

# Supplemental Table 1: Enriched GO categories per cluster

Cluster	Enriched with	#genes	Raw p-value	Corrected p-value	Frequency in set (%)
Cluster 1	immune response - GO:0006955	32	2.36E-14	0.001	13.5
Cluster 1	cellular defense response - GO:0006968	12	1.10E-11	0.001	5.06
Cluster 1	defense response - GO:0006952	25	3.21E-10	0.001	10.54
Cluster 1	cell motility - GO:0006928	18	5.36E-08	0.001	7.59
Cluster 1	cytolysis - GO:0019835	5	4.71E-07	0.002	2.1
Cluster 1	leukocyte chemotaxis - GO:0030595	5	3.02E-06	0.005	2.1
Cluster 1	taxis - GO:0042330	10	3.27E-06	0.007	4.21
Cluster 1	viral genome replication - GO:0019079	5	3.88E-06	0.008	2.1
Cluster 1	cell adhesion - GO:0007155	22	3.88E-06	0.008	9.28
Cluster 1	extracellular space - GO:0005615	18	5.30E-06	0.008	7.59
Cluster 1	signal transducer activity - GO:0004871	44	8.09E-06	0.014	18.56
Cluster 1	antigen processing - GO:0002504	4	1.02E-05	0.018	1.68
Cluster 2	mitotic cell cycle - GO:0000278	15	9.04E-18	0.001	30.61
Cluster 2	cell cycle - GO:0007049	19	2.84E-15	0.001	38.77
Cluster 2	microtubule cytoskeleton - GO:0015630	10	2.08E-09	0.001	20.4
Cluster 2	cell cycle checkpoint - GO:0000075	5	9.40E-08	0.001	10.2
Cluster 2	microtubule-based process - GO:0007017	7	1.58E-07	0.001	14.28
Cluster 2	spindle organization and biogenesis - GO:0007051	4	1.62E-07	0.001	8.16
Cluster 2	establishment of organelle localization - GO:0051656	4	1.96E-07	0.001	8.16
Cluster 2	chromosome segregation - GO:0007059	4	7.34E-06	0.014	8.16
Cluster 3	regulation of metabolic process - GO:0019222	28	3.69E-05	0.046	25
Cluster 4	immune response - GO:0006955	6	2.57E-06	0.004	33.33

Each of the four clusters of Figure 1C was analyzed for enrichment of GO categories using the TANGO algorithm in Expander. Only GO categories are reported that are significant after correction for multiple testing (corrected  $P \leq 0.05$ ). # genes: number of genes that appear in the cluster and that are also annotated with the GO annotation. Raw P-value: hypergeometric enrichment P-value. Corrected P-value: significance level after the multiple testing correction performed by TANGO. Frequency in set: percentage of genes in a cluster that are annotated with the GO annotation.

## Supplemental Table 2

### Changes in expression of different categories of genes: Cell cycle

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
			Peak	1 year	Latency	Effector type	Memory
<b>TYMS</b>		NM_001071	109.5	10.8	7.3	<i>1.1</i>	<i>1.6</i>
<b>CDCA7</b>	JPO1	NM_031942	82.3	17.1	8.8	<i>1.4</i>	<i>2.2</i>
<b>UHRF1</b>		NM_013282	55.5	2.7	1.3	<i>1.0</i>	<i>-1.5</i>
<b>SAP30</b>		NM_003864	29.9	24.0	17.7	13.7	7.9
<b>NCAPG</b>	Condensin G	NM_022346	27.7	7.6	2.4	<i>1.0</i>	<i>1.5</i>
<b>MKI67</b>	Ki67	NM_002417	23.1	2.3	<i>-1.0</i>	<i>-1.5</i>	<i>-1.0</i>
<b>RBBP8</b>	CtIP	NM_002894	17.3	2.8	1.7	3.4	4.8
<b>CDCA5</b>		NM_080668	15.6	1.3	1.7	<i>1.4</i>	<i>1.9</i>
<b>CDC6</b>		NM_001254	15.4	1.6	1.3	<i>-1.0</i>	<i>-1.1</i>
<b>BIRC5</b>	Survivin	BC000784	15.4	1.1	1.2	<i>1.1</i>	<i>1.0</i>
<b>CEP55</b>		NM_018131	15.0	2.0	<i>-1.1</i>	<i>1.0</i>	<i>1.6</i>
<b>TK1</b>		NM_003258	14.9	1.7	1.4	<i>1.2</i>	<i>1.1</i>
<b>MCM4</b>		NM_005914	14.0	2.3	2.7	<i>1.6</i>	<i>1.4</i>
<b>CENPF</b>	Mitosin	NM_016343	13.8	1.1	1.2	<i>-1.3</i>	<i>1.3</i>
<b>G0S2</b>		NM_015714	10.6	18.2	29.5	<i>-1.9</i>	<i>1.5</i>
<b>NUSAP1</b>		NM_018454	10.3	2.4	3.1	<i>1.1</i>	<i>1.3</i>
<b>CDC2</b>		NM_001786	10.2	1.4	1.6	<i>1.1</i>	<i>1.2</i>
<b>CDC7</b>		NM_003503	6.2	3.5	3.0	<i>1.6</i>	<i>1.3</i>
<b>DTYMK</b>	CDC8	AF258562	5.4	3.0	1.3	<i>-1.3</i>	<i>-2.2</i>
<b>MCM10</b>		AB042719	5.0	<i>-1.1</i>	1.0	<i>1.1</i>	<i>1.0</i>
<b>CDC50B</b>		AK091169	-7.3	-6.1	-4.5	<i>1.6</i>	<i>1.3</i>
<b>TCEAL3</b>		NM_032926	-12.4	-5.6	-3.0	<i>1.4</i>	<i>1.5</i>
<b>CSNK1D</b>		NM_152675	-13.5	-9.1	-15.0	<i>1.5</i>	<i>1.3</i>

