SUPPLEMENTARY MATERIAL AND METHODS

Clinical course of the melanoma patient

A 56-year-old patient was diagnosed with malignant melanoma in 2008 and underwent resection of the primary tumor in the same year. In 2013 metastatic disease with pulmonary and intestinal metastases were detected. A biopsy from the lung metastasis (B_{Lung}) was performed for histologic confirmation of metastatic status of malignant melanoma. Subsequently, the patient underwent two cycles of chemotherapy resulting in a mixed response with regression of the intestinal metastasis (M_{Int}) but progression of lung metastasis (M_{Lung}). In November 2013, the patient became eligible for administration of anti-CTLA-4-antibody lpilimumab for a total of four cycles. In March 2014, restaging revealed response of M_{Lung}, whereas M_{Int} progressed and was therefore surgically removed, together with two non-malignant lymph nodes (M_{Int}-LN1 and -LN2). The residual M_{Lung} previously targeted by biopsy, initially regressed, but later progressed and was therefore surgically removed in January 2016, together with one adjacent non-malignant lymph node (M_{Lung}-LN). Treatment with the PD-1-directed monoclonal antibody Pembrolizumab was subsequently applied for one year and the patient is in complete remission since then (Supplementary Fig. S1).

Cultivation of cell lines and primary human cells

All target cell lines were maintained in RPMI 1640, MEM or DMEM (Invitrogen), according to manufacturer's instructions, supplemented with Penicillin and streptomycin antibiotics (Pen/Strep), L-glutamine, non-essential amino acids (NEAA), sodium pyruvate (NaP) and 10% heat-inactivated fetal calf serum (FCS). T cells were cultured in RPMI supplemented with: L-glutamine, 5% human serum and 5% FCS, Hepes, Pen/Strep, NEAA, NaP and gentamycin.

T-cell antigen-experience recall responses

For stimulation with peptides, PBMCs were cultured as previously described^{1 2}. Briefly, frozen PBMCs were thawed and cultured in AIM-V medium supplemented with 100 ng/ml of IL-4 and 100 ng/ml GM-CSF. After 24h, Poly:IC (20 μg/ml), IL-7 (0.5 ng/ml) and peptide pools (1 μM/peptide) were added to the culture. After 20-24h incubation, PBMCs were transferred on a pre-coated IFN-γ ELISpot plate, which was developed after additional 20-24h, prior transfer of PBMCs to culture for expansion of T cells in RPMI medium supplemented with IL-7 (5 ng/ml) and IL-15 (5 ng/ml) for 10-15 days. IFN-γ ELISpot assay was repeated on expanded T cells co-cultured for 72h with T2-A3 cells (E:T = 1:1) pulsed with single peptides from sub-pool A4 shared by Pool 4 and 9.

Arrangement of peptide pools for immunogenicity assessment of predicted ligands

The first 25 predicted binders to each allele were synthetized and used for stimulation assays, excluding previously identified neoantigens (NCAPG2^{P333L}, ranked 24th and SYTL4^{S363F} ranked 6th). In total 48 peptides were assembled in 11 pools. Each pool contained 10 peptides: 5 HLA-A03:01-predicted binders (sub-pool A) and 5 HLA-B27:05-predicted binders (sub-pool B) were arranged as depicted in Supplementary Table S3. Sub-pools A5 and B2 contained 9 peptides, due to the exclusion of known immunogenic peptides¹. Pool 11 contained peptide SYTL4^{S363F} and served as positive control for peptide pool approach. Following screening of peptide pools, T cells were expanded for two weeks and co-cultured with single-peptide-pulsed target T2 cells to define the peptides eliciting reactivity in the pool.

