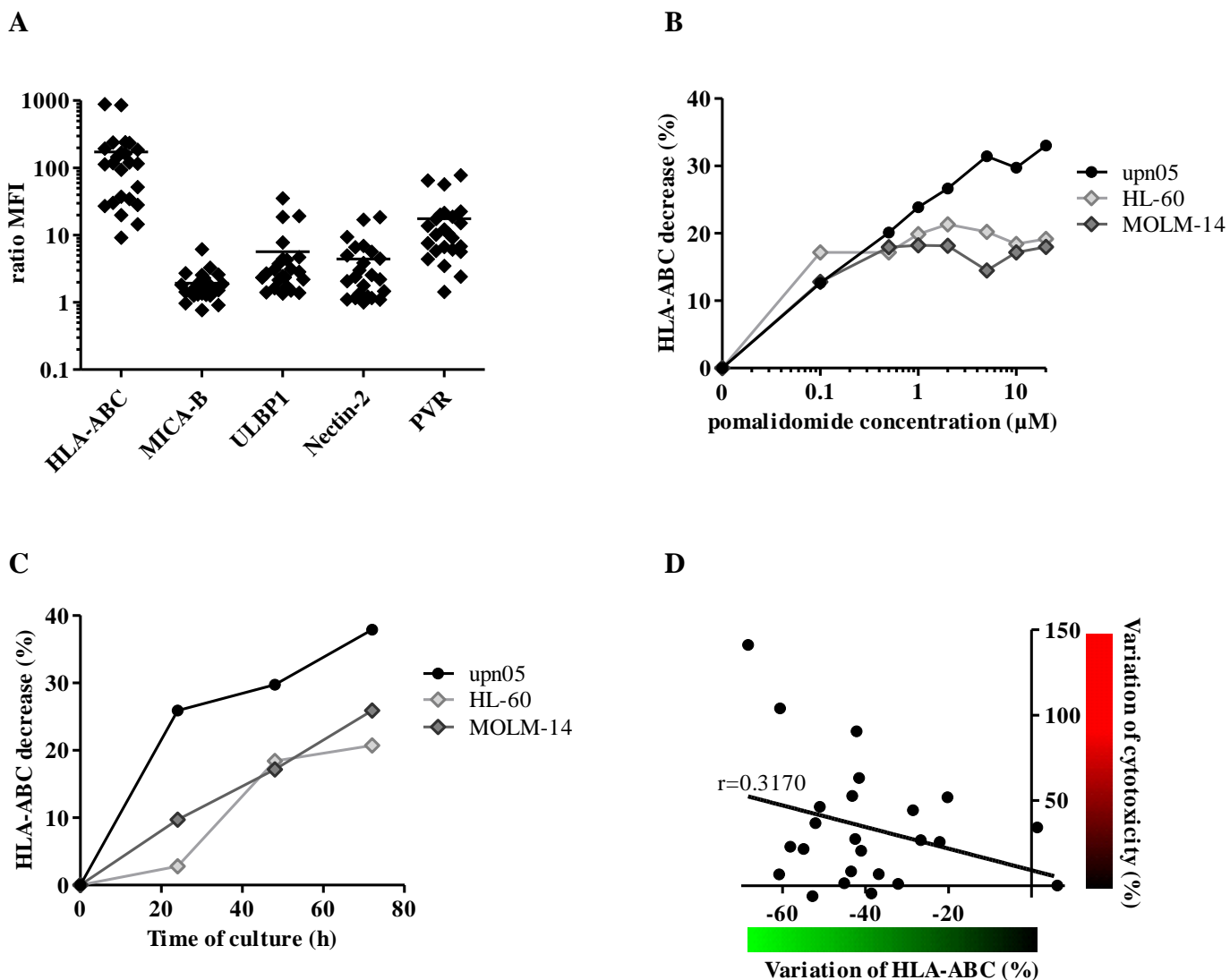


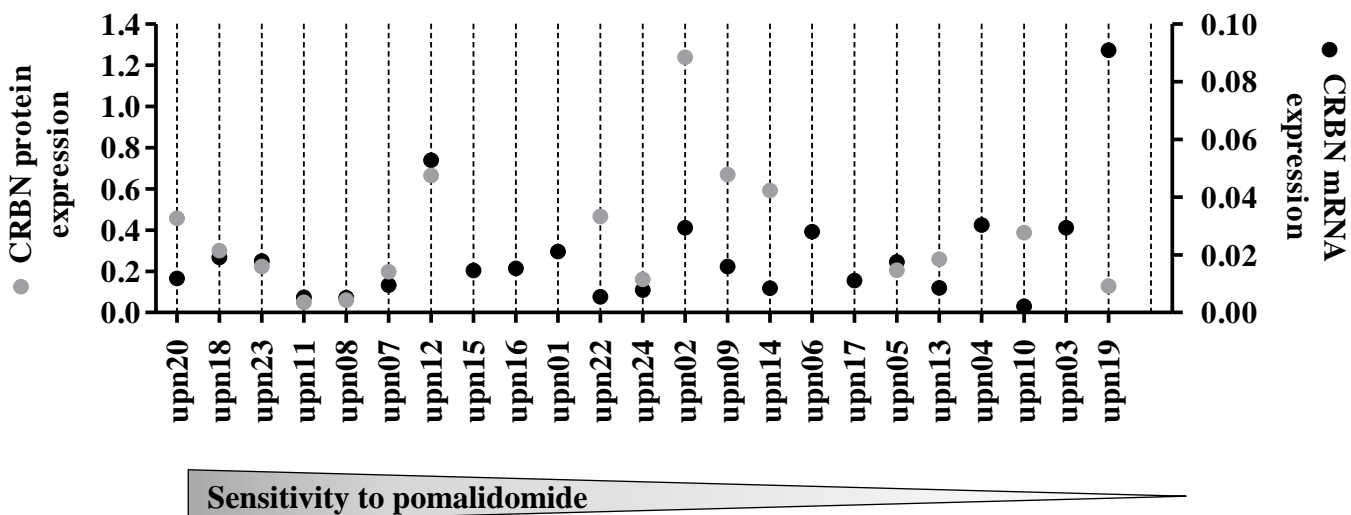
**Supplementary Figure 1.** Pomalidomide sensitizes AML blasts to NK cell lysis. (A and B) NK-mediated lysis of K562 cells and AML blasts ( $n=24$ ) after treatment with (A) pomalidomide or DMSO control, or (B) pomalidomide, lenalidomide or DMSO. Data are shown for E:T 2:1 and 15:1. (C) Sensitivity of blasts from 24 AML patients to lysis by allogeneic NK cell ( $n=2-12$ ) (E:T 15:1). Results are expressed as mean $\pm$ sem and statistical significance was established using paired Student  $t$  test (A).



**Supplementary Figure 2.** Effect of IMiDs on NK cell phenotype and functions. (A-C) Purified NK from HV were pre-incubated for 48 hours with pomalidomide (10  $\mu$ M) or DMSO. (A) Standard [ $^{51}$ Cr]-release assay was used to evaluate specific lysis of allogeneic NK cells ( $n=4$ ) against primary AML blasts (upn20). (B) Percentage of NK cells ( $n=2-3$ ) degranulation (CD107a), and IFN- $\gamma$  and TNF- $\alpha$  production, in response to AML cells ( $n=12$ ) was monitored using cytometry. (C) Primary AML blasts from one patient and allogeneic NK from 3 HV were pre-incubated separately for 48 hours with pomalidomide (+) (10  $\mu$ M) or DMSO (-) as control treatment. They were extensively washed before the co-culture. Standard [ $^{51}$ Cr]-release assay was used to evaluate specific lysis. Results were expressed as mean $\pm$ sem and statistical significance was established using Wilcoxon matched-pairs test.