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

## Supplemental Table 3

### Changes in expression of different categories of genes: Metabolism

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
			Peak	1 year	Latency	Effector type	Memory
HBB		NM_000518	55.8	23.3	6.8	<i>1.6</i>	<i>2.2</i>
ATP2B4		AK026443	27.8	35.1	7.9	5.4	2.4
SCD5		AL831891	26.9	30.3	6.2	<i>1.7</i>	<i>-1.0</i>
RRM2		BC030154	26.8	7.7	2.4	<i>1.0</i>	<i>1.0</i>
SLC27A2		NM_003645	23.5	9.6	3.9	<i>1.2</i>	<i>1.4</i>
HBA2		NM_000517	14.6	9.6	3.0	<i>1.3</i>	<i>1.1</i>
SLC14A1		AF263545	13.8	12.2	5.2	<i>1.8</i>	<i>1.2</i>
SLCO4C1		AF119865	11.1	22.1	11.5	3.3	2.0
AYTL2		NM_024830	10.1	12.0	6.0	5.8	3.3
GFOD1		NM_018988	10.1	12.4	7.0	7.2	2.7
IDH2		NM_002168	8.1	3.6	1.9	3.4	2.1
RRM2		BC030154	8.0	<i>1.7</i>	<i>1.0</i>	-2.5	-4.7
ENTPD1		NM_001776	7.0	10.2	1.3	<i>1.0</i>	<i>1.0</i>
AQP9		NM_020980	6.0	3.6	4.9	<i>1.2</i>	<i>1.4</i>
GLUL		NM_002065	5.9	8.2	10.4	8.7	6.8
ACADM		NM_000016	5.7	2.7	-1.8	<i>1.4</i>	<i>1.2</i>
ADCY7		NM_001114	5.3	6.1	2.1	<i>1.8</i>	<i>1.1</i>
G6PD		M12996	-8.1	-7.1	-12.8	-8.7	-4.8
EPHX2		NM_001979	-12.3	-9.0	-10.9	-5.1	-4.5
SLC16A10		NM_018593	-28.8	-25.6	-24.4	<i>-1.6</i>	<i>-1.1</i>
AK5		BC012467	-30.6	-20.7	-12.4	-4.7	-10.3

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

## Supplemental Table 4

### Changes in expression of different categories of genes: BCL-2 family members

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
			Peak	1 year	Latency	Effector type	Memory
BAD		NM_004322	<i>1.4</i>	<i>1.3</i>	<i>1.3</i>	<i>1.2</i>	<i>1.1</i>
BAK		BC004431	<i>3.1</i>	<i>2.1</i>	<i>1.6</i>	<i>1.9</i>	<i>1.8</i>
BAX		NM_004324	<i>-1.1</i>	<i>-1.5</i>	<i>-1.1</i>	<i>1.0</i>	<i>1.0</i>
BCL2		AK022111	<i>-1.3</i>	<i>-1.2</i>	<i>-1.3</i>	<i>-3.3</i>	<i>-2.6</i>
BCL2A1		NM_004049	<i>1.7</i>	<i>1.6</i>	<i>1.5</i>	<i>-1.8</i>	<i>1.4</i>
BCL2L12		NM_138639	<i>1.2</i>	<i>-1.0</i>	<i>1.1</i>	<i>1.3</i>	<i>1.1</i>
BCLG	BCL2L14	NM_030766	<i>2.0</i>	<i>-1.2</i>	<i>-1.2</i>	<i>-1.0</i>	<i>1.1</i>
BCL-RAMBO	BCL2L13	NM_015367	<i>1.8</i>	<i>1.4</i>	<i>-1.8</i>	<i>-1.3</i>	<i>-1.3</i>
BCL-W		NM_004050	<i>1.2</i>	<i>1.0</i>	<i>-1.5</i>	<i>1.3</i>	<i>1.2</i>
BCL-XL		NM_001191	<i>-1.0</i>	<i>1.1</i>	<i>-1.1</i>	<i>-1.2</i>	<i>-1.1</i>
BCL-XS	BCL2L1	NM_001191	<i>-1.0</i>	<i>1.1</i>	<i>-1.1</i>	<i>-1.2</i>	<i>-1.1</i>
BIK		NM_001197	<i>1.2</i>	<i>-1.1</i>	<i>1.5</i>	<i>2.1</i>	<i>2.6</i>
BIM	BCL2L11	AF455755	<i>2.7</i>	<i>1.3</i>	<i>2.3</i>	<i>1.2</i>	<i>1.2</i>
BOK		NM_032515	<i>-1.2</i>	<i>-1.5</i>	<i>-1.2</i>	<i>-1.9</i>	<i>-1.4</i>
DIVA	BCL2L10	NM_020396	<i>-1.8</i>	<i>-1.8</i>	<i>-1.4</i>	<i>-1.2</i>	<i>-1.2</i>
MCL1		NM_021960	<i>1.9</i>	<i>1.3</i>	<i>1.9</i>	<i>1.6</i>	<i>2.2</i>