IC₅₀ in vitro measurement of predicted peptide candidates and neoantigens

Binding of selected peptides to HLA was further investigated through a peptide exchange assay. HLA-A03:01, HLA-B27:05, and human β2m (hβ2m) were expressed in E. coli and purified from inclusion bodies as described previously³. Purified proteins were stored at -80 °C until use. Folding of heavy chain-h\u00ed2m-peptide complexes was performed by diluting purified denatured proteins to a final concentration of 30 µg/mL of heavy chain and 30 µg/mL hβ2m folding buffer (100 mM Tris Cl, pH 7.5, 0.4 M arginine, 2 mM EDTA, 0.5 mM oxidized glutathione, 5 mM reduced glutathione, and 0.5 mM PMSF) and stirring at 4 °C (2 days for HLA-A03:01, 14 days for HLA-B27:05) with 10 µM high-affinity peptide (KLIETYFJK for HLA-A03:01, and RRKJRRWHL for HLA-B27:05, where J is the photolabile aa residue)4. After folding, samples were ultracentrifuged at 15,000 x g for 20 min and further purified by gel filtration. For peptide exchange reaction, 0.5 µM HLA class I monomers (HLA-hβ2m- photolabile peptide complex) were exposed to UV radiation (345 nm, 1000 W) for 5 min, followed by incubation for 18 h at 4 °C with 10nM fluorophorelabeled peptide (KLIE-FITC-YFSK for HLA-A3:01 and RRKW-FITC-RWHL for HLA-B27:05, FITC λ ex = 494 nm, λ em = 517 nm) and varying concentration of the measured peptide. The binding was measured by fluorescence anisotropy using a Victor 3V reader (Perkin Elmer) in a black 96-well plate (Corning). Data were fitted and IC₅₀ values were calculated by using GraphPad Prism 7.

TCR in situ hybridization

RNA in situ hybridization for identification of neoantigen-specific TCR on FFPE tumor slides was performed using BaseScopeTM Detection Reagent Kit v2 - RED (ACD). TCR-specific Probes were designed to anneal on the TCR CDR3 sequence. Probes against PPIB (Cyclophilin B) and a bacterial protein (DapB, Bacillus subtillis) served as respective positive and negative controls. For each paraffin tumor block, slides of 4 μm were trimmed

with a microtome. Tissue slides were deparaffinized, pretreated using Protease IV (ACD) and stained with target probe, negative control and positive control probes following the manufacturer's instructions on an automated immunostainer. For localization of T-cell infiltration, Immunohistochemistry (IHC) was performed using anti-CD3-antibody (clone MRQ, Cell Marque Cat# 103R) as previously described¹. Slides were scanned on a Leica AT2 (Leica, Wetzlar, Germany) system and visualized using Aperio ImageScope software (v12.4.3).

HLA-peptide complex structural modelling and SASA calculation

Each model was solvated in a rectangular box of TIP3P⁵ water with a minimum distance of 12 Å between solute and box boundary, neutralized, and energy minimized. All modelling steps were performed using AMBER17⁶. The force field FF14SB was selected⁷. Subsequently, all 6 models were progressively heated up to 300 K over 3 ns gradually releasing initial positional restraints from the solute (Supplementary Table S4). The last heat-up step was performed in constant number, pressure and temperature (NPT) thermodynamic ensemble whereas the other steps were performed in constant number, volume and temperature (NVT). Temperature was controlled using a Langevin thermostat with a collision frequency (gamma_ln) of 4.00 ps⁻¹. Pressure was controlled using a Berendsen barostat⁸ with default settings. SHAKE algorithm⁹ was applied for all bonds including hydrogen atoms. Particle mesh Ewald (PME) method¹⁰ was used to compute long range electrostatic interactions. A cut-off for non-bonded interactions of 12 Å was applied. After equilibration models were simulated for 200 ns at 300 K using the NPT ensemble with a 1 fs time step. For each model 3 replicas were simulated resulting in a cumulative simulation time of 600 ns per system.

To quantitatively analyse the HLA-p interface, solvent-accessable surface area (SASA) was calculated for each peptide residue and the electrostatic potential of the interaction surface

as previously described^{11 12}. Briefly, frames were extracted every 200 ps from the last 180 ns of each replicon and analyzed. To select representative structures for visualization, frames were clustered, and central structure of the highest populated cluster was picked. The clustering was based on non-hydrogen peptide atoms using the hierarchical agglomerative algorithm with an epsilon of 2.0 and default settings. Trajectory processing and clustering was conducted with the CPPTRAJ¹³ tool provided in AmberTools17⁶. Molecule images were generated using PyMOL (version 1.7.X, Schrödinger, LCC). Electrostatic potential was computed with PyMOL plugin APBS Tools 2.1¹⁴ using default settings. Hydrogen bonds were identified using the VMD software HBonds plugin (version 1.2)¹⁵.

