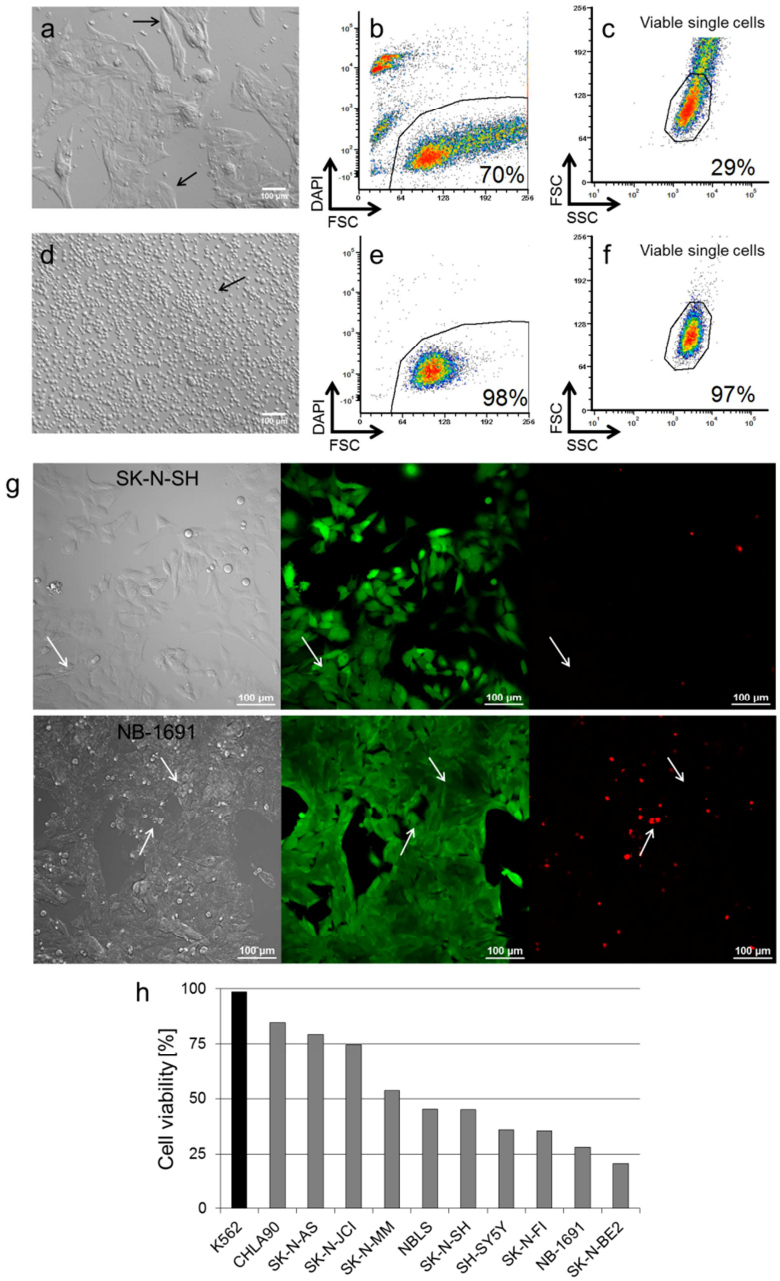
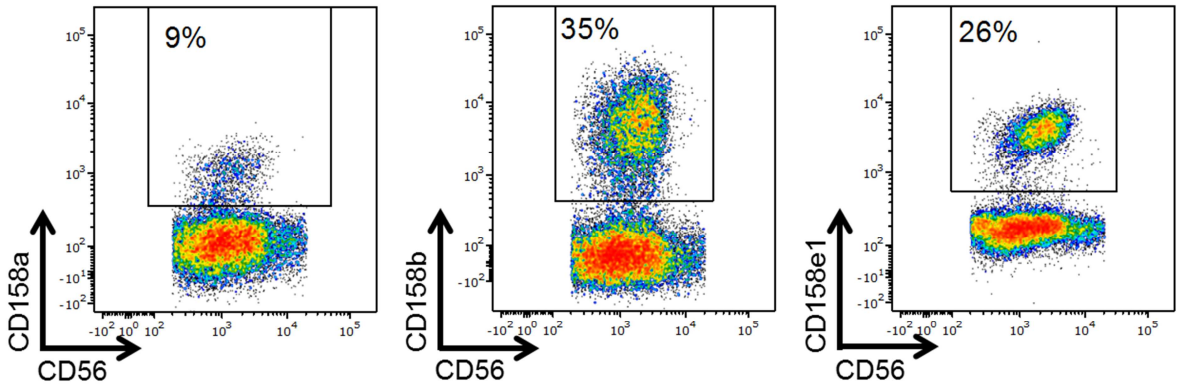
