Supplementary Materials: Key role of the CD56^{low}CD16^{low} Natural Killer cell subset in the recognition and killing of Multiple Myeloma cells

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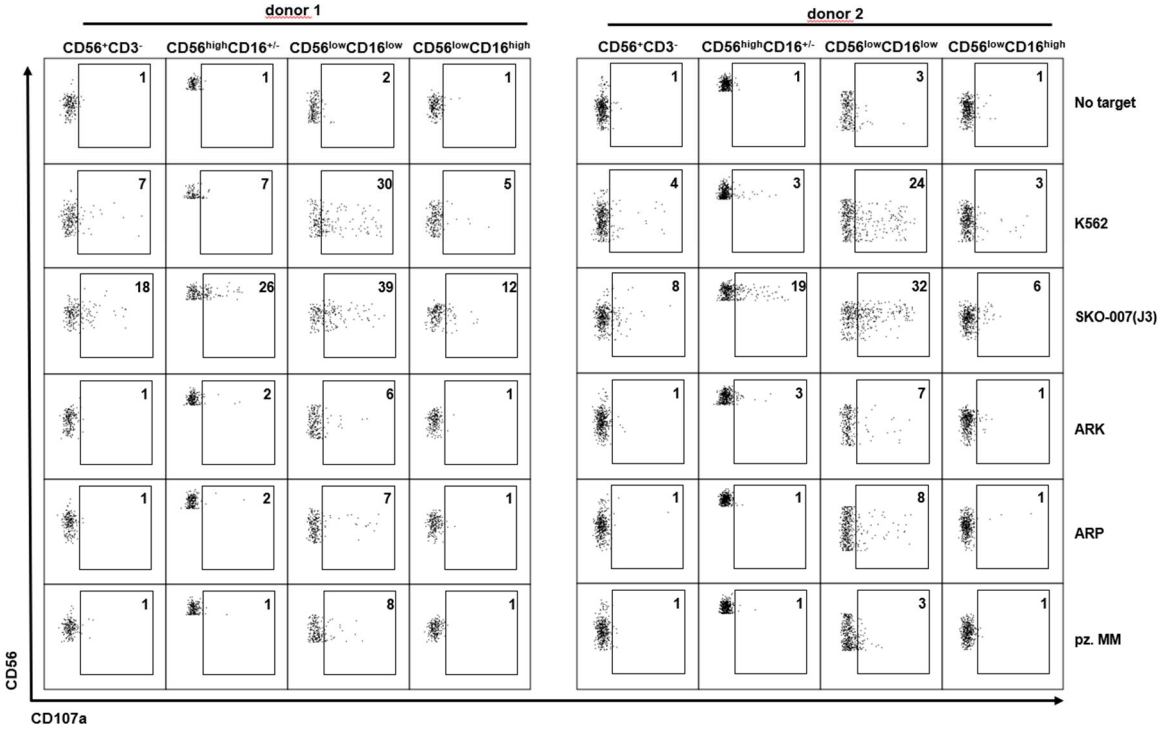

Figure S1. PB derived cells from two representative healthy donors were incubated for two hours without target or with distinct target cells including K562 and various MM cell lines (SKO-007(J3), ARK, ARP) and primary plasma cells (pz MM) as indicated. Cells were harvested and stained with anti-CD3, anti-CD56, anti-CD16 and anti-CD107 antibodies. NK cell subsets were analyzed considering the expression levels of CD56 and CD16. The percentage of CD107^{+} cells is shown in each plot.

