SUPPLEMENTARY TABLES AND FIGURE

Supplementary Table 1: Assay-specific reagents and equipment.

Device for cam1615TEM8 Protein Production Item	Manufacturer	Catalog #
AKTA Avant Chromatography System	GE Healthcare	Catalog #
AKTA Avant Chromatography System	(Chicago, IL, USA)	-
Reagents for ANTXR1 RT-qPCR	(Cincago, IL, COA)	
Item	Manufacturer	Catalog #
ANTXR1 TaqMan Probe (Human)	Thermo Fisher Scientific	4351372
ANTAKT Taqivian Trobe (Human)	(Waltham, MA, USA)	4331372
ANTXR1 TaqMan Probe (Mouse)	Thermo Fisher Scientific	4331182
The Tadivian Flore (Mouse)	(Waltham, MA, USA)	1331102
GAPDH TaqMan Probe (Human)	Thermo Fisher Scientific	4331182
, ,	(Waltham, MA, USA)	
GAPDH TaqMan Probe (Mouse)	Thermo Fisher Scientific	4453320
	(Waltham, MA, USA)	
MicroAmp TM EnduraPlate TM Optical 384-Well Clear	Applied Biosystems	4483285
Reaction Plate	(Foster City, CA, USA)	
QIAshredder	Qiagen	796565
	(Germantown, MD, USA)	
RNEasy Mini Kit	Qiagen	74104
DV 14 1'C (' C 1	(Germantown, MD, USA)	10040015
DNase I, Amplification Grade	Invitrogen	18068015
SuperScript TM IV Reverse Transcriptase	(Carlsbad, CA, USA)	18000050
SuperScript IV Reverse Transcriptase	Invitrogen	18090050
Tagman Fast Advanced Master Mix	(Carlsbad, CA, USA) Applied Biosystems	4444557
Taqinan Fast Advanced Master Mix	(Foster City, CA, USA)	4444337
Thermo Scientific TM dNTP Mixes	Thermo Fisher Scientific	R0192
Thermo Scientific divit whites	(Waltham, MA, USA)	R0192
Reagents for PBMC Isolation, NK Cell Enrichment, NK Cel		
Item	Manufacturer	Catalog #
Ficoll®-Paque Premium	GE Healthcare	17544202
	(Chicago, IL, USA)	
EasySep TM Human NK Cell Enrichment Kit	STEMCELL Technologies	19055
• •	(Vancouver, Canada)	
G-REX® 6 Well Plate	Wilson Wolf	80240M
_	(Saint Paul, MN, USA)	
IncuCyte® NucLight Red Lentivirus Reagent	Sartorius	4625
	(Göttingen, Germany)	
Reagents for Generating A549 TEM8 Knockout Cell Line		
Item	Manufacturer	Catalog #
Alt-R S.p. HiFi Cas9 Nuclease V3	IDT	1081060
THE CONTRACTOR OF THE CONTRACT	(Coralville, IA, USA)	GL C. L. VIOLOGIA
Lipofectamine TM CRISPRMAX TM Cas9 Transfection	Invitrogen	CMAX00001
1		
Reagent	(Carlsbad, CA, USA)	
Reagent Reagents and Devices for NK Cell Degranulation and Cytok	ine Production Assay	
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item	ine Production Assay Manufacturer	Catalog #
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item	ine Production Assay Manufacturer BD Biosciences	Catalog # 555029
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM	Manufacturer BD Biosciences (San Jose, CA, USA)	555029
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM	Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences	
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM	BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA)	555029
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM	Ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences	555029
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer	BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA)	555029
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer Reagents and Devices for Tumor Spheroid Killing Assay	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA)	555029 554724 -
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer Reagents and Devices for Tumor Spheroid Killing Assay Item	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA) Manufacturer	555029 554724 - - Catalog #
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer Reagents and Devices for Tumor Spheroid Killing Assay Item	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA) Manufacturer Corning	555029 554724 -
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer Reagents and Devices for Tumor Spheroid Killing Assay Item Round Bottom Ultra-Low Attachment 96 Well Plate	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA) Manufacturer Corning (Corning, NY, USA)	555029 554724 - Catalog #
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer Reagents and Devices for Tumor Spheroid Killing Assay Item Round Bottom Ultra-Low Attachment 96 Well Plate	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA) Manufacturer Corning (Corning, NY, USA) Essen Bioscience	555029 554724 - Catalog #
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer Reagents and Devices for Tumor Spheroid Killing Assay Item Round Bottom Ultra-Low Attachment 96 Well Plate IncuCyte® S3	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA) Manufacturer Corning (Corning, NY, USA) Essen Bioscience (Ann Arbor, MI, USA)	555029 554724 - Catalog #
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM GolgiStop TM LSR II Flow Cytometer Reagents and Devices for Tumor Spheroid Killing Assay Item Round Bottom Ultra-Low Attachment 96 Well Plate IncuCyte® S3 Reagents and Devices for NK Cell and T Cell pSTAT5 Indus	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA) Manufacturer Corning (Corning, NY, USA) Essen Bioscience (Ann Arbor, MI, USA)	555029 554724 - - Catalog # 7007
Reagent Reagents and Devices for NK Cell Degranulation and Cytok Item GolgiPlug TM	ine Production Assay Manufacturer BD Biosciences (San Jose, CA, USA) BD Biosciences (San Jose, CA, USA) BD Biosciences (East Rutherford, NJ, USA) Manufacturer Corning (Corning, NY, USA) Essen Bioscience (Ann Arbor, MI, USA)	555029 554724 - - Catalog #

