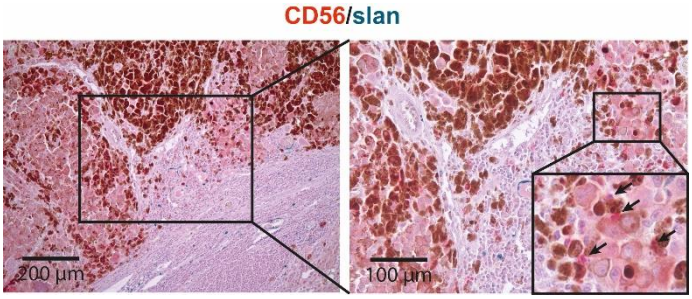
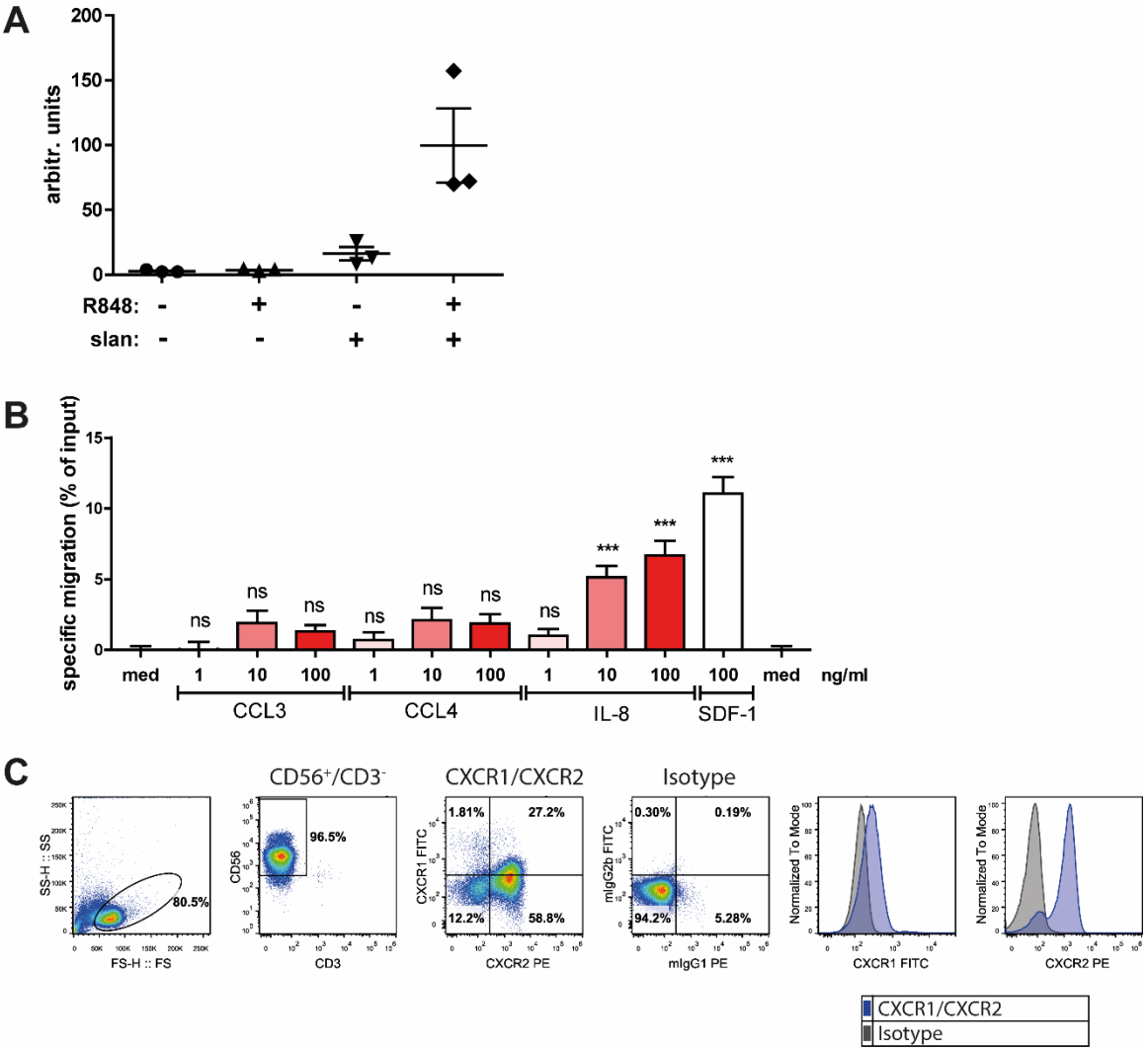
Supplementary Figure S1