Molecular cloning and retroviral transduction of TCRs, minigenes and HLA

TCR repertoire PCR analysis followed by Sanger sequencing was performed to determine variable alpha and beta chain usage of neoantigen reactive T-cell clones¹⁶ ¹⁷. V-D-J rearrangements of complementarity-determining regions (CDR3) were investigated using IMGT/V-Quest (http://www.imgt.org/IMGT_vquest/vquest) and the complete sequences were in silico reconstructed with Ensembl database. TCR sequences were modified by in silico murinization, insertion of an additional cysteine bridge and codon optimization (BioCat)¹⁸ ¹⁹. Optimized TCR constructs were retrovirally transduced in CD8⁺ healthy donor derived T cells as described before and expanded for 7 to 10 days with IL-7 and IL-15 (5ng/mL; Peprotech) before functional characterization ¹⁶ ²⁰.

SYTL4 and NCAPG2 mutated and WT minigenes were cloned as previously described¹. KIF2C minigenes were in silico designed, comprising 100 bp up- and downstream of mutated position, synthetized (Genscript) and cloned into pMP71 backbone. Additionally, tandem constructs were in silico designed, synthetized (Genscript) and cloned into the pMP71 backbone with single or tandem constructs for minigenes containing mutated

sequences of all three neoantigens and WT counterparts separated in two different vectors. All minigene vectors included a reporter gene dsRed ExpressII to allow sorting of transgenic cells. Neoantigen-coding and WT counterpart minigenes were transduced in different cell lines as LCL-1, U-698-M, A2058 and MDST8 as previously described¹ with small changes for adherent cell lines omitting RetroNectin (Clontech). LCL-1 was transduced with single minigenes, while other cell lines with tandem constructs, followed by single clone selection.

TCR beta and alpha chains as well as tandem constructs of minigenes were separated by a self-cleaving P2A element¹⁶. All vectors were amplified using NEB® 5-alpha Competent E. coli (New England BioLabs) and purified with NucleoBond® Xtra Midi/Maxi (Macherey-Nagel).

T2 were retrovirally transduced with the HLA restriction elements HLA-A03:01 and B27:05 as described before ¹⁶.

In-vitro cytotoxicity assessment

For monitoring of T-cell mediated killing in vitro, two different adherent cell lines were chosen according to the naturally expressed HLA allotypes. MDST8 cell line expressing HLA-B27:05 was selected for SYTL4^{S363F}-specific TCRs; A2058 expressing HLA-A03:01 for KIF2C^{P13L} and NCAPG2^{P333L}-specific TCRs. Killing assays were performed with impedance-based xCELLigence assays (ACEA BioSciences)²¹. Target cell culturing media was added to each well of 96 well E-Plates (ACEA Biosciences) for background impedance measurement²². Dissociated adherent target cells were seeded on E-Plate at different densities depending on the cell line (A2058 – 50,000/well; MDST8 – 20,000/well). Cell density on plates is measured within the RTCA MP instrument inside a cell culture incubator for 24h. For addition of T cells, data acquisition was paused and effector cells were added. Data recording was initiated immediately at 15-min intervals for the first 8 h

and then at 30-min intervals for remaining 16 h. Target cells only as well as target cells and non-transduced T cells served as controls. For calculation of percentage of cytolysis, the following formula was adopted: $\frac{Cytotoxicity}{(\%)} = 100 - \left(\frac{CI_{TCR}}{CI_{bul}}\right) \times 100$.

Activation/dysfunction patterns of stimulated and restimulated enriched TCR-transgenic T cells

A near-infrared fluorescent protein (iRFP) linked with a T2A element was cloned downstream of TCR constructs KIF2-PBC2 and SYTL4-TIL1 to allow for flow-cytometry based enrichment of TCR-transduced T cells. Retroviral transduction was performed as stated above and iRFP-positive T cells were sorted on a FACSAria III Cell Sorter (BD Biosciences). Sorted T cells were coincubated with minigene-transduced U-698-M in an E:T ratio of 1:1. To analyze repeated antigen exposure, transduced and enriched T cells were co-cultured with irradiated U-698-M expressing mutated tandem minigene (E:T = 1:1), fed with IL-7 and IL-15 (5 ng/ml each) every three days and restimulated with respective target cells after 11 days. For flow cytometry assessment, T cells were stained with anti-CD8, **TCRmu** and Zombie UV **Fixable** Viability Kit (BioLegend). Expression activation/dysfunction markers was assessed using anti-PD-1-antibody (BioLegend, Cat# 329930) and, in combination with True-Nuclear Transcription Factor buffer set (BioLegend), anti-T-bet (BioLegend, Cat# 644816). Proliferation after 6 days of target stimulation was assessed with CellTrace Violet Cell Proliferation Kit, (ThermoFisher) according to the manufacturer's recommendations. Flow cytometry data acquisition and analysis was performed as stated in respective section within the main manuscript.