Reagents for NK-92 Metabolic Activity Assay					
Item	Manufacturer	Catalog #			
96-Well, Cell Culture-Treated, Flat-Bottom Microplate	Thermo Fisher Scientific	07-200-565			
	(Waltham, MA, USA)				
Resazurin	R&D Systems	AR002			
	(Minneapolis, MN, USA)				
Reagents and Devices for A549 In Vivo Assay					
Item	Manufacturer	Catalog #			
Matrigel TM Membrane Matrix High Concentration	Corning	354262			
	(Corning, NY, USA)				
VWR Digital Caliper	VWR International	62379-531			
	(Radnor, PA, USA)				
Gibco TM ACK Lysing Buffer	Thermo Fisher Scientific	A1049201			
	(Waltham, MA, USA)				

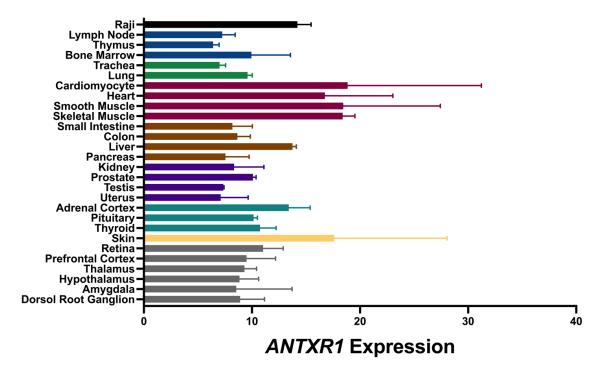
Supplementary Table 2: Cell culture reagents.