NK cells can be distinguished from CD56 positive tumor cells

CD56 and slan were stained in human FFPE melanoma tissue. Inlet shows CD56 positive NK cells (black arrows) surrounded by CD56 weak positive melanoma cells. Original magnification x100 (left image), x200 (right image).

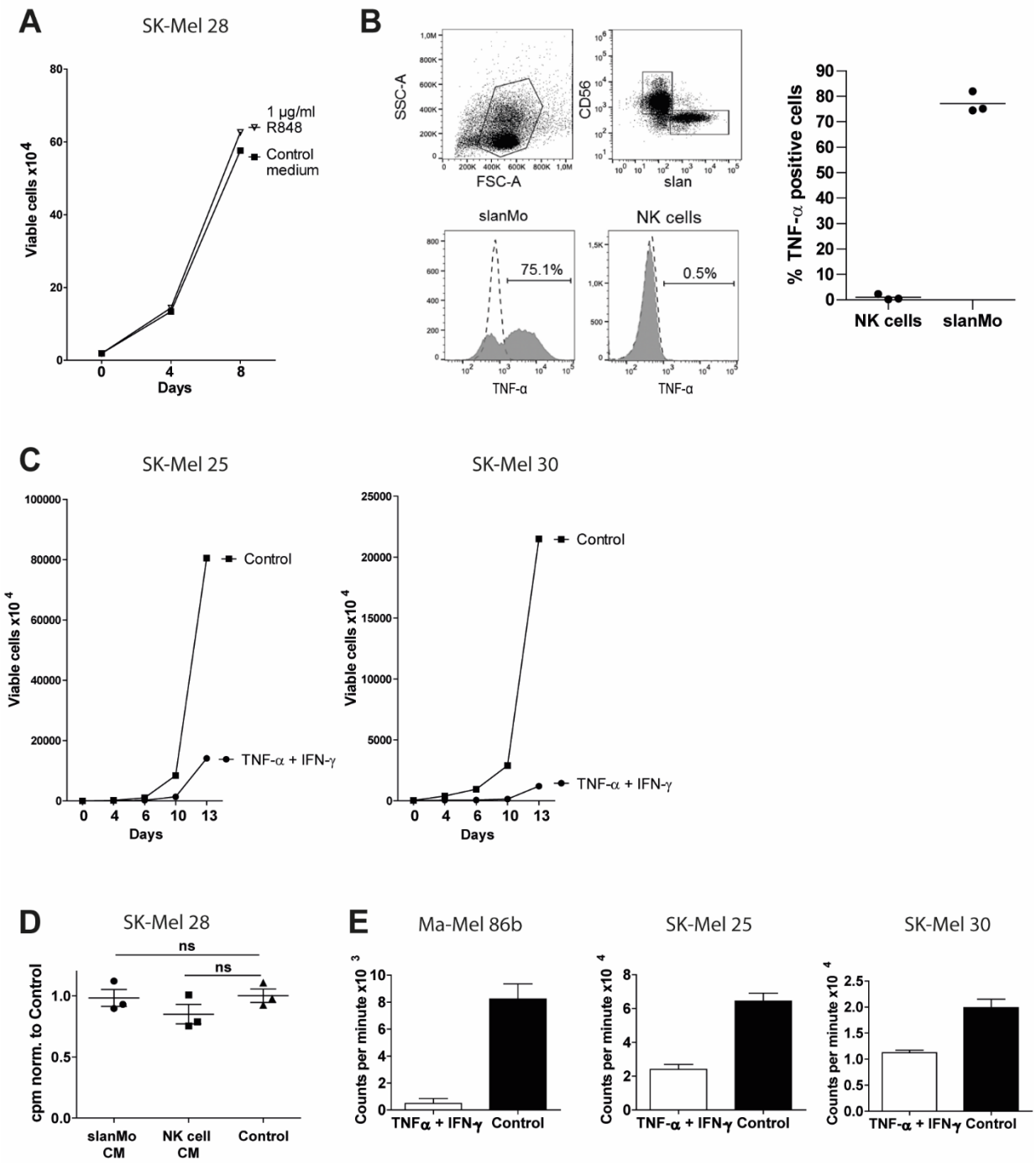
Supplementary Figure S2



NK cell migration towards recombinant chemokines present in slanMo supernatants

A, Specific migration of 1 day cultured NK cells towards different stimuli including recombinant R848 (1 µg/ml) and conditioned medium from unstimulated and R848-activated slanMo displayed as arbitrary units. Data from 3 donors (SEM). **B,** Specific migration of 1 day cultured NK cells towards different stimuli as indicated or control medium (med). Cumulative data from 4 donors. p values were calculated by 1 way Anova comparing each chemokine group with the medium control with *p<0.05, **p<0.01, ***p<0.001. **B,** Chemokine receptor expression (CXCR1 and CXCR2) on 1 day cultured NK cells. Pre-gating on $CD56^{+}CD3^{-}$ NK cells and CXCR1/CXCR2 gating according to isotype staining. Representative data out of 4 donors.

