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Supplemental Information

Tissue Determinants of Human NK

Cell Development, Function, and Residence

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Table S1. Related to Figures 1,2,3,4,5,6,7. Information about donors used in the study

Donor number	Age (years)	Sex	Ethnicity/race	Cause of death	EBV Status	CMV status
339	5	MALE	Black or African American	OTHER SPECIFY : INFECTION: BACTERIAL	Negative	Negative
251	9	MALE	White	ANOXIA	Positive	Negative
392	9	FEMALE	Hispanic/Latino	ANOXIA	Positive	Negative
351	11	FEMALE	Black or African American	ANOXIA	Positive	Negative
360	16	MALE	Hispanic/Latino	HEAD TRAUMA	Positive	Positive
430	18	MALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Negative
400	18	MALE	White	ANOXIA	Positive	Positive
408	18	MALE	Black or African American	ANOXIA	Negative	Positive
Npod6503	18	MALE	Unknown	ANOXIA	Unknown	Positive
442	19	MALE	Hispanic/Latino	HEAD TRAUMA	Positive	Positive
340	23	MALE	Black or African American	HEAD TRAUMA	Positive	Positive
361	24	MALE	Black or African American	HEAD TRAUMA	Positive	Positive
358	24	MALE	Hispanic/Latino	ANOXIA	Positive	Negative
365	28	FEMALE	Hispanic/Latino	ANOXIA	Positive	Positive
425	30	FEMALE	White	ANOXIA	Positive	Negative
331	32	MALE	Black or African American	HEAD TRAUMA	Positive	Negative
346	32	MALE	White	HEAD TRAUMA	Positive	Negative
397	34	MALE	White	ANOXIA	Positive	Negative
429	36	MALE	Hispanic/Latino	ANOXIA	Positive	Positive
359	38	FEMALE	Asian	ANOXIA	Positive	Positive
419	38	MALE	White	ANOXIA	Positive	Negative
332	38	MALE	Black or African American	HEAD TRAUMA	Positive	Positive
441	40	MALE	Hispanic/Latino	ANOXIA	Positive	Negative
447	40	FEMALE	Hispanic/Latino	CEREBROVASCULAR/STROKE	Positive	Positive
344	44	MALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Negative
390	45	MALE	Asian	ANOXIA	Positive	Negative
309	45	FEMALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Positive
407	45	MALE	Hispanic/Latino	CEREBROVASCULAR/STROKE	Positive	Positive
445	47	MALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Positive
413	48	FEMALE	White	ANOXIA	Positive	Positive
341	49	MALE	White	CEREBROVASCULAR/STROKE	Positive	Negative
338	49	MALE	Hispanic/Latino	ANOXIA	Positive	Positive
350	49	FEMALE	White	ANOXIA	Positive	Positive
448	50	FEMALE	White	ANOXIA	Positive	Positive
418	52	MALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Negative
456	53	MALE	White	ANOXIA	Positive	Negative
380	53	FEMALE	White	CEREBROVASCULAR/STROKE	Positive	Negative
367	54	FEMALE	Unknown	ANOXIA	Positive	Positive
396	56	MALE	Black or African American	ANOXIA	Positive	Positive
342	59	MALE	Hispanic/Latino	ANOXIA	Positive	Positive
422	60	MALE	White	ANOXIA	Positive	Negative
374	62	FEMALE	White	ANOXIA	Positive	Positive
348	62	FEMALE	Hispanic/Latino	CEREBROVASCULAR/STROKE	Positive	Positive
439	62	FEMALE	White	CEREBROVASCULAR/STROKE	Positive	Negative
438	64	MALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Positive
412	66	MALE	White	ANOXIA	Positive	Negative
308	68	MALE	Hispanic/Latino	HEAD TRAUMA	Positive	Positive
349	69	FEMALE	Hispanic/Latino	CEREBROVASCULAR/STROKE	Positive	Positive
427	69	MALE	Hispanic/Latino	HEAD TRAUMA	Positive	Positive
455	70	MALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Positive
450	71	FEMALE	Hispanic/Latino	ANOXIA	Positive	Positive
424	71	FEMALE	Black or African American	CEREBROVASCULAR/STROKE	Positive	Positive
411	72	MALE	Hispanic/Latino	ANOXIA	Positive	Positive
347	73	FEMALE	Asian	CEREBROVASCULAR/STROKE	Positive	Positive
345	73	FEMALE	White	ANOXIA	Positive	Positive
464	75	FEMALE	Asian	ANOXIA	Positive	Positive
337	76	FEMALE	White	CEREBROVASCULAR/STROKE	Positive	Positive
423	83	MALE	White	ANOXIA	Positive	Positive
364	87	FEMALE	White	CEREBROVASCULAR/STROKE	Positive	Positive
391	92	FEMALE	Hispanic/Latino	CEREBROVASCULAR/STROKE	Positive	Positive