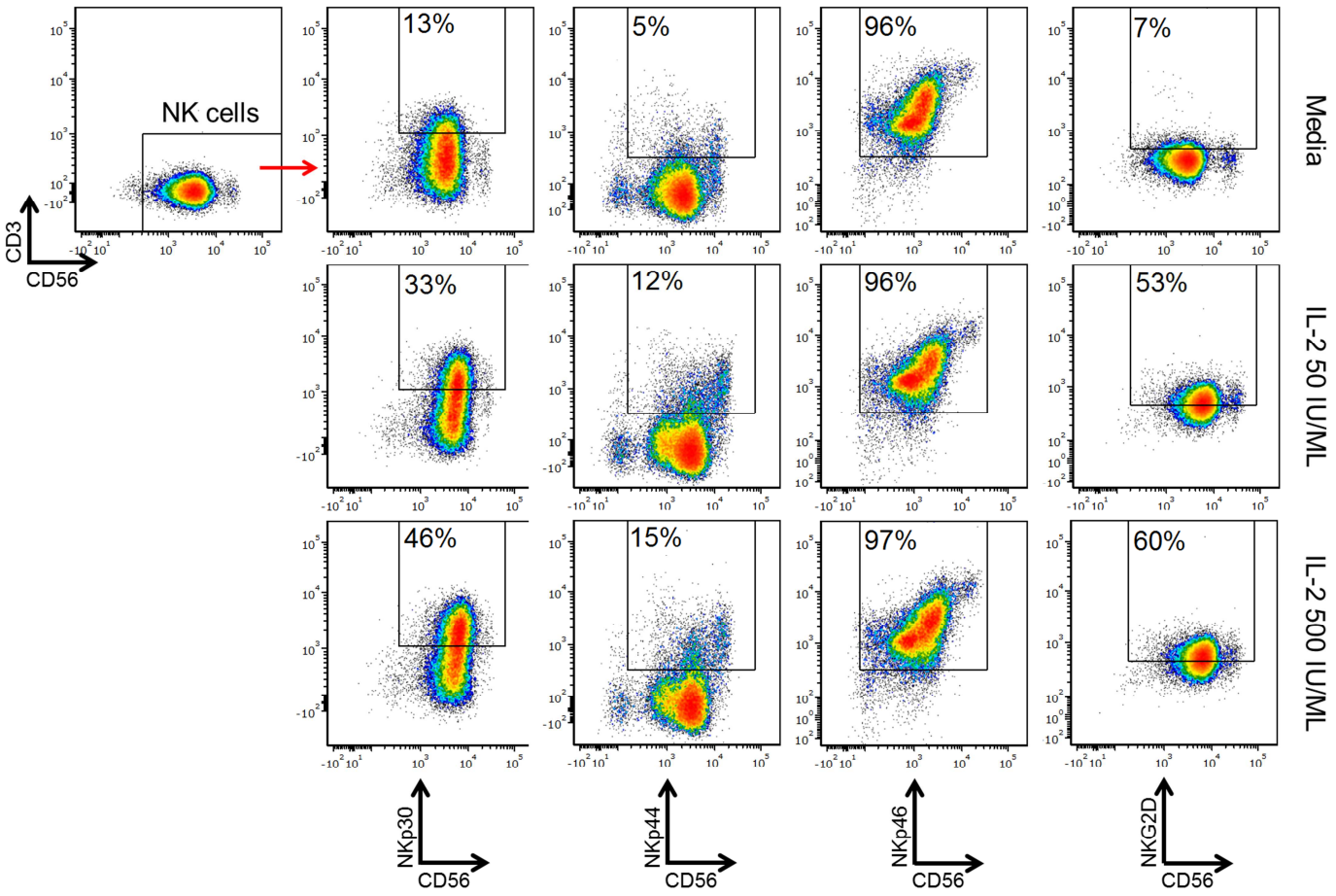