**Supplementary Figure 3.** Pomalidomide-induced down-regulation of MHC class I and change of the expression of NK cell ligands on AML blasts. (A) Expression levels of NK cell ligands for activating receptors (MICA, ULBP1, Nectin-2 (CD112) and PVR (CD155)) and inhibitory receptors (HLA-ABC), expressed as the ratio of the mean fluorescence intensity (MFI) for each marker divided by the MFI for the isotype control, were determined on primary AML blasts ( $n=24$ ) by flow cytometry. (B and C) HLA-ABC downregulation (%) induced by pomalidomide on AML cell lines (HL-60 and MOLM-14) and primary AML blasts from one patient (upn05), was presented as described in Fig. 4 and evaluated in a (B) dose and (C) time-manner using flow cytometry. (D) The relative variation of cytotoxicity is correlated with the relative variation of HLA-ABC for each patient ( $n=24$ ).



**Supplementary Figure 4.** CRBN protein and mRNA expression (normalized to GAPDH) from primary AML blasts ( $n=23$ ). CRBN protein expression was evaluated by western-blot. CRBN mRNA expression was evaluated by qRT-PCR and presented as a ratio  $R = 2^{-\Delta Ct}$ . AML blasts are classified according to a gradient of sensitivity to pomalidomide as described in Fig.2C (increased AML lysis by NK cell induced by pomalidomide treatment).