

Hepatosplenic T-cell lymphoma displays an original oyster-shell cytological pattern and a genomic profile distinct from that of $\gamma\delta$ T-cell large granular lymphocytic leukemia

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Supplemental data: Hepatosplenic T-cell lymphoma displays an original oyster-shell cytological pattern and distinct genomic profile from $\gamma\delta$ T-Large Granular Lymphocytic Leukemia

Supplemental Figure 1: Immunophenotypic and oncogenetic profiles of HSTCL and $\gamma\delta$ -LGLL patients.

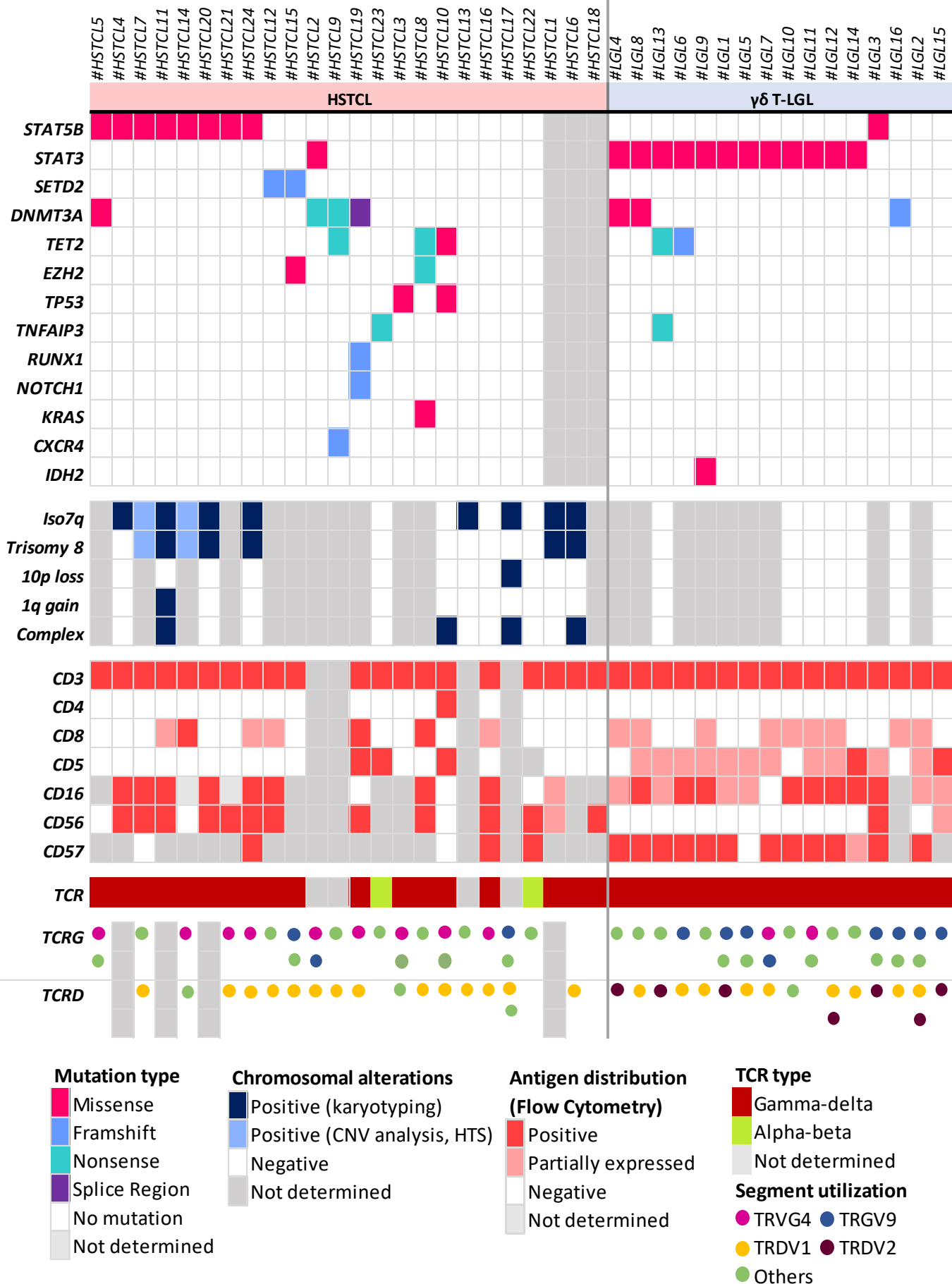
Heatmap of mutations, cytogenetic alterations, antigen expression and TCR gene utilization in dominant clonotypes from 24 HSTCL and 16 $\gamma\delta$ T-LGLL patients.