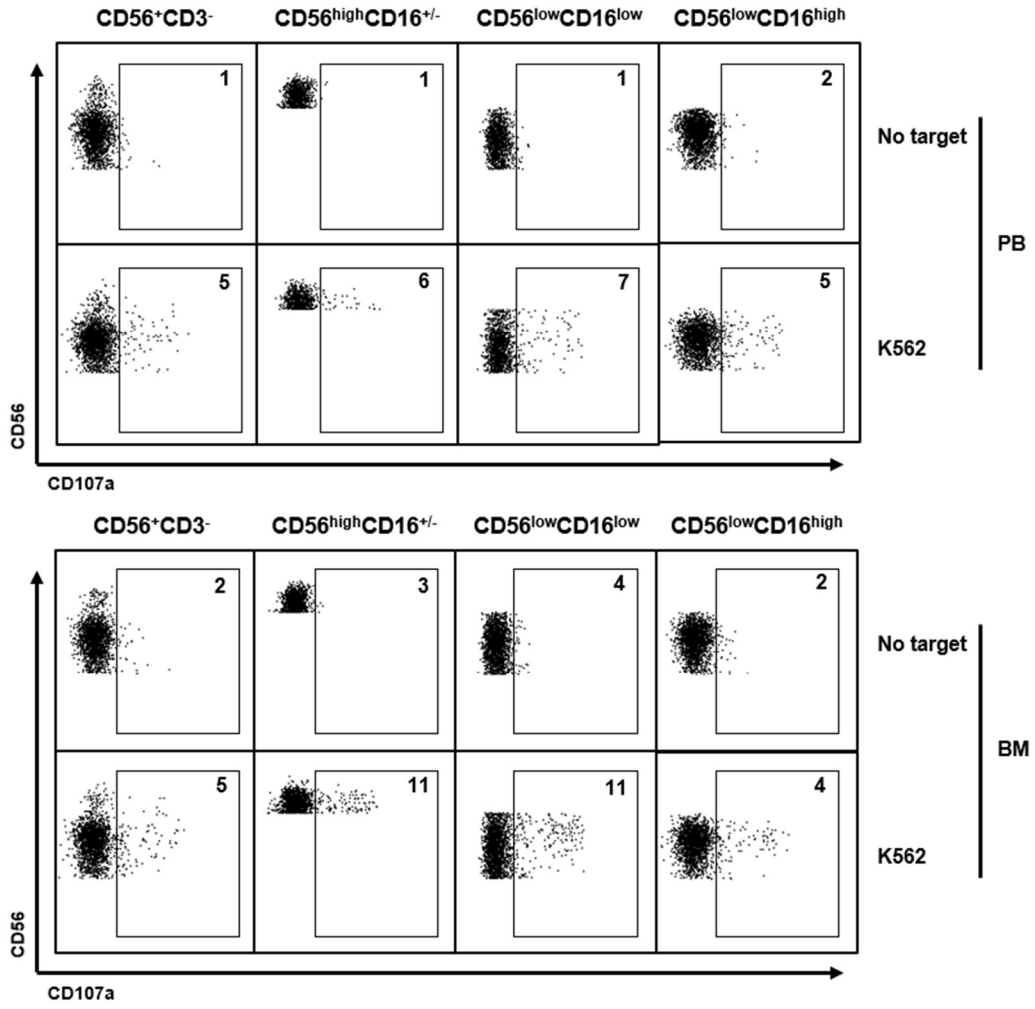

Figure S2. PB and BM derived cells from the same representative patient were incubated for two hours with or without the target cell line, K562. Cells were harvested and stained with anti-CD3, anti-CD56, anti-CD16 and anti-CD107 antibodies. Total NK cells and NK cell subsets were analyzed considering the expression levels of CD56 and CD16. The percentage of $CD107^+$ cells is shown in each plot.