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

## Supplemental Table 5

### Changes in expression of different categories of genes: Apoptosis

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV* donor	Healthy HCMV* donor	
			Peak	1 year	Latency	Effector type	Memory
<b>ANXA2</b>		NM_004039	20.5	18.2	7.8	7.2	6.8
<b>ANXA4</b>		NM_0011153	16.6	8.3	2.3	<i>1.3</i>	<i>-1.1</i>
<b>BIRC4BP</b>	XAF-1	AK091799	16.1	5.7	<i>1.4</i>	<i>1.4</i>	<i>1.3</i>
<b>ANXA2P3</b>		NR_001446	11.7	10.3	5.3	3.6	5.3
<b>DIP</b>		AB018310	10.7	10.7	2.9	2.3	2.7
<b>ANXA5</b>		NM_0011154	10.6	7.9	4.6	2.9	3.2
<b>UBE2C</b>		NM_181803	10.5	<i>1.4</i>	<i>1.0</i>	<i>1.1</i>	<i>1.3</i>
<b>CASP1</b>		NM_033292	10	4.5	2.5	2.6	1.7
<b>TNFSF10</b>	TRAIL	NM_003810	8.8	2.7	2.4	<i>1.1</i>	<i>1.0</i>
<b>FASLG</b>	TNFSF6	NM_000639	7.2	6.5	8.1	3.0	2.7
<b>FAS</b>	CD95	AK026195	5.0	4.0	4.7	<i>1.3</i>	<i>1.8</i>
<b>ENC1</b>		AY049781	4.5	6.6	11.4	8.2	9.7
<b>PMAIP1</b>	NOXA	BC032663	4.2	1.9	17.1	4.5	5.1
<b>TP53</b>	p53	NM_000546	3.6	2.9	<i>-1.0</i>	<i>-1.1</i>	<i>-1.1</i>
<b>TP53I3</b>	PIG3	NM_004881	3.6	2.2	<i>1.2</i>	<i>-1.1</i>	<i>1.3</i>
<b>TNFAIP3</b>		M59465	-4.8	-3.5	<i>-1.1</i>	<i>1.6</i>	<i>2.1</i>

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

# Supplemental Table 6

## Changes in expression of different categories of genes: Transcription factors

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
			Peak	1 year	Latency	Effector type	Memory
EOMES		NM_005442	23.5	27.0	14.4	5.3	6.1
CEBPD		NM_005195	19.9	12.8	7.5	5.1	21.6
CTBP2		NM_022802	18.4	23.7	5.4	11.3	2.2
ZC3HAV1L		BC020784	18.0	2.5	<i>1.1</i>	<i>1.8</i>	<i>1.5</i>
ZEB2	SIP1	BC035706	17.9	13.6	14.7	4.0	4.1
MELK		NM_014791	16.1	6.4	2.7	1.2	1.2
JAZF1		NM_175061	15.6	18.4	10.1	5.9	2.1
TBX21	T-bet	NM_013351	15.2	22.1	15.5	17.6	6.8
ZNF683		NM_173574	11.9	10.1	12.1	17.7	4.7
RNF135		NM_032322	11.8	9.5	6.0	2.6	3.1
ASCL2		BC028140	11.1	24.8	4.6	7.6	<i>1.0</i>
PRDM1	Blimp-1	NM_001198	10.9	10.5	12.0	3.1	5.4
BATF		NM_006399	10.7	10.8	2.6	6.7	2.0
ZBTB32		NM_014383	10.3	5.7	6.0	2.5	3.6
E2F2		BC007609	10.1	3.4	<i>1.3</i>	<i>1.1</i>	<i>1.3</i>
IRF4		NM_002460	10.0	5.2	4.0	5.6	2.7
MYBL1		X66087	8.9	17.0	12.5	4.8	2.8
ZEB2		NM_014795	8.7	12.1	21.1	9.8	4.4
ZFHX1B	SIP1	AK098835	7.6	11.6	12.7	7.0	6.4
SMAD3		NM_015400	7.6	11.5	9.7	3.4	3.6
ZNF365		NM_014951	<i>-1.2</i>	6.6	48.4	3.0	1.8
MYC		NM_002467	<i>-1.2</i>	-6.9	-8.9	-6.2	-2.1
MYB		NM_005375	-3.6	-11.3	-8.4	-2.6	-3.0
LEF1		AF086339	-13.2	-17.0	-15.2	-5.0	-5.3
ZNF165		NM_003447	-14.6	-15.1	-4.5	-3.5	1.3
ZNF395	PBF	NM_017606	-14.9	-8.2	<i>-1.3</i>	<i>-1.3</i>	<i>-1.5</i>
ZNF516		NM_014643	-16.3	-9.6	-18.2	4.9	1.0
ZMAT1		AL831883	-16.4	-6.5	-2.3	-2.5	-2.9
BACH2		NM_021813	-17.4	-12.1	-9.8	-1.7	-1.7
KLF7		NM_003709	-17.7	-13.2	-13.6	-1.2	-1.8
ZSCAN18		NM_023926	-18.5	-9.6	-10.9	-5.6	-2.5
ZNF238		NM_006352	-19.6	-17.0	-6.4	<i>1.0</i>	<i>-1.4</i>
PLAG1		NM_002655	-30.5	-25.6	-25.8	-13.3	-11.2
ZNF516		BM471507	-30.6	-37.5	-26.3	-9.9	-9.5
NR3C2		NM_000901	-54.4	-28.1	-4.8	-6.2	-4.0
SCML1		NM_006746	-117.5	-76.0	-35.0	-4.2	-3.5