HSTCL: Hepatosplenic T-cell lymphoma; LGLL: Large Granular Lymphocytic Leukemia.

Supplemental Table 1: Somatic mutations detected in HSTCL and $\gamma\delta$ T-LGLL samples.

Supplemental Table 2: TRG and TRD productive clonotypes detected in HSTCL and $\gamma\delta$ T-LGLL samples.

Supplemental figure 1



Supplemental Table 1 : Somatic mutations detected in HSTCL and LGLL

Sample	Gene	Exon	Nucleotide change	Amino acid substitution	VAF (%)	Class
#HSTCL2	STAT3	21	c.1919A>T	p.(Tyr640Phe)	14.6	5
	DNMT3A	9	c.1024G>T	p.(Glu342Ter)	9.7	4
#HSTCL3	TP53	5	c.461G>T	p.(Gly154Val)	9.6	4
#HSTCL4	STAT5B	16	c.1924A>C	p.(Asn642His)	4.8	5
#HSTCL5	STAT5B	16	c.1924A>C	p.(Asn642His)	20.3	5
	DNMT3A	19	c.2207G>A	p.(Arg736His)	15.4	3
#HSTCL7	STAT5B	15	c.1883C>G	p.(Thr628Ser)	76.8	4
#HSTCL8	TET2	10	c.4393C>T	p.(Arg1465Ter)	13.2	4
	EZH2	20	c.2199C>G	p.(Tyr733Ter)	17.1	4
	KRAS	2	c.35G>T	p.(Gly12Val)	18.3	5
#HSTCL9	TET2	11	c.5038C>T	p.(Gln1680Ter)	49.5	5
	TET2	11	c.5558_5559insC	p.(Phe1854LeufsTer5)	9.4	4
	DNMT3A	14	c.1584C>A	p.(Tyr528Ter)	47.2	5
	CXCR4	2	c.954del	p.(Ser319LeufsTer2)	5.9	4
#HSTCL10	TET2	11	c.5907G>T	p.(Lys1969Asn)	10.1	3
	TP53	6	c.671A>C	p.(Glu224Ala)	56.9	4
	TP53	6	c.581T>A	p.(Leu194His)	6.4	4
#HSTCL11	STAT5B	16	c.1924A>C	p.(Asn642His)	2.6	5
#HSTCL12	SETD2	15	c.6366_6367insGA	p.(Lys2123GlufsTer25)	12.4	4
#HSTCL14	STAT5B	15	c.1883C>G	p.(Thr628Ser)	34.2	4
#HSTCL15	SETD2	21	c.7614_7615del	p.(His2538GlnfsTer7)	6.4	4