Supplementary Figure 1 Detachment of neuroblastoma cell lines from culture greatly reduces cell viability. **a,d** The adherent neuroblastoma cell line NB-1691 (**a**) and non-adherent erythroid leukemia cell lines K562 (**d**) were grown to subconfluence for comparison. Cell viability was assessed with flow cytometry by using 4',6-diamidino-2-phenylindole as a viability dye (**b–f**). **g** SK-N-SH and NB-1691 were stained at a subconfluent state with the live-cell stain calcein-AM (green) and dead-cell stain ethidium bromide (red) for evaluation of cell viability prior to detachment from culture. Cells were imaged with differential interference contrast and fluorescence microscopy. The majority of cells are viable in culture. Arrows facilitate comparison of the same area in between the different imaging modalities. **h** Following detachment from culture, cell viability for each neuroblastoma cell line (grey bars) is plotted against K562 (black bar).The percentage of viable single cells ranges from 21% (SK-N-BE2) to 84% (CHLA90).



Supplementary Figure 2 KIR phenotype analysis by flow cytometry.



Supplementary Figure 3 Example of flow cytometry analysis of natural cytotoxicity receptors in IL-2–stimulated NK cells.

Supplementary Table 1 Characterization of neuroblastoma cell lines.

Neuroblastoma cell line	HLA genotype	KIR mismatch	HLA expression[1]	GD2 expression[2]	Cell type[3]	Differentiation[4]
CHLA90	C*05:01, 12:03	CD158e1	Intermediate	High	S	Poor
NB-1691	C*05, 07:01	CD158e1	Low	High	I	Good
NBLS	C*02, 06	CD158b	Low	High	N	Poor
SK-N-AS	C*08, 03:04	CD158a	Normal	High	S	Poor
SK-N-BE2	C*04, 07:01	No mismatch	Low	Intermediate	I	Good
SK-N-FI	C*04, 07:01	No mismatch	Intermediate	High	N	Good
SK-N-Jci	C*12:03, 03:04	CD158a	Normal	High	S	Poor
SK-N-MM	C*04, 12:03	No mismatch	Normal	High	I	Good
SK-N-SH	C*07:01, 07:01	CD158a	Low	Intermediate	I	Good
SH-SY5Y	C*07:01, 07:01	CD158a	Low	Low	N	Good

[1]Normal: comparable to buffy coat; low: comparable to K562; intermediate: in between buffy coat and K562
[2]High: MFI ratio ≥90; intermediate: MFI ratio <90 and ≥25; Low: MFI ratio <25
[3]N-type: ≥90% of cells have neurite outgrowth; S-type: cells ≥90% of cells do not have neurite outgrowth; I-type: neither criteria for N or S-type cells are met
[4]Good: ≥50% of cells have neurite outgrowth after ATRA exposure; Poor: <50% have neurite outgrowth after ATRA exposure

Supplementary Table 2 HLA and KIR genotype information on donors used for experiment to study CD107a expression of NK cells following ADCC.