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SUPPLEMENTARY FIGURE LEGENDS

Figure S1.

Clinical course of disease of the melanoma patient. He was diagnosed with malignant melanoma in 2008 and underwent resection of the primary tumor that year. In 2013, pulmonary and intestinal metastases were detected and a lung biopsy (B_{Lung}) was performed for histological analysis. Carboplatin and paclitaxel were administered, resulting in a mixed response of metastatic disease. The patient was subsequently treated with the anti-CTLA-4-antibody lpilimumab. In 2014, the progressing abdominal lesion (M_{Int}) and two non-malignant lymph nodes (LNs) were surgically removed. In 2016, one primarily responding lung metastasis (M_{Lung}) progressed and was resected with one adjacent non-malignant LN. Treatment with Pembrolizumab was subsequently administered for 18 months. The patient is currently in complete remission without therapy. Analyses performed on tissue samples and time points of blood withdrawals are depicted.

Figure S2.

Detection of immunogenicity of predicted neoantigen KIF2C^{P13L} in autologous PBMCs of the melanoma patient. **A**, PBMCs derived from time point 925 were cultured in presence of IL-4 and GM-CSF following addition of Poly:IC, IL-7 and peptide pools (1 μ M/peptide). After 24h, IFN- γ ELISpot assay was performed. **B**, IFN- γ ELISpot assay with T cells expanded after stimulation with Pool 4 and 9 (Supplemental Table 3). Expanded T cells were incubated with T2-A3 cells (E:T = 1:1) pulsed with single peptides of subpool A4 shared by Pool 4 and 9 for 72h. Subpool B4 containing peptides only present in Pool 4 but not Pool 9, served as negative control.

Figure S3.

Expression of transgenic neoantigen-specific TCRs on the surface of human CD8+ T cells assessed by TCRmu staining. Representative flow cytometry plots of single-cell suspension of TCR-transduced-CD8+ T cells stained (7-10 days after transduction) for CD8, TCRmu, and 7-AAD; the dot plots were gated on living cells (7-AAD-) and CD8-TCRmu+ T cells. The numbers in the gate represent the percentage of CD8+-T cells expressing the murinized TCR. Gates were set on the basis of isotype control for TCRmu-Ab, for each single TCR. Transduction efficiency was assessed for all transgenic T cells showing consistent results for the different TCR constructs.

Figure S4.

Expression of transgenic neoantigen-specific TCRs on the surface of CD8⁺ T cells assessed by multimer staining. Representative flow cytometry plots show stainings with indicated multimers: HLA-B27:05-SYTL4 (**A**), HLA-A03:01-KIF2C (**B**) and HLA-A03:01-NCAPG2 (**C**). TCR-transduced-CD8⁺ T cells were then stained for CD8 and 7-AAD; the dot plots were gated on living cells (7-AAD). The values in the gate represent the percentage of multimer-positive CD8⁺-T cells. The quadrants were set on the basis of non-transduced T cells and isotype control. One representative out of three experiments with T cells from two different healthy donors is shown.

Figure S5.

Functional avidity of neoantigen-specific TCRs. Representative plots of IFN-γ secretion of TCR-transduced T cells upon stimulation with T2 target cells pulsed with titrated peptide concentrations of SYTL4^{S363F} (**A**), KIF2C^{P13L} (**B**) and NCAPG2^{P333L} (**C**). EC₅₀ values of all experiments were calculated by fitting a non-linear curve and results are summarized in Fig. 1D.

Figure S6.