	SETD2	21	c.7570dup	p.(Cys2524LeufsTer2)	6.6	4
	EZH2	18	c.2079T>G	p.(Asn693Lys)	5.1	4
#HSTCL19	DNMT3A	21	c.2478+2T>C	-	96.1	3
	NOTCH1	34	c.7355_7356insAC	p.(Val2453ArgfsTer25)	40.0	4
	RUNX1	5	c.505dup	p.(Arg169LysfsTer44)	49.5	4
#HSTCL20	STAT5B	16	c.1924A>C	p.(Asn642His)	7.1	5
#HSTCL21	STAT5B	16	c.1924A>C	p.(Asn642His)	7.2	5
#HSTCL23	TNFAIP3	7	c.1690A>T	p.(Lys564Ter)	9.1	4
#HSTCL24	STAT5B	16	c.1994A>T	p.(Tyr665Phe)	26.4	5
#LGL1	STAT3	21	c.1919A>T	p.(Tyr640Phe)	26.9	5
#LGL3	STAT5B	16	c.1994A>T	p.(Tyr665Phe)	3.7	4
#LGL4	STAT3	21	c.1919A>T	p.(Tyr640Phe)	16.0	5
	DNMT3A	8	c.982G>T	p.(Val328Phe)	3.0	4
#LGL5	STAT3	21	c.1981G>T	p.(Asp661Tyr)	78.4	5
#LGL6	STAT3	21	c.1940A>T	p.(Asn647Ile)	35.8	4
	TET2	3	c.2273del	p.(Gln758Argfs*55)	3.0	4
	TET2	11	c.5284A>G	p.(Ile1762Val)	35.3	4
#LGL7	STAT3	21	c.1975A>C	p.(Ile659Leu)	33.1	4
	STAT3	21	c.2087A>G	p.(Glu696Gly)	1.8	4
#LGL8	STAT3	21	c.1940A>T	p.(Asn647Ile)	15.9	4
	DNMT3A		c.1969G>A	p.(Val657Met)	15.8	4
#LGL9	STAT3	21	c.1919A>T	p.(Tyr640Phe)	38.4	5
	IDH2	4	c.364C>T	p.(Arg122Cys)	11.0	4
#LGL10	STAT3	21	c.1919A>T	p.(Tyr640Phe)	26.2	5
#LGL11	STAT3	21	c.1919A>T	p.(Tyr640Phe)	24.0	5
#LGL12	STAT3	21	c.1919A>T	p.(Tyr640Phe)	19.6	5
#LGL13	STAT3	21	c.1919A>T	p.(Tyr640Phe)	37.1	5
	TET2	3	c.1692G>A	p.(Trp564Ter)	34.5	4
	TNFAIP3	5	c.777_778insTT	p.(Leu260Phefs*3)	2.6	4
	TNFAIP3	7	c.1221C>A	p.(Cys407Ter)	17.6	4
#LGL14	STAT3	20	c.1852G>C	p.(Gly618Arg)	33.2	4
#LGL16	DNMT3A	19	c.2305_2311del	p.(Ile769AspfsTer8)	11.3	4