Donor	HLA genotype							Licensed KIR[1]			KIR genotype						KIR mismatch
	A	A	B	B	C	C	Bw4	2DL1	2DL2/3	3DL1	2DL1	2DL2	2DL3	3DL1	3DL1v[2]	3DS1	
1	02	03	07	07	07	07	-	-	+	-	+	-	+	-	+	+	2DL1
2	01	02	27	52	02	12	+	+	+	+	+	+	+	+	-	-	-
3	03	31	07	40	03	07	-	-	+	-	+	+	+	+	-	+	2DL1, 3DL1

[1]KIRs that are inhibited by the donor's HLA
[2]KIR3DL1 variant: this KIR is expressed intracellularly and therefore regarded as functionally negative.
[3]KIR3DS1 is listed because it is co-expressed with the KIR3DL1 variant

Supplementary Table 3 Differentially expressed genes in neuroblastoma cells after exposure to ATRA for 72 h.

	Good differentiators										Poor differentiators											
Gene ID	NB-1691		SK-N-SH		SK-N-BE2		SK-N-MM		SH-SY5Y		CHLA90		SK-N-AS		IMR32		NBLS		SK-N-FI		SK-N-JCI	
	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM	Fold	FPKM
Retinoic acid metabolism and binding																						
CRABP1	0.2	138.7	0.0	3.8			7.0	14.7	0.4	3.7												
CRABP2	49.3	659.4	578.0	1861.5	36.1	612.8	40.4	213.4	88.2	5.7	14.5	90.4	7.3	1874.2	3.7	72.8			0.1	3.2	0.0	2.4
CYP26A1	82.9	176.6	84.0	168.6	13.3	24.7	28.2	55.8	356.1	5.5												
CYP26B1	20.2	40.7	39.9	78.7	41.4	82.0	14.0	26.7	64.8	727.4	6.7	11.4	12.0	23.5	3.2	6.2	6.3	10.8				
DHRS3	25.6	60.0	90.7	184.8	37.2	113.8	4.2	57.3	45.9	5.8	2.0	133.4	31.4	136.8	29.1	64.1	13.4	48.0	2.1	8.9	5.9	96.5
RARB	8.1	15.4	20.9	40.4	8.7	18.6	2.7	12.3	21.8	101.0												
RBP1	3.8	151.9	6.2	76.4	4.2	170.3	7.1	27.0	3.7	62.5												
Neuroblastoma, neuronal differentiation, transmitter																						
ADAM22			2.3	16.2			2.1	2.9	2.5	11.1												
ASCL1	0.2	24.0	0.0	0.4	0.2	0.3			0.2	1.9												
ASIC4	2.4	6.4	4.7	8.4	3.2	8.4			4.1	2.1												
C1QL1	0.5	7.7	0.2	2.9			2.1	6.5	0.4	17.3												
C4orf6	41.7	100.7			58.5	120.1	8.4	16.0	9.0	6.6			2.2	2.8			4.5	13.6	24.9	48.7	0.5	0.0
CHAC1			0.5	4.3	0.3	8.7	0.2	8.0														
CHGA	0.2	103.2	0.1	13.1	0.2	36.0	2.4	6.2	0.2	0.9												
CRLF1			6.7	30.3	2.8	4.5	6.3	11.1														
DCLK1													4.8	19.0			2.8	12.9	5.5	24.7	0.3	0.2
DDC													0.3	10.2	2.5	12.7			0.4	27.9	0.0	0.0
DOK4	0.2	65.0	0.2	13.0	0.4	11.4			0.3	19.8												
HTR2B	2.4	3.6	3.7	7.4	2.7	3.6			2.0	1.6												
KCNH1	0.5	0.3	0.3	0.1	0.3	1.2			0.2	64.8												
MAOA	0.3	17.1	0.2	3.5			6.8	21.7	0.4	2.8												
MB21D2			12.1	23.5	3.7	20.9	2.7	14.7														
MCHR1															2.2	3.2	2.2	6.9	10.6	19.4		
METRN			4.7	38.4			2.4	21.6	2.5	9.7												
MRAP2													0.5	0.7			0.4	9.2	2.1	12.2	0.1	0.0
MYCN	0.5	144.6	0.1	0.1	0.3	318.7			0.4	4.3												