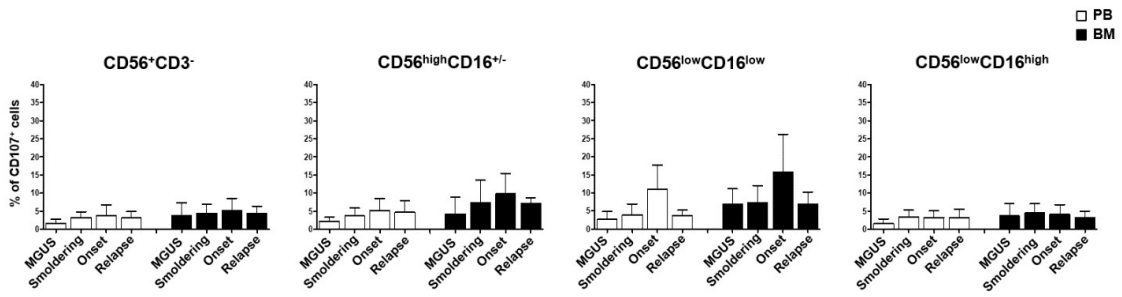

Figure S3. PB and BM derived cells were incubated for two hours with or without the target cell line, K562. Cells were harvested and stained with anti-CD3, anti-CD56, anti-CD16 and anti-CD107 antibodies. NK cell subsets were analyzed considering the expression levels of CD56 and CD16. The percentage of $CD107^+$ cells is shown and represents the net value of CD107 degranulation obtained as follow: (% of $CD107^+$ cells with target)-(% of $CD107^+$ cells without target). No significant differences were found between PB and BM NK cell degranulation in all the subsets analyzed. Patients are the same showed in figure 3 (MGUS, $n = 6$; Smoldering, $n = 4$; Onset, $n = 5$; Relapse, $n = 4$).

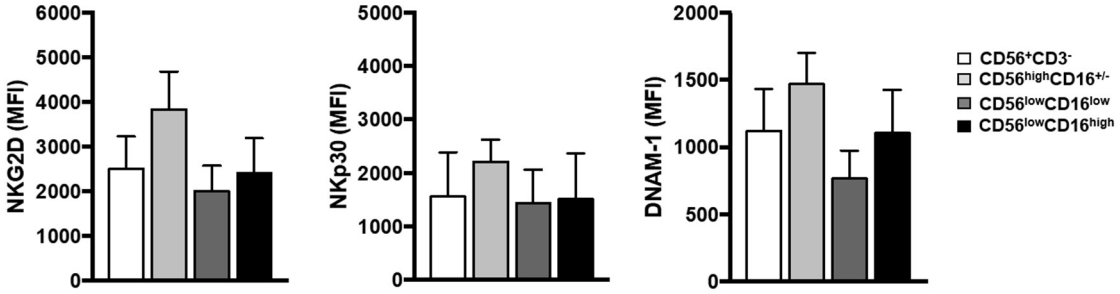

Figure S4. Expression levels of NK cell receptors on NK cell subsets derived from healthy PB donors. FACS analysis of surface expression of NKG2D, NKp30 and DNAM-1 on total NK cells and NK cell subsets in PB derived cells from 8 healthy donors. Values are expressed as mean of the MFI value and error bars represent SD.

Table S1. Therapeutic history of relapsed patients.

Patient	Chemotherapy First line	Second line	Third line	Number of relapse
R1	Lenalidomide Dexamethasone	Melphalan Prednisone Lenalidomide		2
R2	Bortezomib Prednisone			1
R3	Lenalidomide Cyclophosphamide Prednisone			1
R4	Bortezomib Melphalan Prednisone	Lenalidomide Dexamethasone		2
R5	Adriablastin Dexamethasone Vincristine			1
R6	Adriablastin Dexamethasone Vincristine			1
R8	Adriablasin Dexamethasone Vincristine	Melphalan Prednisone Talidomide Lenalidomide		2
R9	Bortezomib Melphalan Prednisone			1
R10	Adriablastin Dexamethasone Vincristine	Bortezomib	Lenalidomide	3
R11	Melphalan Prednisone Talidomide			1
R12	Velcade Doxorubicin Dexamethasone	Bortezomib Melphalan Prednisone	Velcade	3
R13	Adriablastin Dexamethasone Vincristine	Bortezomib		2
R14	Melphalan Prednisone			1

	Talidomide			
R16	Velcade Cyclosphosphamide	Velcade Doxorubicin Dexamethasone		2
R17	Adriablastin Dexamethasone Vincristine	Talidomide Dexamethasone	Velcade Dexametha sone	3
R18	Lenalidomide			1