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

## Supplemental Table 7

### Changes in expression of different categories of genes: Adhesion and migration

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
			Peak	1 year	Latency	Effector type	Memory
ITGAD	CD11D	I_964636	28.8	17.4	-1.3	10.1	-1.5
CX3CR1		NM_001337	83.5	94.4	12.9	10.1	-1.5
CCR1		NM_001295	34.8	7.9	2.9	-1.7	1.6
CCR5		NM_000579	33.5	11.1	2.4	2.1	3.6
VCAM1		NM_001078	23.7	19.2	8.9	1.4	1.9
CXCR6		I_948770	19.7	11.0	5.0	2.3	22.8
CD36		NM_000072	17.3	13.1	4.4	1.0	1.0
ADAM8	CD156	NM_001109	9.9	13.1	8.4	9.0	5.7
ITGB2	LFA-1	NM_000211	9.6	11.3	4.6	5.3	2.0
Tetraspan 2		I_937677	6.3	7.3	1.9	2.7	1.9
VCL	Vinculin	I_932014	3.4	8.7	2.1	-1.2	-1.6
ITGAL	LFA-1	NM_002209	4.9	9.0	3.8	3.0	2.0
ITGB1		NM_002211	3.8	11.5	4.8	6.7	4.1
PECAM1		NM_000442	3.1	2.8	-3.4	-2.9	-1.7
SELL	L-selectin, CD62L	BC020758	1.2	-1.4	-14.0	-3.8	-2.7
ITGA6	CD49f	NM_000210	-4.1	-3.9	-10.7	-4.3	-3.9
AMIGO1		AB032989	-4.8	-2.9	-7.0	-1.9	-2.5
NRCAM		NM_005010	-6.6	-5.9	-5.1	-2.2	-2.1
JAM3		NM_032801	-8.2	-6.6	-1.8	1.2	1.3
ROBO1		NM_133631	-27.2	-24.6	-26.1	-2.5	-4.7
CCR7		NM_001838	-29.1	-26.6	-29.5	-18.3	-3.4

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

## Supplemental Table 8

### Changes in expression of different categories of genes: Cytokine receptors

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
			Peak	1 year	Latency	Effector type	Memory
IL28RA		NM_170743	8.4	8.4	4.3	3.3	3.5
IL2RB	CD122	NM_000878	5.5	4.8	2.8	4.0	4.1
IL2RG	CD132	NM_000206	4.9	5.1	1.6	<i>1.1</i>	<i>1.0</i>
IL18R1		NM_003855	4.7	6.3	9.1	2.7	3.3
IL6R		X12830	-5.4	-3.7	-6.6	-4.1	-8.3
IL7RA		I_1002172	-30.8	-14.7	-5.0	-6.0	-1.2

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.



## Supplemental Table 9

### Changes in expression of different categories of genes: Exhaustion and differentiation

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
			Peak	1 year	Latency	Effector type	Memory
CD38		NM_001775	37.0	3.0	1.5	1.5	2.4
F2R		NM_020182	22.8	27.6	22.0	5.5	9.7
SLAMF7		NM_003242	21.0	25.7	15.4	5.8	3.1
LAG3		NM_002286	18.3	17.3	13.0	7.2	6.8
VSTM3		NM_003243	18.1	10.7	4.3	2.7	3.1
PDGFD		NM_000218	17.1	24.8	6.3	1.7	1.2
TSPAN5		NM_002526	13.6	9.8	3.6	4.2	2.9
CD160		NM_007053	13.6	14.5	10.1	1.3	-1.1
CD244	2B4	NM_016382	13.5	10.6	7.1	1.4	1.3
TSPAN2		NM_003498	13.1	12.9	1.0	1.3	-1.0
EDG8		AK026295	12.5	15.6	16.3	12.8	9.2
HAVCR2	TIM3	BC020843	11.6	7.2	2.4	-1.3	1.2
SLAMF6		NM_015103	11.5	11.7	1.9	1.3	1.2
CD70		NM_001252	10.1	4.5	2.7	1.6	1.4
KLRG1		NM_005810	9.6	17.5	8.0	1.1	1.0
KLRC1	NKG2A	NM_002259	9.0	8.0	1.2	8.2	2.1
TGFBR3		BC024020	7.7	11.1	11.8	9.5	6.1
PTGER2		NM_000956	7.3	6.1	3.4	1.6	1.1
TMEM49		NM_030760	6.1	8.7	5.0	6.7	6.4
PDCD1	PD-1	NM_005018	2.9	6.2	3.5	1.2	3.4
CTLA4		AY209009	2.4	2.2	1.2	-1.3	-1.3
CD27		NM_001242	2.3	1.6	-3.1	-1.9	-1.3
PLXND1		NM_015103	1.0	6.9	13.8	9.0	13.1
CD28		NM_006139	-2.8	-14.2	-12.5	-13.3	-1.0
SERINC5	TPO1	NM_005725	-6.0	-15.1	-9.9	-7.2	-4.4
TGFBR2		NM_005723	-7.1	-5.9	-3.8	-2.6	-3.1
SNN	Stannin	AL833175	-8.0	-10.0	-12.6	-10.4	-4.3
NT5E	CD73	NM_002526	-10.2	-5.9	-5.6	-1.3	-1.8
KCNQ1		NM_052931	-12.02	-9.5	-10.0	-19.9	-4.8
TMEPAI		NM_001992	-14.4	-15.8	-2.1	-1.7	5.1
VIPR1		NM_004624	-17.5	-7.5	-9.4	-2.8	-1.8
MAL		NM_001775	-23.7	-17.6	-18.4	-7.8	-3.8