NCAM2			17.6	33.7	3.9	24.5	2.5	3.4	28.6	3.0												
NEFM	5.4	31.7	2.6	40.1			3.6	7.9	3.7	60.4												
NPY	0.1	6.8	0.0	0.1			3.4	5.3	0.1	16.8												
PMP22			0.2	6.3	0.3	2.4			0.3	19.5												
PRSS12	6.8	74.2	0.3	49.8			3.6	60.8	5.7	20.8												
SLC44A5	3.0	10.8	3.5	10.3	3.3	9.1			6.3	1.9												
STMN2											0.3	25.3	0.4	9.2	2.6	82.6			0.2	85.1	0.0	0.5

Cell structure

ABTB2	3.4	7.4	5.8	10.1			2.4	10.2	8.1	3.7												
ADAMTS9																						
ADD3	2.9	58.2	2.0	44.0	2.8	26.1	0.4	13.4	4.6	57.0												
CCBE1	4.9	10.1			2.1	2.4	2.0	3.1	4.8	16.6												
CNN2	3.1	17.4	23.9	46.8	2.3	5.6	0.2	9.1	4.2	16.1												
COL23A1			3.0	3.9	3.9	14.7			7.4	16.3												
COL3A1											0.4	113.0	2.0	612.7					0.0	0.3	0.2	5.0
CRYGC	28.5	62.0	3.0	4.1	11.9	21.7	7.3	13.4	3.9	1213.4												
FBLIM1	4.1	7.9	9.2	18.2	3.3	11.5	5.0	20.2														
GALNT6					2.2	7.5	5.6	10.5	5.1	12.7												
ITGA1	10.2	73.0	5.6	46.2	4.3	11.4			9.7	8.2												
KRT18											2.3	265.9	2.6	138.3					0.1	0.1	5.9	215.8
MFAP4	0.1	4.0	7.8	13.8	0.2	3.2			0.5	24.0												
TGM2											7.0	37.1	8.3	210.3					0.0	0.5	39.8	454.7
VIM	0.3	34.9			0.2	45.7	0.4	462.1	0.1	154.5												

Cellular metabolism and growth

AC017048.3	7.8	101.2	5.1	66.0	10.3	44.6	2.3	55.1	6.7	16.4												
ATP7A	4.1	135.7	2.4	20.1	3.6	26.3	3.6	15.8	3.6	19.0												
BTG2	2.7	23.0	6.0	20.2			2.6	5.0	2.2	62.2												
CD9	0.4	26.7	0.0	5.0			2.0	58.1	0.4	7.8												
ENPP2	5.5	19.0	4.8	8.7	2.5	106.9			5.8	0.4												
GDF15	37.8	184.3	12.5	82.7	6.8	57.9	30.0	109.3	3.1	45.0												
HK2	0.4	1.6	0.3	5.6	0.2	4.0			0.3	94.6												
MARCH11	0.4	4.2	0.3	5.0	0.5	10.6			0.2	6.1												
OTUD1	4.4	10.6	3.1	7.2	2.9	13.0			3.0	12.6												
PLK2			11.8	123.4	5.2	14.3			6.1	11.3												

RP11-474O21.5	11.4	22.1	19.4	36.8	35.6	74.2	10.3	38.5	5.9	13.5	2.9	94.8	23.3	82.1	5.7	9.8	3.4	5.1			3.1	17.7
SYT4			2.9	68.0	0.5	5.0	3.0	4.6	4.8	16.1												
TMSB4X	3.3	236.0	20.9	1010.4	2.8	73.0	5.9	728.0														