TCR-transduced CD8⁺ T cells mediate specific lysis of target cells expressing defined neoantigens. **A**, **B** and **C**, growth of target cells transduced with MUT/WT minigenes is monitored for ca. 24h (impedance measurement every 15 min) before addition of transgenic T cells to the culture and observation of cytolysis. MDST8MUT/WT cells were seeded at density 20,000/well and 40,000 TCR-T cells/well were added at time 0 (**A**). A2058MUT/WT cells were seeded at density 50,000/well and 100,000 TCR-T cells/well were added (**B** and **C**). Cell index values of target cell lines are depicted on left y axis. Percentage of target cell lysis, calculated on non-transduced T cell, is depicted on right y axis and indicated by the colored line. **D**, Comparison of cytolysis mediated by all TCRs. TCR transduction efficiency is indicated in the figure legend.

Figure S7.

Investigation of peptide-dependent and – independent HLA alloreactivity of neoantigen-specific TCR. Reactivity of all defined TCRs was tested to different LCLs expressing common HLA allotypes, pulsed with 1 μ M mutated peptides SYTL4 S363F, KIF2C and NCAPG2 P333L (pLCL) in comparison to non-pulsed condition (LCL). All experiments were performed three times on two different healthy-donor-derived sets of transduced T cells showing consistent results. For co-cultures, E:T ratio was 1:1 and read-out consisted of IFN- γ secretion, assessed by ELISA on culture supernatants after 20h incubation

Figure S8.

Venn diagrams with distribution of TCR CDR3 sequences. **A**, Overlap of TCR CDR3 clonotypes obtained from TCR- β sequencing on B_{Lung}, M_{Int} and M_{Lung}. **B**, Overlap of TCR CDR3 clonotypes from removed metastases and associated lymph nodes. Arrows indicate shared compartments in which defined TCRs with validated neoantigen-specificity were detectable. The overlap was calculated using the Venn diagram tool from Bioinformatics & Systems Biology available online (http://bioinformatics.psb.ugent.be/webtools/ Venn/).

Figure S9.

RNA in situ hybridization of neoantigen-specific T cells within tumor tissue M_{Lung} . **A**, CDR3-specific probe visualizes T cells expressing TCR KIF2C-PBC2, which show polarization of detected RNA within single cells. **B**, anti-CD3 staining show an inhomogenous T-cell infiltrate. **C**, Negative control probe DapB (Bacillus subtillis). **D**, positive control probe Cyclophilin B.

Figure S10.

Expanded TIL from M_{Lung}^{1} were analyzed for specific responses against mutated peptide ligands. IFN- γ secretion upon stimulation with peptide-pulsed autologous LCL line and analyzed by IFN- γ ELISpot.

Figure S11.

Longitudinal monitoring of activation of TCR-transgenic T cells upon neoantigen encountering. **A-B**, percentage of T-bet positive cells within TCRmu⁺CD8⁺ fraction of TCR-transduced T cells after 24 and 96 hours of co-culture with U-698-M expressing the mutated (**A**) or wildtype (**B**) tandem minigene. **C-D**, T-bet expression of SYLT4-TIL1-iRFP and KIF2C-PBC2-iRFP transduced T cells as shown in Fig. 6C including analysis after 96 hours after coincubation with mutated (**C**) or wildtype (**D**) transduced U-698-M.

SUPPLEMENTARY TABLES

Rank	Gene	Peptide seq (aa)	Mutation (aa)	Predicted affinity (nM)	Experimental IC ₅₀ (nM)
		HL	A-A03:01		
1	CRMP1	KIFN <u>F</u> YPRK	L > F	6.8	11.5
2	FUT9	KMKNFF <u>F</u> TK	S > F	7.4	135.7
3	ANO7	RMLRRRAQ <u>K</u>	E > K	8.7	791.3
4	ADAMDEC1	TLYSPRGE <u>K</u>	E > K	9.2	416.9
5	ASAH2	AMYQRAK <u>L</u> K	S > L	9.5	27.1
6	SLC5A3	SLLTPP <u>S</u> TK	P > S	9.6	211.4
7	CRYBB1	RLM <u>F</u> FRPIK	S > F	9.8	57.6
8	ZNF234	SLYL <u>K</u> IHLK	L > K	11	
9	ZNF234	KI <u>Y</u> AAGTFY	H > Y	11.2	975
10	DNAH5	YL <u>F</u> FIQGYK	S > F	12.5	932.8
11	TENM1	TTYSPIG <u>E</u> K	G > E	14.5	81.51
12	NCAPG2	RLYK <u>L</u> ILWR	P > L	14.7	707.1
13	TGM5	KTYPCKI <u>F</u> Y	S > F	16.6	248.1
14	FHDC1	<u>S</u> LQPRGSFK	P > S	18.2	36.0
15	CCDC7	KVINLSPF <u>K</u>	E > K	18.6	474.3
16	PCDHGA10	CLFFG <u>I</u> PWK	S > I	19.2	2391
17	SGK3	KQF <u>S</u> AMALK	P > S	21.4	208.2
18	KIF2C	RLF <u>L</u> GLAIK	P > L	21.6	277.4
19	AKAP6	KLKLP <u>I</u> IMK	M > I	23.3	35.1
20	FREM1	LLI <u>N</u> RGFSK	D > N	25.2	931.2
21	UVSSA	RLKCPF <u>Y</u> GK	H > Y	26.1	249
22	USP37	K <u>V</u> MTDPSRK	A > V	28.7	16,29
23	ARHGEF17	RIAGKA <u>L</u> KK	P > L	31.5	669
24	NCAPG2	K <u>L</u> ILWRGLK	P > L	32.6	263.9
25	ZFN226	K <u>L</u> YQCNECK	S > L	32.7	3502