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

# Supplemental Table 10

## Changes in expression of different categories of genes: Effector molecules

Gene symbol	Alias	Accession Nr.	Primary CMV infection		Healthy HCMV* donor	Healthy HCMV* donor	
			Peak	1 year	Latency	Effector type	Memory
<b>Cytokines</b>							
IL32		NM_004221	8.3	9.9	1.6	2.0	1.6
IL1B		NM_000576	1.2	6.4	24.6	-1.6	-1.0
IL23A		NM_016584	-14.2	-14.4	-5.2	-5.3	-1.6
<b>Chemokines</b>							
IL8	CXCL8	NM_000584	29.2	24.4	73.7	1.8	2.3
CCL4	Mip-1 $\beta$	NM_002984	26.5	47.2	52.4	16.1	8.7
CCL5	Rantes	NM_002985	11.4	21.2	16.2	12.7	10.2
CKLF		NM_016326	10.8	8.0	2.2	1.5	1.8
XCL1		NM_002995	8.3	5.0	4.7	4.9	3.4
CXCL7		NM_002704	8.2	6.2	3.8	1.0	-1.2
CCL3	Mip-1 $\alpha$	NM_002983	7.9	7.5	14.8	5.9	2.8
CCL3L1		NM_021006	7.0	6.5	13.3	2.2	1.3
XCL2		NM_003175	6.7	4.6	4.1	3.9	2.8
CMTM1		NM_052999	6.5	4.0	2.6	1.0	1.0
CXCL4		NM_002619	5.7	3.8	1.6	-1.2	-1.1
CXCL10	IP10	NM_001565	4.9	1.6	7.3	1.1	1.2
CCL23		NM_005064	4.5	1.6	7.6	1.2	1.4
CXCL2		NM_002089	2.1	3.0	8.1	1.1	1.3
CMTM8		NM_178868	-2.6	-7.8	-5.6	-6.7	-2.7
<b>Effector molecules</b>							
GZMA		I_958171	69.9	64.0	27.1	33.0	16.1
S100A8		NM_002964	63.8	50.2	24.2	1.6	2.1
GZMB		NM_004131	51.2	49.4	48.6	22.3	1.8
LYZ		NM_000239	24.8	28.8	29.2	-1.2	1.0
GZMH		NM_033423	23.1	32.7	27.6	23.9	4.4
GNLY		NM_006433	19.5	25.4	19.5	16.9	5.3
SPON2		NM_012445	18.6	17.8	16.7	19.3	1.9
CKLF		NM_016951	10.2	7.1	2.0	1.1	1.0
S100A9		NM_002965	17.6	20.3	17.8	1.0	1.0
FGFBP2		NM_031950	13.8	30.5	29.2	20.8	2.6
GZMK		NM_002104	13.5	7.3	3.0	4.3	10.4
PRF1		NM_005041	10.3	12.7	5.5	4.4	2.6
PROK2		NM_021935	1.3	9.8	32.4	41.6	1.4
TGFB1		NM_000660	-1.1	2.3	2.8	4.8	6.4
LTB		NM_002341	-8.1	-10.3	-11.3	-7.5	-1.3
SECTM1		NM_003004	15.3	14.7	5.2	1.1	1.0
BTBD11		NM_152322	-10.3	-19.3	-5.6	-2.7	1.2
PCSK5		AK023096	-11.9	-11.8	-19.6	-1.8	-3.9
NELL2		NM_006159	-13.2	-12.6	-36.5	-11.4	-2.3
TANC2		AB032974	-14.6	-14.1	-1.5	1.2	-1.3
SCGB3A1		NM_013409	-18.3	-10.4	-9.9	-2.1	-2.3
SPINK2		NM_052863	-18.7	-21.6	-17.8	-10.5	-7.8
CA6		NM_021114	-43.9	-31.2	-24.7	-4.3	-5.5

Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

## Supplemental Table 11

### Changes in expression of different categories of genes: Genes regulated by IFN $\gamma$

Gene symbol	Accession Nr.	Primary CMV infection		Healthy HCMV <sup>+</sup> donor	Healthy HCMV <sup>+</sup> donor	
		Peak	1 year	Latency	Effector type	Memory
IFNG	NM_000619	38.8	42.4	53.6	16.8	7.7
IFI27	NM_005532	25.3	17.3	<i>1.5</i>	<i>1.3</i>	<i>1.3</i>
IFI16	I_1997689	20.5	25.6	15.8	11.4	7.4
OAS1	NM_002534	18.2	4.7	<i>1.4</i>	<i>1.7</i>	<i>1.2</i>
IFI44L	NM_006820	11.5	-1.4	<i>-1.6</i>	<i>-1.3</i>	<i>-1.3</i>
IFI30	J03909	11.5	10.9	4.8	<i>-1.1</i>	<i>-1.1</i>
IRF4	NM_002460	10.0	5.2	4.0	5.6	2.7
ISG15	NM_005101	9.0	2.5	<i>1.6</i>	<i>1.6</i>	<i>1.5</i>
IFIT1	NM_001548	7.8	-1.2	13.7	3.9	2.0
IFIT3	NM_001549	7.0	<i>1.2</i>	24.8	5.8	2.8
MX1	NM_002462	5.3	<i>-1.6</i>	<i>-2.0</i>	<i>-2.8</i>	<i>-1.1</i>
ISG20	NM_002201	4.6	1.9	<i>2.0</i>	<i>1.8</i>	<i>1.8</i>
OASL	NM_003733	4.4	2.1	18.9	15.2	6.1
IFIT2	NM_001547	2.7	<i>1.2</i>	18.9	7.9	2.3
IFIT2	BC005987	2.3	<i>1.5</i>	20.5	17.1	4.8
IFNAR1	NM_000629	-1.6	-1.7	-2.6	<i>-1.4</i>	<i>1.3</i>
IFNGR2	NM_005534	-3.7	-4.0	-3.7	-3.0	-3.3

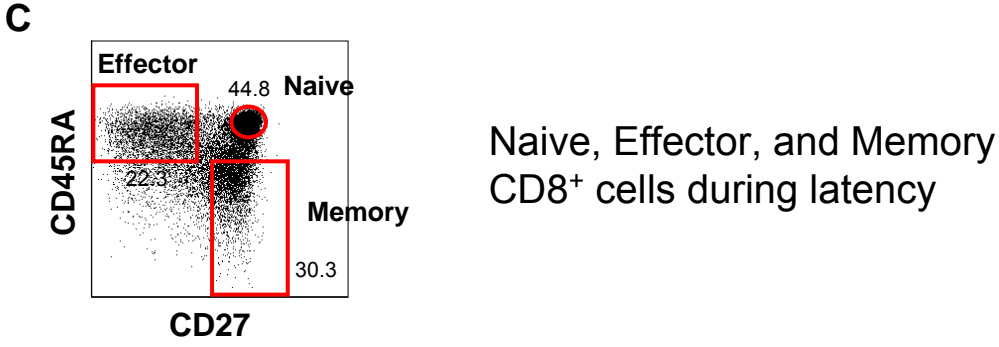
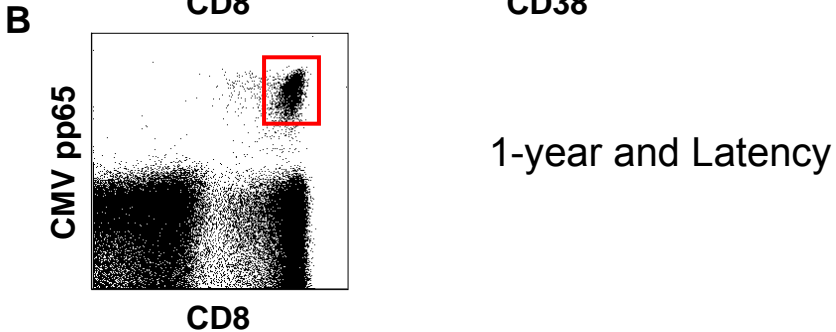
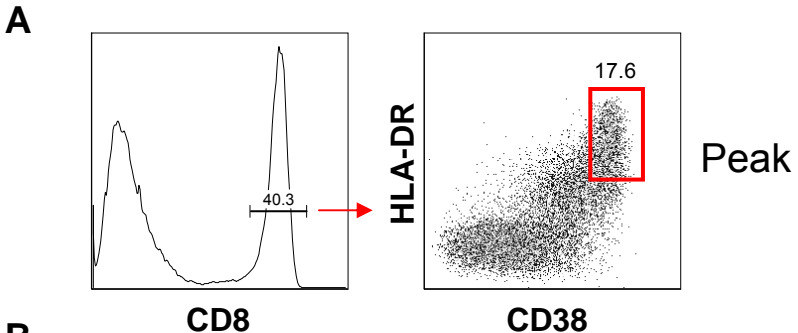
Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells. Fold changes < 2 are denoted in italics.

Supplemental Table 12: Genes with similar fold change between latent HCMV and exhausted LCMV CD8<sup>+</sup> T cells

Agilent ID	Symbol	Affymetrix ID	HCMV	LCMV
A_23_P343398	CCR7	104443_at	-29.55	-5.99
A_24_P20630	LEF1	103629_g_at	-24.96	-5.39
A_23_P213045	LEF1	103629_g_at	-15.25	-5.39
A_23_P103522	SELL	102838_at	-14.03	-3.15
A_23_P204208	KLRD1	93677_at	33.57	-2.5
A_23_P105957	ACTN1	104578_f_at	-19.28	-2.43
A_23_P93348	LTB	102940_at	-11.26	-2.31
A_23_P68601	CST7	102638_at	23.31	2.12
A_24_P261760	KLRG1	95320_at	11.96	2.59
A_23_P116942	LAG3	98392_at	13.02	3.25
A_23_P213562	F2R	95474_at	22.03	3.26
A_23_P350451	PRDM1	92904_at	12.02	3.56
A_23_P206284	GPR56	102787_at	10.58	3.85
A_23_P207564	CCL4	94146_at	52.38	4.01
A_23_P354341	CD160	102272_at	10.09	4.08
A_23_P151294	IFNG	99334_at	53.62	9.12
A_24_P97374	EOMES	103532_at	14.4	10.58
A_24_P228130	CCL3L3	102424_at	13.3	10.69
A_23_P133445	GZMA	102995_s_at	27.07	11.18
A_23_P117602	GZMB	102877_at	48.56	15.09
A_23_P152838	CCL5	98406_at	16.18	23.46