Cell Line	Vendor	Growth Media ¹	Growth Media Vendor	Growth Media Catalog #
A549	American Type Culture Collection (Manassas, VA, USA)	DMEM	Corning (Corning, NY, USA)	10-013-CV
DU145	American Type Culture Collection (Manassas, VA, USA)	RPMI 1640	Thermo Fisher Scientific (Waltham, MA, USA)	11875119
Raji	American Type Culture Collection (Manassas, VA, USA)	RPMI 1640	Thermo Fisher Scientific (Waltham, MA, USA)	11875119
HT-29	American Type Culture Collection (Manassas, VA, USA)	RPMI 1640	Thermo Fisher Scientific (Waltham, MA, USA)	11875119
HUVEC (Human Umbilical Vein Endothelial Cell)	Lonza (Basel, Switzerland)	EGM TM -2	Lonza (Basel, Switzerland)	CC-3162
HMVEC-L (Human Microvascular Endothelial Cell-Lung)	Lonza (Basel, Switzerland)	EGM TM -2 MV	Lonza (Basel, Switzerland)	CC-3202
2Н-11	American Type Culture Collection (Manassas, VA, USA)	DMEM	Corning (Corning, NY, USA)	10-013-CV
NHLF	American Type Culture Collection (Manassas, VA, USA)	DMEM	Corning (Corning, NY, USA)	10-013-CV
NK-92 [®]	American Type Culture Collection (Manassas, VA, USA)	MEM a-nucleosides	Thermo Fisher Scientific (Waltham, MA, USA)	12571071
Expi293F TM	Thermo Fisher Scientific (Waltham, MA, USA)	Expi293 TM Expression Medium	Thermo Fisher Scientific (Waltham, MA, USA)	A1435101

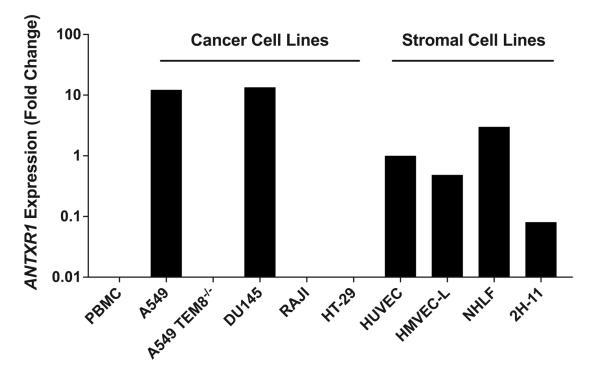
¹DMEM and RPMI 1640 were supplemented with 10% Fetal Bovine Serum (FBS), while MEM α nucleosides was supplemented with 0.1 mM 2-mercaptoethanol, 500 U/mL recombinant human IL-2, 12.5% horse serum, and 12.5% fetal bovine serum.

Supplementary Table 3: Antibodies and other fluorescent markers.