Table S1. Measured binding activity of top 25 neoantigen candidates for HLA-A03:01 predicted by NetMHC4.0.

Rank	Gene	Peptide seq (aa)	Mutation (aa)	Predicted affinity (nM)	Experimental IC ₅₀ (nM)
HL	A-B27:05				
1	TECTB	R R FSSLYSF	G > R	11.5	48.0
2	CLDN24	RRLLILG R I	G > R	11.5	311.0
3	KAT2A	FRMF <u>L</u> TQGF	P > L	15	2.0
4	TMPRSS11E	ARWTA F FGV	S > F	17.1	525.0
5	SDK2	GRWALHSA <u>F</u>	S > F	17.5	68.0
6	SYTL4	GRIAF F LKY	S > F	18.4	224.0
7	Ac087289.2, MRP L38, Ac087289.3 ^a	KRF <u>L</u> HRQPL	P > L	20.2	73.0
8	B3GAT1	A <u>R</u> FAVNLRL	G > R	20.7	8.0
9	ITLN1	WRNS <u>F</u> LLRY	S > F	24	29.0
10	Af241726.2, CYBB ^a	YR <u>I</u> YDIPPK	V > I	24	60.0
11	KIF2C	ARLF L GLAI	P > L	25.7	
12	P2RX1	YRHLFKVF <u>R</u>	G > R	26.6	70.0
13	SCN2A	FRFFTR K SL	E > K	26.9	4.0
14	RNF216	RRHCRSY <u>N</u> R	D > N	27.6	55.0
15	CLDN24	KRRLLILG <u>R</u>	G > R	28.0	111.0
16	ZFN234	FRQSLYL <u>K</u> I	L > K	29.2	7.0
17	NEK10	rrtqryfm <u>k</u>	E > K	29.3	46.0
18	ERCC5	FRI <u>C</u> PIFVF	R > C	32.3	877.0
19	DSG1	K RTNVGILK	E > K	33.3	136.0
20	LIPH	LRILR <u>I</u> KLR	M > I	35.6	109.0
21	SI	KR <u>H</u> EVPVPL	Y > H	36.8	907.0
22	MBOAT1	HRY <u>F</u> FFVAM	S > F	37.5	353.0
23	SCN4A	FRF <u>F</u> ATPAL	S > F	38.3	13.0
24	INO80C	LRFS <u>I</u> IEEF	T > I	45.9	
25	STON2	SRVILF <u>S</u> PL	N > S	46.0	

a) Overlapping genes

Table S2. Measured binding activity of top 25 neoantigen candidates for HLA-B27:05 predicted by NetMHC4.0.