Signaling pathways

AURKB			0.2	2.5	0.5	5.2	0.4	9.8		1.3												
CXCR4	0.3	1.7	0.3	1.7	0.5	0.4			0.1	5.8			0.3	1.4	0.4	0.9			0.2	3.7		
DKK2			4.2	38.2	4.5	8.2			7.5	104.4												
DLK1	0.2	39.4	0.0	0.5	0.1	0.7			0.0	15.3												
EGLN3	0.4	3.8	0.1	0.1			2.6	3.3	0.5	3.9												
GNG8	13.1	47.5	41.7	341.5	8.0	23.2	8.7	15.3	3.6	20.2												
IGFBP4	0.3	36.8	13.0	48.7			0.4	8.9	0.4	9.0					0.5	4.4	2.3	19.0	0.1	1.0	0.5	20.1
IGFBP6	2.4	3.2	42.0	214.9	2.1	4.3			2.4	3.5	4.6	122.3	4.8	42.1					0.4	6.8	9.2	236.6
LPAR3					0.4	3.5	0.2	0.3	0.3	20.2												
LTBP1	3.3	6.3	17.2	61.6			0.1	9.5	2.1	1.7												
NTRK2			4.0	6.0	2.9	4.2			7.2	3.2												
PRKAR2B	2.0	32.4	0.4	13.9	2.1	26.9	2.8	19.5	2.0	1.1												
RASL10B			7.1	43.6	2.2	33.4			4.8	57.6												
RET	8.0	184.4	5.7	218.3	14.5	161.6	29.7	72.2	13.3	107.3												
RP3-422G23.4															2.2	2.6	4.8	17.5	10.4	18.7		
TRIB2	2.2	72.2	0.5	38.4	2.5	39.9	2.7	18.3	7.1	6.2												

Angiogenesis

HAND1	0.3	20.7	0.3	8.1	0.4	6.2	2.0	2.5														
PLAT	9.4	42.0	85.2	351.6	9.8	34.1	9.1	349.8	5.7	14.7												
TMEM100					0.4	0.8	0.2	1.7	0.4	0.9												

Histones

HIST1H2AL	0.4	147.0	0.2	38.1	0.3	53.8	0.5	85.8														
HIST1H2BB	0.5	261.2	34.7	85.1	0.2	12.1	0.0	0.2														
HIST1H2BF	0.4	75.5	0.3	28.7	0.2	28.1	0.5	48.6														
HIST1H2BI	0.4	231.8	6.0	97.5	0.4	132.2	0.0	0.1														
HIST1H2BM	0.4	214.1	0.4	77.4	0.3	81.0	0.1	9.3														
HIST1H3F			0.1	91.0	0.3	287.1	0.5	289.8														
HIST1H3I			0.3	97.9	0.4	305.8	0.1	29.5														
HIST1H4H	0.5	709.9	0.2	157.5	0.3	334.0	0.4	328.3														

Unknown significance

AC017048.4	2.4	5.2	2.8	6.4	3.8	7.4			4.7	117.8												
C1QTNF1-AS1			2.7	3.4	2.2	5.8	5.6	9.3	2.3	4.1												
DNM3OS			10.4	23.6			2.4	23.0	3.1	1.8												
FABP3	2.8	4.0			4.5	19.8	3.6	5.3	3.5	0.8												
FNDC5															3.1	73.2	2.2	4.9	3.0	7.7	0.2	0.1
PDZRN3			2.0	10.1	6.0	14.7			3.0	2.9												
RP11-116D17.3	3.7	8.2	0.3	0.7	4.8	8.8	3.9	6.1	3.3	261.9												
RP11-124O11.1	4.8	10.3			7.1	14.4	4.3	6.5	4.1	5.0												
RP11-45F15.2	2.6	12.0	2.4	4.3	2.3	8.0			2.4	7.9												
RP5-998N21.10															0.4	13.7	0.4	4.4	0.2	13.3	0.2	5.6
SLC10A4	0.3	33.3	0.1	6.2	0.4	26.2			0.4	13.1												
TOX			0.2	2.3	0.4	3.2			0.5	1.5												