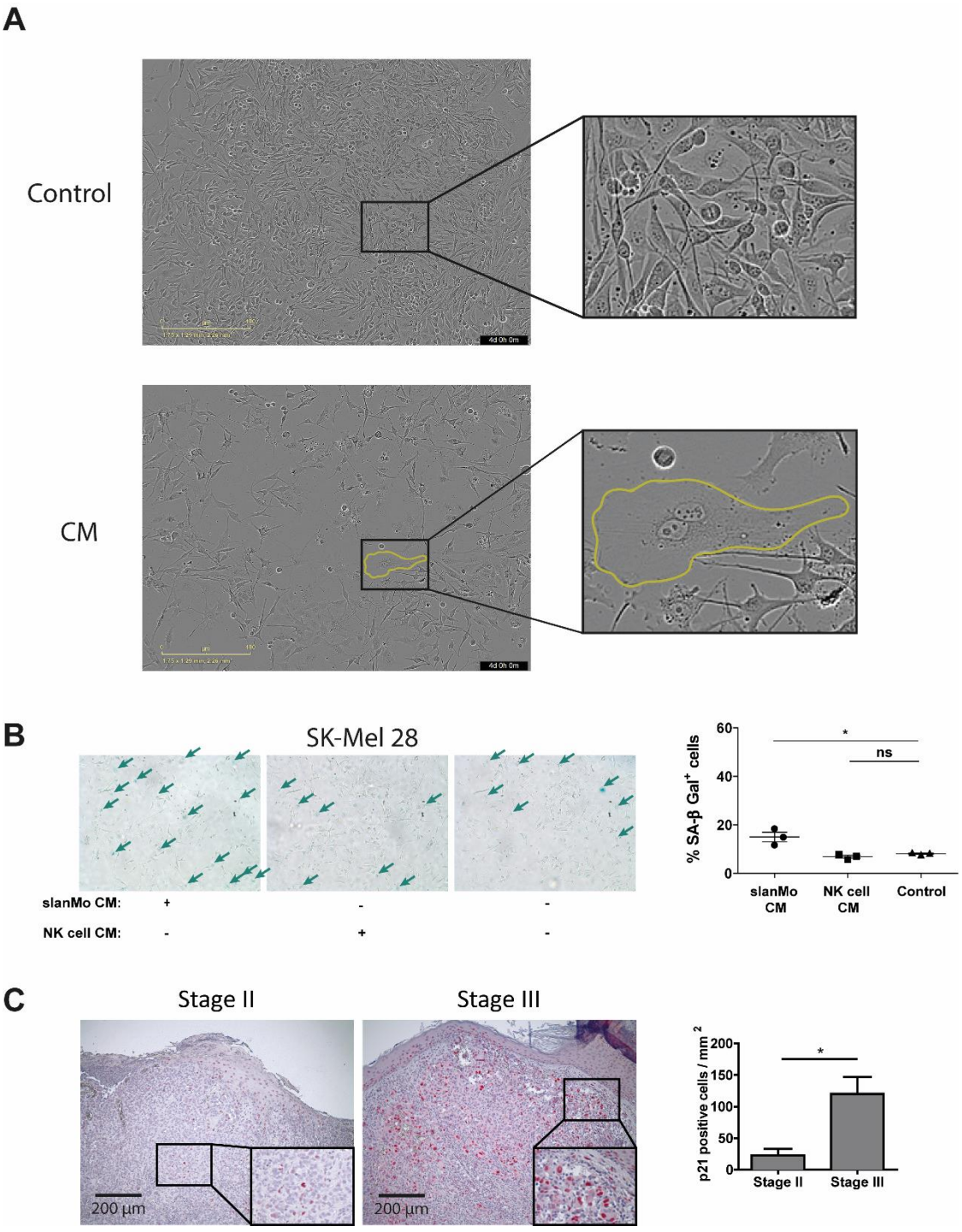
Supplementary Figure S3



The TNF-α and IFN-γ mediated growth arrest is slanMo/NK cell co-culture dependent

A, Prolonged culture of SK-Mel-28 melanoma cells after 4 day treatment with 1 µg/ml R848. After the treatment, the cells were washed, counted and cultured in normal medium. **B,** Freshly purified slanMo were cultured for 6 hours before co-culture with NK cells and activation with 1 µg/ml R848. After 6 hours of co-culture, the cells were fixed, permeabilized and stained for TNF-α (filled gray) or isotype (dotted line). Representative data out of 3 donors. **C,** Prolonged culture of melanoma cell lines SK-Mel 25 and SK-Mel 30. Melanoma cells were treated for 4 days with recombinant TNF-α and IFN-γ (10 ng/ml and 100 ng/ml, respectively). Afterwards, the cells were washed, counted and cultured in normal medium for 3 additional passages. **D,** SK-Mel-28 cells were treated with slanMo and NK cell mono-culture CM. The cells were reseeded and pulsed for 12 h with ^{3}H-Thymidine for measurement of ^{3}H-Thymidine incorporation. **E,** ^{3}H-Thymidine incorporation in melanoma cell lines after treatment with TNFα and IFN-γ (10 ng/ml and 100 ng/ml, respectively).

Supplementary Figure S4



Co-culture CM treatment results in the formation of morphologically distinct melanoma cells. **A,** SK-Mel-28 cells were treated with co-culture CM as described before and 100x magnification images of tumor growth were taken every two hours over a total incubation time of 96 hours. A representative image after 96 hours for each condition is depicted. Yellow line marks cellular margins of a characteristic enlarged and multinucleated (2) cell. **B,** SA-β Galactosidase assay for growth inhibition induced by slanMo and NK cell mono-culture conditioned medium in comparison to control medium. Green arrows indicate representative positive cells. Percentage of SA β-galactosidase positive cells evaluated by staining intensity. **C,** Cutaneous stage II/stage III FFPE melanoma samples were stained for p21 and p21 positive cells were quantified. Numbers for stage II (n=4) and stage III (n=9). Original magnification 100x. Statistical significance was analyzed using Mann-Whitney test with *p<0.05, **p<0.01, ***p<0.001.