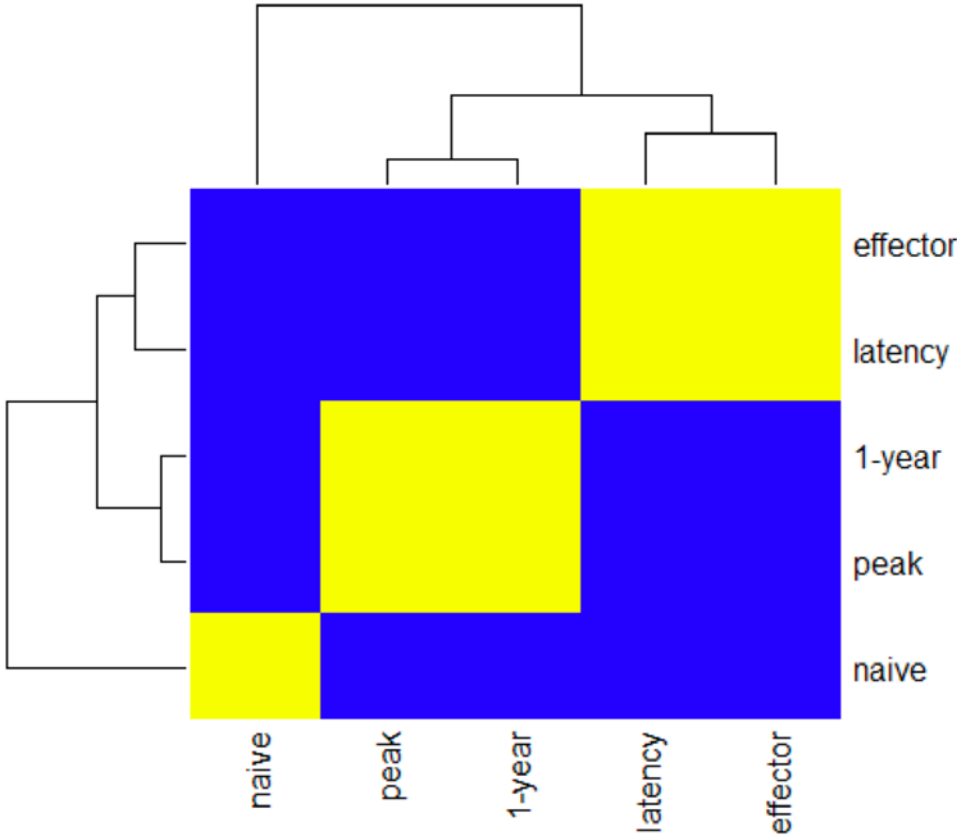
Numbers denote mean changes of replicate samples compared to the pool of purified naive CD8<sup>+</sup> T cells.

# Supplemental Figure 1



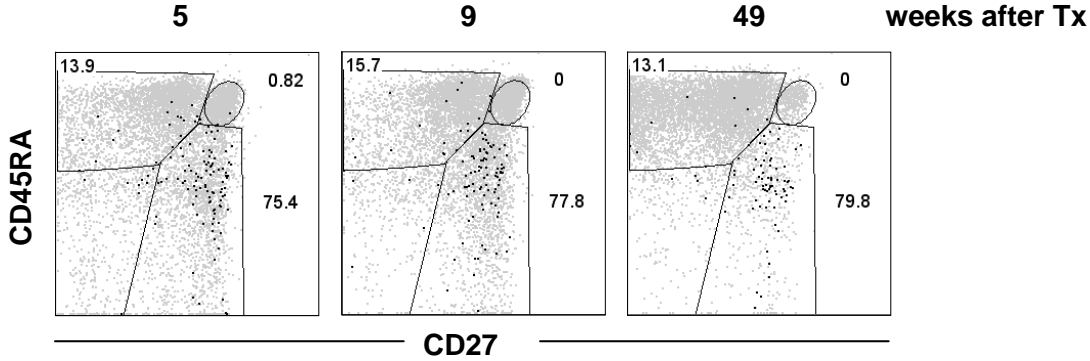
Sort windows of microarray samples. (A) To obtain HCMV-specific cells for RNA isolation, at the peak of the HCMV infection all highly activated cells were sorted (CD8<sup>+</sup>CD38<sup>+</sup>HLA-DR<sup>+</sup>). (B) Cells at 1-year and latency were sorted with HCMV-pp65 tetramers. (C) Sort windows for naive (CD8<sup>+</sup>CD45RA<sup>+</sup>CD27<sup>+</sup>), effector-type (CD8<sup>+</sup>CD45RA<sup>+</sup>CD27<sup>-</sup>), and memory-type cells (CD8<sup>+</sup>CD45RA<sup>-</sup>CD27<sup>+</sup>).