Supplemental Table 2 : TRG and TRD productive clonotypes detected in HSTCL and LGLL samples

Sample	Locus	Rearrangement name	lenCDR3	seq_CDR3aa
#HSTCL2	TRG	TRGV9*01 3/CCCTCAGTCGCCACTCCT/1 TRGJ1*01	51	CALWEPSVATPYTGWFKIF
	TRG	TRGV4*01 0/CC/4 TRGJ1*01	32	CATWDGPIRNS
	TRD	TRDV1*01 1/AAAAGACAA/0 TRDD2*01 0//3 TRDD3*01 2/ACGCCGATT/5 TRDJ1*01	60	CALGEQKTTFLRGITPIDKLI
#HSTCL3	TRG	TRGV10*02 2/CCT/3 TRGJ1*01	32	CAAWDSFIIRNS
	TRG	TRGV4*01 3//4 TRGJ1*01	27	CATWDFYKLI
	TRD	TRDV3*01 4/A/2 TRDD2*01 2/TTGG/3 TRDD3*01 1/CTGTGTGG/3 TRDJ1*01	45	CAYSFGGDTLACDKLI
#HSTCL5	TRG	TRGV4*01 0/CTAGGA/4 TRGJ1*01	36	CATWDGLGYKLI
#HSTCL6	TRD	TRDV1*01 1/CTCGGCCTCT/1 TRDD3*01 0/CCGGGTA/0 TRDJ1*01	60	CALGEPRLGDTPGNNDKLI
#HSTCL7	TRG	TRGV5*01 0/CACCCCG/0 TRGJ1*01	42	CATWDRHPRNYKLI
	TRD	TRDV1*01 2/TACTCTCCGGT/0 TRDD3*01 1/AAGTTGG/2 TRDJ1*01	57	CALGEYSPVLGDTSWTDKLI
#HSTCL8	TRG	TRGV8*01 4/CGT/3 TRGJ1*01	30	CATWVDYKLI
	TRD	TRDV1*01 1/CAGTGGGGACCCGGTGGTGGGCT/3 TRDJ1*01	51	CALGEPVGRWVWWSDKLI
#HSTCL9	TRG	TRGV8*01 0/CAGAGAGAG/3 TRGJ1*01	44	CATWDRQREVVISRR
	TRG	TRGV11*01 6/CTTCTCGG/7 TRGJ1*01	32	CACWILLGIRNS
	TRG	TRGV2*01 0/CCGTCGGG/3 TRGJ1*01	43	CATWDGSPGVGLDQDV
#HSTCL10	TRG	TRGV2*01 0/CCAGGA/4 TRGJ1*01	36	CATWDGPGYKLI
	TRD	TRDV1*01 0//0 TRDD2*01 2/GTGCCTT/1 TRDD3*01 7/CTTTTGAGAG/3 TRDJ1*01	57	CALGELLVPVSGLLRADKLI
#HSTCL12	TRG	TRGV2*01 4/TTT/3 TRGJ1*01	30	CATWDFYKLI
	TRD	TRGV8*01 5/GGG/11 TRGJ1*01	21	CAIRGEKLI
#HSTCL13	TRD	TRDV1*01 1/GAGGATGGCCGACCTAGT/0 TRDD3*01 0/TATAGGCAC/8 TRDJ1*01	63	CALGERGWPTLVLDGTYRHKLI
	TRG	TRGV3*01 0/G/3 TRGJ1*01	36	CATWWDGSDWKI
#HSTCL14	TRD	TRDV1*01 3/CTCTGTGG/0 TRDD2*01 2/CC/3 TRDD3*01 3/CCCCAGT/0 TRDJ1*01	60	CALGDPVAFRLRIPSYTDKLI
	TRG	TRGV4*01 6/AA/0 TRGJ1*01	30	CATWKNYKLI
#HSTCL15	TRD	TRDV3*01 4/GCCCTCTAGGGG/2 TRDD3*01 0/CGGATCT/4 TRDJ1*01	51	CACPRLGGGYADLDKLI
	TRG	TRGV9*01 3/CCGACCTGG/7 TRGJ1*01	33	CALWEPTYKLI
#HSTCL16	TRD	TRDV1*01 0/ACGAGTCCGACTT/0 TRDD3*01 2/GGA/2 TRDJ1*01	57	CALGELRVPYTWIGTDKLI
	TRD	TRDV1*01 0/TAAGA/1 TRDD2*01 3/ACCTGCGCTA/3 TRDD3*01 0/GGTGTTGG/11 TRDJ1*01	59	CALGELKTSTCARGIRVLGSS