Table S3. Related to Figure 4. Pathways enriched in CD56^{bright}CD16⁻ vs. CD56^{dim}CD16⁺ NK cells

Term	Overlap	Enrich_log2FC	P.value	Adjusted.P.value	Genes	Direction	Source
Cytokine-cytokine receptor interaction_Homo sapiens_hsa04060	20/265	2.714301874	3.43E-11	6.37E-09	IL1R1;FLT3;IL23R;IFNGR2;FLT4;LIF;IL18;CXCR6;BMP2;CXCR3;KIT;XCL2;CD27;XCL1;TNFSF8;CCR7;LTB;CCR5;IL6ST;IL7R	up	KEGG
Jak-STAT signaling pathway_Homo sapiens_hsa04630	8/158	2.13844158	0.000497145	0.011558613	SOCS3;CDKN1A;MYC;IL23R;IFNGR2;LIF;IL6ST;IL7R	up	KEGG
Chemokine signaling pathway_Homo sapiens_hsa04062	8/187	1.895327869	0.001483821	0.021926169	CXCR3;XCL2;ADCY3;XCL1;CCR7;CXCR6;CCR5;GNAI1	up	KEGG
Focal adhesion_Homo sapiens_hsa04510	7/202	1.591365768	0.009013482	0.062092877	COL4A4;FLT4;ITGA1;TNR;FLNB;COL9A2;BIRC3	up	KEGG
interferon-gamma-mediated signaling pathway (GO:0060333)	11/204	2.229228605	2.54E-05	0.010921785	SOCS3;GREM2;CIITA;FLT3;IFNGR2;KIT;XCL2;XCL1;HLA-DRA;HLA-DRB3;IL6ST	up	GO-BP
positive regulation of MAPK cascade (GO:0043410)	10/194	2.164237581	8.66E-05	0.022400282	BMP2;FLT3;INSR;LRRK2;FLT4;KIT;LPAR1;LIF;DAB2IP;AXIN2	up	GO-BP
interleukin-1-mediated signaling pathway (GO:0070498)	9/157	2.317526581	8.72E-05	0.022400282	SOCS3;GREM2;IL1R1;FLT3;KIT;XCL2;DAB2IP;XCL1;IL6ST	up	GO-BP
Notch signaling pathway (GO:0007219)	5/46	3.240588467	0.000179759	0.022400282	BMP2;MAML2;MYC;DTX1;MAML3	up	GO-BP
regulation of natural killer cell proliferation involved in immune response (GO:0032820)	10/190	1.947027725	0.000293849	0.054212009	NCR3;FCGR3A;SIGLEC9;KIR2DS2;LILRB1;KIR3DL1;CD247;KIR2DL1;KIR2DL2;KIR2DL3	down	GO-BP
regulation of natural killer cell differentiation involved in immune response (GO:0032826)	10/190	1.947027725	0.000293849	0.054212009	NCR3;FCGR3A;SIGLEC9;KIR2DS2;LILRB1;KIR3DL1;CD247;KIR2DL1;KIR2DL2;KIR2DL3	down	GO-BP
positive regulation of cell migration (GO:0030335)	13/193	1.421280471	0.001244519	0.107302814	PDGFRB;INSR;SPHK1;SYNE2;DAB2;BMP2;ABI3;FAM110C;CTSH;FLNA;SPRY2;CCR7;LGR6	both	GO-BP
plasmacytoid dendritic cell chemotaxis (GO:0002410)	5/16	3.635225885	3.42E-05	0.017421465	CXCR1;GPR183;CXCR2;CCR7;CCR5	both	GO-BP

Table S6. Related to Figure 7. Cluster contribution

Cluster ID	% of total NK cells analyzed
1	8.7
2	9.8
3	2.5
4	1.7
5	11
6	8.8
7	1.3
8	7.7
9	6.7
10	4.2
11	6.6
12	0.9
13	5.6
14	9.7
15	14.8