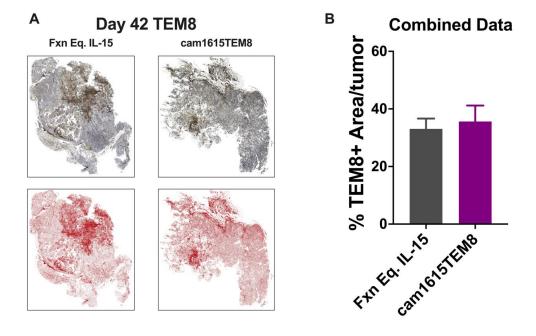
Antibodies for N	K Cell Degranulation	and Cytokine Production A	ssay			
Target	Clone	Manufacturer	Catalog #	Host Species	Target Species	Application
CD3	UCHT1	BD Biosciences	562280	Mouse	Human	Flow Cytometry
		(San Jose, CA, USA)				
CD56	HCD56	Biolegend	318318	Mouse	Human	Flow Cytometry
		(San Diego, CA, USA)				
CD107a	H4A3	Biolegend	328606	Mouse	Human	Flow Cytometry
		(San Diego, CA, USA)				
IFNγ	4S.B3	Biolegend	502538	Mouse	Human	Flow Cytometry
		(San Diego, CA, USA)				
Antibodies for N	K Cell and T Cell Pro	liferation Assay				
Target	Clone	Manufacturer	Catalog #	Host Species	Target Species	Application
CD3	UCHT1	BD Biosciences	562280	Mouse	Human	Flow Cytometry
		(San Jose, CA, USA)				
CD56	HCD56	Biolegend	318318	Mouse	Human	Flow Cytometry
		(San Diego, CA, USA)				
Antibodies for N	K Cell and T Cell pS	TAT5 Induction Assay		•	•	•
Target	Clone	Manufacturer	Catalog #	Host Species	Target Species	Application
CD3	OKT3	Biolegend	317330	Mouse	Human	Flow Cytometry
		(San Diego, CA, USA)	11,550			2 12 // Cytomony
CD56	HCD56	Biolegend	318336	Mouse	Human	Flow Cytometry
		(San Diego, CA, USA)				
STAT5/pY694	A17016B.Rec	Biolegend	936904	Mouse	Human	Flow Cytometry
r ·		(San Diego, CA, USA)	1			1
Kappa Isotype	MOPC-21	Biolegend	400140	Mouse		Flow Cytometry
Control		(San Diego, CA, USA)				1
	K-92 CD16 Surface S					
Target	Clone	Manufacturer	Catalog #	Host Species	Target Species	Application
CD16	3G8	Biolegend	302038	Mouse	Human	Flow Cytometry
CDIO	300	(San Diego, CA, USA)	302038	Wiousc	Tuman	Flow Cytollicity
Kappa Isotype	MOPC-21	Biolegend	400158	Mouse		Flow Cytometry
Control	WIOI C-21	(San Diego, CA, USA)	400130	Wiouse		1 low Cytollicity
	viva Mausa Parinhar	al Blood Human NK Cell Qu	untification			
	Clone	Manufacturer		Host Cuosias	Towart Curation	Auuliaatiau
Target			Catalog #	Host Species	Target Species	Application
CD3	UCHT1	BD Biosciences	562280	Mouse	Human	Flow Cytometry
CD45	HI30	(San Jose, CA, USA)	304042	Mouse	Human	Flass Cutamatus
CD45	пізо	Biolegend (Sep Diago CA USA)	304042	Mouse	numan	Flow Cytometry
CD45	30-F11	(San Diego, CA, USA) Biolegend	103149	Rat	Mouse	Flow Cytometry
CD43	50-1-11	(San Diego, CA, USA)	103147	Nat	MIOUSC	1 10 w Cytollicity
		LUMB DESCRIPTION (A USA)	1	I	1	Flans Cutamatus
CD56	HCD56		318318	Mouse	Human	
CD56	HCD56	Biolegend	318318	Mouse	Human	Flow Cytometry
		Biolegend (San Diego, CA, USA)	318318	Mouse	Human	Flow Cytometry
Primary Antiboo	lies for <i>in vivo</i> Tumor	Biolegend (San Diego, CA, USA) Immunohistochemistry				, ,
Primary Antiboo Target	lies for in vivo Tumor	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer	Catalog#	Host Species	Target Species	Application
Primary Antiboo	lies for <i>in vivo</i> Tumor	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam				, ,
Primary Antiboo Target TEM8	lies for in vivo Tumor Clone EPNCI-R173-37	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK)	Catalog # ab241067	Host Species Rabbit	Target Species Mouse, Human	Application Immunohistochemistry
Primary Antiboo Target	lies for in vivo Tumor	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research	Catalog#	Host Species	Target Species	Application
Primary Antiboo Target TEM8	lies for in vivo Tumor Clone EPNCI-R173-37	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc.	Catalog # ab241067	Host Species Rabbit	Target Species Mouse, Human	Application Immunohistochemistry
Primary Antiboo Target TEM8	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA)	Catalog # ab241067 DIA-310	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry
Primary Antiboo Target TEM8	lies for in vivo Tumor Clone EPNCI-R173-37	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma	Catalog # ab241067	Host Species Rabbit	Target Species Mouse, Human	Application Immunohistochemistry
Primary Antiboo Target TEM8 CD31 Granzyme B	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA)	Catalog # ab241067 DIA-310	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry
Primary Antiboo Target TEM8 CD31 Granzyme B	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA)	Catalog # ab241067 DIA-310 262R-15	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry
Primary Antiboo Target TEM8 CD31 Granzyme B Other Fluorescen	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA)	Catalog # ab241067 DIA-310 262R-15 Catalog #	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry Application
Primary Antiboo Target TEM8 CD31 Granzyme B	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA) Manufacturer BD Biosciences	Catalog # ab241067 DIA-310 262R-15	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry
Primary Antiboo Target TEM8 CD31 Granzyme B Other Fluorescer Item Annexin V	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230 nt Markers	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA) Manufacturer BD Biosciences (San Jose, CA, USA)	Catalog # ab241067 DIA-310 262R-15 Catalog # 556419	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry Application Flow Cytometry
Primary Antibod Target TEM8 CD31 Granzyme B Other Fluorescer Item Annexin V Live/Dead TM Fixa	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA) Manufacturer BD Biosciences (San Jose, CA, USA) Thermo Fisher Scientific	Catalog # ab241067 DIA-310 262R-15 Catalog #	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry Application
Primary Antiboo Target TEM8 CD31 Granzyme B Other Fluorescer Item Annexin V	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230 nt Markers	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA) Manufacturer BD Biosciences (San Jose, CA, USA)	Catalog # ab241067 DIA-310 262R-15 Catalog # 556419	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry Application Flow Cytometry
Primary Antibod Target TEM8 CD31 Granzyme B Other Fluorescentem Annexin V Live/Dead TM Fixa Cell Stain Kit	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230 nt Markers	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA) Manufacturer BD Biosciences (San Jose, CA, USA) Thermo Fisher Scientific (Waltham, MA, USA)	Catalog # ab241067 DIA-310 262R-15 Catalog # 556419 L34976	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry Application Flow Cytometry Flow Cytometry
Primary Antibod Target TEM8 CD31 Granzyme B Other Fluorescen Item Annexin V Live/Dead TM Fixa Cell Stain Kit	lies for in vivo Tumor Clone EPNCI-R173-37 SZ31 EP230 nt Markers	Biolegend (San Diego, CA, USA) Immunohistochemistry Manufacturer Abcam (Cambridge, UK) American Research Products Inc. (Waltham, MA, USA) MilliporeSigma (Burlington, MA, USA) Manufacturer BD Biosciences (San Jose, CA, USA) Thermo Fisher Scientific	Catalog # ab241067 DIA-310 262R-15 Catalog # 556419	Host Species Rabbit Rat	Target Species Mouse, Human Mouse	Application Immunohistochemistry Immunohistochemistry Immunohistochemistry Application Flow Cytometry