	TRG	TRGV4*01 4/CGCTGC/6 TRGJ1*01	30	CATWDAAYKLI
#HSTCL19	TRD	TRDV1*01 1/CCCC/0 TRDD2*01 0/GCT/0 TRDD3*01 8/CCAGACCGT/0 TRDJ1*01	60	CALGEPPLTLARPYTDKLI
	TRG	TRGV5*01 5/TTACC/7 TRGJ1*01	27	CATWVTKLI
	TRD	TRDV1*01 0/CCCTAGGGGAAGGT/0 TRDD3*01 1/CCTATT/3 TRDJ1*01	60	CALGLDPRGRYWGIPYSKLI
#HSTCL21	TRD	TRDV3*01 0/GAG/3 TRDD2*01 0/G/2 TRDD3*01 2/GGGTAGT/1 TRDJ1*01	51	CAFRSPTWRDRVTDKLI
	TRG	TRGV4*01 0/CGGGG/12 TRGJ1*01	27	CATWDGRKLI
	TRD	TRDV1*01 9/CAGTCTCTCGT/0 TRDD3*01 0/GGGG/7 TRDJ1*01	42	CALSLRTGGYGGKLI
#HSTCL22	TRG	TRGV4*01 1/TTT/3 TRGJ1*01	33	CATWDFYKLI
	TRD	TRDV1*01 6/TAGTAGGACCCCTCTA/0 TRDD2*01 0/GTTT/4 TRDD3*01 2/GGT/2 TRDJ1*01	63	CALGSRTPFLRLGIGTDKLI
#HSTCL23	TRG	TRGV8*01 6//2 TRGJ1*01	26	CATWIIIRNS
	TRB	TRBV5-1*01 4/CCAGTCCGAGAGCGGCC/0 TRBJ2-7*01	42	CASSPVRERPLYEQY
#HSTCL24	TRG	TRGV8*01 3/TTAACG/5 TRGJ1*01	32	CATWDLTIIRNS
	TRB	TRBV19*01 1//2 TRBD1*01 3/T/3 TRBJ2-7*01	33	CATSKDRVYEQY
#HSTCL24	TRG	TRGV4*01 0/AGAAAGCCGAGGA/7 TRGJ1*01	39	CATWIGESRGYKLI
	TRD	TRDV1*01 0/CCCGTTTGGGTTTCTTGTATACATACCG/3 TRDD3*01 3/TCC/0 TRDJ3*01	78	CALGELPLVSVLHYTGGIPSWDRQMFF
#LGL1	TRG	TRGV8*01 11/ACAACTCCCA/4 TRGJ1*01	29	CANNSHIIRNS
	TRD	TRDV2*01 0/GAGTTTGGG/2 TRDD3*01 1/CCCCTAG/0 TRDJ3*01	63	CACDTEFGWGPSPSWDRQMFF
#LGL2	TRG	TRGV9*01 2/GAACCT/9 TRGJ1*01	30	CALWVGLTKLI
	TRD	TRDV2*01 0/GTGAAG/1 TRDD3*01 2/AAGCAATG/0 TRDJ3*01	61	CACDVKLGDKAMLLGHPTDVF
#LGL3	TRD	TRDV1*01 2/TTTTGGCG/10 TRDJ1*01	27	CALGFWRLI
	TRG	TRGV2*01 0/CCGG/9 TRGJ1*01	29	CATWDPVRNS
#LGL4	TRG	TRGV9*01 5/GACCCCTA/4 TRGJ1*01	45	CALWGPQLQELGKIKIV
	TRD	TRDV2*01 1//2 TRDD3*01 2/AGT/1 TRDJ3*01	48	CACDTAGISSWDRQMFF
#LGL5	TRG	TRGV5*01 0//1 TRGJ1*01	33	CATWDRNYKLI
	TRD	TRDV2*02 0/ATTCGGT/0 TRDD3*01 1//2 TRDJ1*01	45	CACDNSGTGGYTDKLI
#LGL6	TRG	TRGV9*01 2/GCCACCTAG/6 TRGJ1*01	36	CALWEGPPSYKLI
	TRD	TRDV1*01 3/CCAGTCAACAA/1 TRDD2*01 0/TTTTCC/0 TRDD3*01 1/TTA/2 TRDJ1*01	66	CALGDQSTTSVSTGGYLDKLI
#LGL7	TRG	TRGV9*01 5/TGTTCC/2 TRGJ1*01	33	CALWVFDYKLI
	TRD	TRDV1*01 2/GTGGGGACCCGAGGGT/0 TRDJ1*01	48	CALGEVGTREGYTDKLI