Supplementary table 1

Patient Characteristics

	stage 1 (n=10)	stage 2 (n=16)	stage 3 (n=10)	stage 3 LN (n=10)	stage 4 (n=8)
sex					
female	6 (60%)	9 (56%)	7 (88%)	2 (20%)	3 (37.5%)
male	4 (40%)	7 (44%)	1 (12%)	8 (80%)	5 (62.5%)
age	60±21	61.9±14	73.3±12	74.7±9.5	58.5±8.9
tumor thickness (mm)	0.6±0.3	4.5±2.5	-	-	-

Supplementary Table S2

Primers used for qPCR analysis

hIL6_fw	AGACAGCCACTCACCTCTTCAG
hIL6_rev	TTCTGCCAGTGCCTCTTTGCTG
hIL8_fw	TTGGCAGCCTTCCTGATTTC
hIL8_rev	TCTTTAGCACTCCTTGGCAAAAC
hIL1A_fw	TGTATGTGACTGCCCAAGATGAAG
hIL1A_rev	AGAGGAGGTTGGTCTCACTACC
hIL1B_fw	CCACAGACCTTCCAGGAGAATG
hIL1B_rev	GTGCAGTTCAGTGATCGTACAGG
hTGFβ1_fw	CGGAGTTGTGCGGCAGTGGT
hTGFβ1_rev	GTTGGTGTCCAGGGCTCGGC
hVEGF-A_fw	AGTTCATGGATGTCTATCAGCGC
hVEGF-A_rev	TCCGCATAATCTGCATGGTG
hMMP1_fw	ATGAAGCAGCCCAGATGTGGAG
hMMP1_rev	TGGTCCACATCTGCTCTTGGCA
hMMP2_fw	CCACTGCCTTCGATACAC
hMMP2_rev	GAGCCACTCTCTGGAATCTTAAA
hMMP9_fw	GCCACTACTGTGCCTTTGAGTC
hMMP9_rev	CCCTCAGAGAATCGCCAGTACT
hMMP3_fw	CACTCACAGACCTGACTCGGTT
hMMP3_rev	AAGCAGGATCACAGTTGGCTGG
hSerpine1_fw = PAI1	GGCCATTACTACGACATCCTG
hSerpine1_rev = PAI1	GGTCATGTTGCCTTTCCAGT
hSerpine2_fw = PAI2	GCTGTTTGGTGAGAAGTCTGCG
hSerpine2_rev = PAI2	CTGCACATTCTAGGAAGTCTACTG
hCXCL1_fw	AGCCAACGTCAAGCATCTCAA
hCXCL1_rev	AATCCACTTTAGCTTCGGGTCAA
hCXCL2_fw	GGCAGAAAGCTTGTCTCAACCC
hCXCL2_rev	CTCCTTCAGGAACAGCCACCAA
hICAM-1_fw	AGCGGCTGACGTGTGCAGTAAT
hICAM-1_rev	TCTGAGACCTCTGGCTTCGTCA
hCCL2_fw	CCGAGAGGCTGAGACTAAC
hCCL2_rev	CTTGCTGCTGGTGATTCTTC
hCCL7_fw	ACAGAAGGACCACCAGTAGCCA
hCCL7_rev	GGTGCTTCATAAAGTCCTGGACC
hGAPDH_fw	CGACCACTTTGTCAAGCTCA
hGAPDH_rev	AGGGGTCTACATGGCAACTG

Supplementary Methods

Intracellular TNF-α staining

Freshly purified slanMo were plated at a concentration of $5x10^5$ cells/ml and cultured for 6 hours. $1x10^6$ NK cells were added and cells were stimulated with 1 µg/ml R848 in the presence of 1 µg/ml brefeldin A (Sigma-Aldrich). After 6 hours of co-culture, the cells were harvested and stained for slan (clone MDC8) and CD56 (clone B159, BD). For intracellular cytokine staining, cells were fixed with 4% paraformaldehyde (PFA), permeabilized using 1% saponin and stained for TNF- α (clone Mab11, BD) or with the respective isotype control.