# Supplemental Figure 2



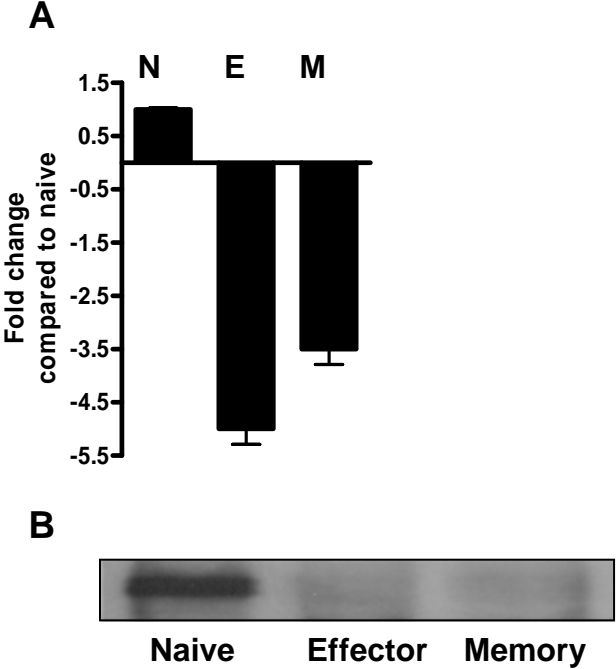
Consensus matrix for the hierarchical clustering of Figure 1A. The consensus matrix is a visual representation of the clustering results and the stability of the sample clusters across 200 bootstrap samples. Samples that remain consistently clustered together across different bootstrap samples have a high consensus. Blue indicates no consensus, yellow indicates maximal consensus across bootstrap samples from the original data. Note that the clustering in three groups (naive), (peak, 1-year), (latency, effector) is highly stable.

# Supplemental Figure 3



EBV-reactive cells during the primary HCMV infection have a memory phenotype. At the timepoints pre and during HCMV infection (weeks 5, 9, and 49) EBV tetramer<sup>+</sup> cells express markers indicating a stable predominantly memory (CD8<sup>+</sup>CD45RA<sup>-</sup>CD27<sup>+</sup>) phenotype.

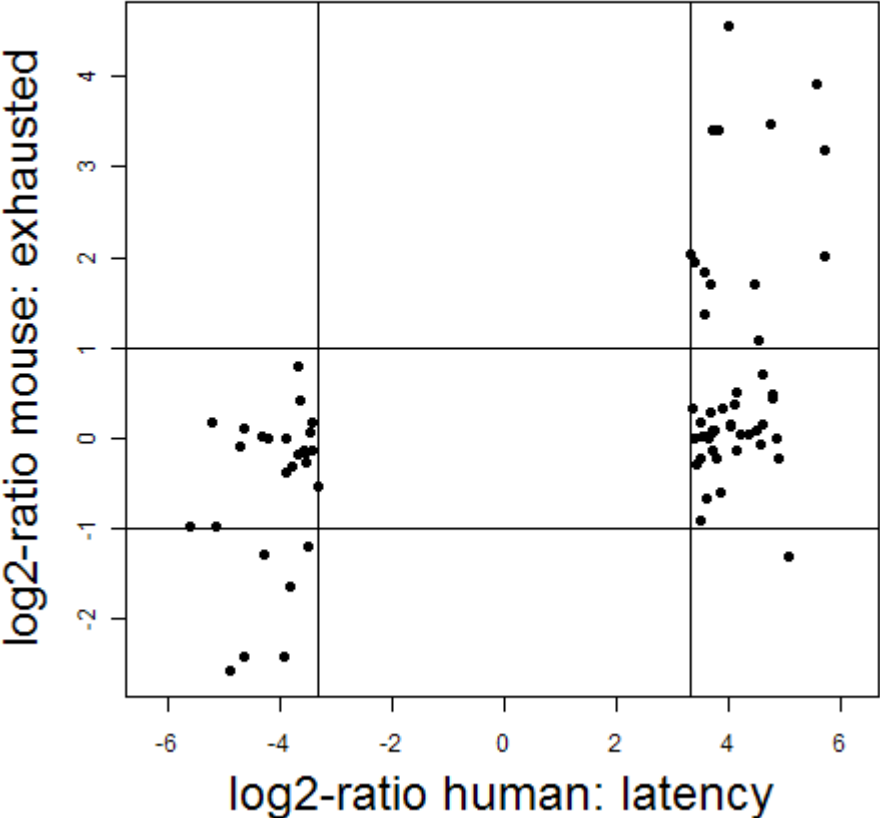
# Supplemental Figure 4



LEF-1 RNA and protein levels. (A) qPCR of sorted effector and memory CD8<sup>+</sup> cells in latency. Expression is measured as fold change compared to a pool of naive CD8<sup>+</sup> cells. (B) Western blot showing low amounts of LEF-1 protein in effector and memory CD8<sup>+</sup> cells.



Supplemental Figure 5



Comparison of expression of genes regulated in latent HCMV-specific cells with exhausted murine LCMV-specific CD8<sup>+</sup> cells. Scatterplot for genes that were up- or downregulated significantly (corrected  $P \leq 1 \times 10^{-10}$ ) and 10-fold or greater in the latent HCMV-specific CD8<sup>+</sup> T cells and that could be mapped to Affymetrix mouse probesets (n = 73) versus the orthologous mouse genes in exhausted LCMV-reactive cells.