#LGL8	TRD	TRDV1*01 0/TGGGGT/0 TRDD3*01 2/AC/0 TRDJ1*01	50	CALGELVGLVNTPISS
	TRG	TRGV4*01 3//5 TRGJ1*01	26	CATWDSIRNS
	TRG	TRGV9*01 6/ATAATAGCCG/3 TRGJ1*01	36	CALWINRRYKLI
#LGL9	TRD	TRDV1*01 4/CT/2 TRDD2*01 0/GTTGGCCCTCTATCCCGT/0 TRDD3*01 2//0 TRDJ1*01	66	CALGAFRLWPSIPVLGNDTKLI
	TRD	TRDV1*01 1/GAAGG/3 TRDD2*01 0/AATTTGT/4 TRDD3*01 3/CA/0 TRDJ1*01	56	CALGERRSYNLWGSTPISS
	TRG	TRGV3*01 0/CTAGGTGA/10 TRGJ1*01	33	CATWDRLGGKLI
#LGL10	TRG	TRGV3*01 0/CCTAGTTGG/12 TRGJ1*01	32	CATWDRPSLGN
	TRD	TRDV1*01 1/AAGAGGCA/2 TRDD3*01 0/GAA/2 TRDJ1*01	50	CALGEQEAECIRKPISS
	TRD	TRDV1*01 1/CAGGCCGTTAA/4 TRDD3*01 0/ATCCA/2 TRDJ1*01	54	CALGEPGLRGYDPTDKLI
#LGL11	TRG	TRGV3*01 0/CAAGGGG/5 TRGJ1*01	36	CATWDRQGDYKLI
	TRD	TRDV1*01 0/AGACCCCTCATGGTCT/4 TRDD3*01 0/GGT/0 TRDJ1*01	60	CALGELDPSMVWGYGYTDKLI
	TRG	TRGV5*01 9/AGCCCTT/3 TRGJ1*01	30	CATSPFYKLI
#LGL12	TRG	TRGV2*01 0/CGGC/4 TRGJ1*01	38	CATWDRLVISRR
	TRD	TRDV3*01 1/AAAG/0 TRDD3*01 4//1 TRDJ1*01	36	CAFRLGDTDKLI
#LGL13	TRG	TRGV4*01 5/TTA/5 TRGJ1*01	27	CATWVNYKLI
	TRD	TRDV3*01 0/CTTCAAG/8 TRGJ1*01	33	CATWDRLQDKLI
#LGL14	TRD	TRDV1*01 0/AAACCAACCA/0 TRDD2*01 0/CTT/1 TRDJ1*01	54	CALGELNPTLPTFTDKLI
	TRD	TRDV2*01 0/GTG/3 TRDD3*01 2/T/0 TRDJ1*01	41	CACDVTGGYTPISS
#LGL15	TRG	TRGV5*01 4/TAC/0 TRGJ1*01	33	CATWDTNYKLI
	TRD	TRDV2*02 2/TCATACGGGAAGGGT/1 TRDJ1*01	39	CAWDHTGRVTDKLI
#LGL16	TRG	TRGV8*01 0/CGGC/5 TRGJ1*01	33	CATWDRRHYYKLI
	TRG	TRGV10*02 3//3 TRGJ1*01	31	CAAWDPRLVQDI
#LGL17	TRD	TRDV1*01 6/AGCCCCACTACTCCCGT/0 TRDD3*01 5/CT/0 TRDJ4*01	51	CALGAPHYSRTGSRPLIF
	TRG	TRGV9*01 0//4 TRGJ1*01	42	CALWEVQELGKIKIV
	TRD	TRDV2*01 0/GT/0 TRDD3*01 1//3 TRDJ3*01	48	CACDVLGDTWDRQMFF
#LGL18	TRD	TRDV2*02 1/CCAGT/0 TRDD3*01 2/AGGTGAC/1 TRDJ1*01	48	CACDPLVGLDKVTDKLI
	TRG	TRGV8*01 1//4 TRGJ1*01	33	CATWDSRDWKI
	TRG	TRGV9*01 1/AGCAGGGG/9 TRGJ1*01	32	CALWEVAGVNS
#LGL19	TRG	TRGV10*02 4/CAACAGAACTT/0 TRGJ1*01	46	CAAWDKQLNYHLVLDQDI
	TRD	TRDV1*01 2/GCGAGGG/4 TRDD2*01 0/CCTCTT/0 TRDD3*01 5/GGCTCTCGGGGCTGT/0 TRD	72	CALGEARPLYWGGSRGLYTDKLI