Supplementary Figure 1. Organ and tissue specific expression of *ANTXR1* **in human tissues.** Gene expression of *ANTXR1* in human tissues in the GeneAtlas U133A, gcrma database with the 220092_s_at probe set. Graph have been adapted from the BioGPS website with tissues grouped and color-coded.



Supplementary Figure 2. *ANTXR1* expression in tumor and stromal cell lines. *ANTXR1* expression was quantified with RT-qPCR of Human Peripheral Blood Mononuclear Cells (PBMC), human tumor cell lines (A549, A549 TEM8^{-/-}, DU145, RAJI, HT29), human endothelial cell lines (HUVEC, HMVEC-L), human fibroblasts (NHLF), and immortalized mouse endothelial cells (2H-11). Expression levels of ANTXR1 are normalized to GAPDH then depicted as a fold change relative to HUVECs. The 2H-11 cell line required mouse *ANTXR1* and *GAPDH* RT-qPCR probes.



Supplementary Figure 3. cam1615TEM8 does not alter TEM8 expression within A549 xenograft tumors. A549 tumor was engrafted as outlined and mice were treated with NK cells and cam1615TEM8 or functionally equivalent IL-15. (A) Top: Representative anti-TEM8 stained whole tumor sections. Bottom: the TEM8 mask used for TEM8 quantification generated with QuPath. (B) Combined data for tumors from all mice. "Fxn Eq. IL-15" indicates "Functionally Equivalent IL-15." n=4 for the functionally equivalent IL-15 treatment group. n=3 for the cam1615TEM8 treatment group.