KIENFYPRK RRESLYSF RRLLLGRI RMLRRRAQK B1 FRMF_TOGF ARWTAFFGV A	Subpool A	A03:01 binders	Subpool B	B27:05 binders	Pools	
A1 RMLRRAOK TLYSPRGEK ARWTAFFGV ARWTAFFGV ARWTAFFGV ARWTAFFGV GRWALHSAF SLLTPPSTK RLMFFRPIK ARFAVNLRL POOL 2 A2 SLYLKIHLK B2 ARFAVNLRL POOL 2 KIYAAGTEY WRNSFLLRY YLFIGOYK YRIYDIPPK TTYSPIGEK ARLFLEKY YLFIGOYK YRIYDIPPK TRYSPIGEK ARLFLEKY YLFIGOYK ARLFLEKY YLFIGOYK ARLFLEKVER ARLFLEKY YLFIGOYK YRIYDIPPK TRYSPIGEK ARLFLEKVER ARLFLEKAL POOL 3 A3 KTYPCKIFY B3 FRFFTRKSL POOL 3 KKYNCKIFY B4 FROSLYLKI RRTORYPMK FROSLYLKI RRTORYPMK KRILLIGR FROSLYLKI KLINFGESK LRILLIGR FRICEPIEVF POOL 4 KLKLPJIMK KRTNVGILK LINIFKLR KRHEVPVPL KVMTOPSRK HRYFFEVAM HRYFFEVAM ANTON FROSL FRIAGKALKK B5 FRFFATPAL POOL 5 KLYOCNECK SRVILFSPL A1 RMLRRAOK B2 ARFAVNLRL POOL 6 KKIFNFYPRK KMKNFFFTK ARLFLERY AMYORAKLK YRIVDIPPK SLLTPPSTK ARLFLERY AMYORAKLK YRIVDIPPK SLLTPPSTK ARLFLERY AMYORAKLK YRIVDIPPK KRELLILGR TTYSPIGEK FROSLYLKI RRICKSTYNR KRELLILGR FROSLYLKI RRICKSTYNR KRELLICGR FROSLYLKI RRICKSTYNR KRELLICGR FROSLYLKI RRICKSTYNR KRELLICGR FROSLYLKI RRICKSTYNR KRELLICGR FR		KIFN <u>F</u> YPRK		R R FSSLYSF		
TLYSPRGEK AMYQRAKLK GRWALHSAF SLLTPPSTK RLMFFRPIK RLMFRPIK RLMFRPIK RLYKLLWR AS KTYPCKIFY BS FRFFTRKSL SLOPRGSFK KVINLSPFK KRRLLLIGR CLFFGIPWK KGPSAMALK RETCRYFMK KLKLPJIMK LLINRGFSK RLKLRPJMK RLKLPJIMK LLINRGFSK RLKLRPFYDRL KLKLPJIMK RSTORYFMK RSTORYFMK AS RIAGKALKK BS FRFFATPAL LRFSJEEF RLMFRPRK KMKNFFFTK ARFANNRL RRMFRRAQK TLYSPRGEK AMYQRAKLK RRMFRPIK AS SLITPPSTK RLMFRPIK RLMFRPIK RLMFRPIK RLMFRPIK RLMFRPIK RLMFRPIK RLMFRPIK RLMFRROK RRHCRSYNR RRH		KMKNFF <u>F</u> TK		rrllilg <u>r</u> i		
AMYGRAKLK SLTPPSTK RLMFRPIK RLMFRAGIK RLMFLILRY YRIPDIPPK TTYSPIGEK RLYKLILWR ARLFLGLAI RLYKLILWR AS KTYPCKIFY RKVINLSPFK RKVINLSPFK RKVINLSPFK RKOPSAMALK RLKLPIMK RLKLPIMK RLKLPIMK RLKLPIMK RLKLPIMK RLKCPFYGK RRHCRYPPL RKMKNFFFTK RLKCPFYGK RRHCRYPPL RKMKNFFFTK RLKCPFYGK RRHCRYPPL RKMKNFFFTK RLKCPFYGK RRHCRYPPL RKMRNAGIK RLKPPPRK RKMKNFFFTK RKMKNFFFTK RMLRRAGIK RLKFJIEEF RKLCALI RRHCRYFK RMRRAGIK RLKFJIEEF ROOI 5 RRHCRSYNR RHCRSYNR RRHCRSYNR RRH	A1	RMLRRRAQ K	B1	FRMF <u>L</u> TQGF	Pool 1	
SLLTPPSTK RLMFFRPIK RLMFFRPIK RLMFFRPIK RLMFRPIK RLYAGTFY YLFFIGGYK TTYSPIGEK RLYKLILWR A3 KTYPCKIFY SLOPRGSFK KVINLSPFK RVINLSPFK RLKLPIMK RLKLPIMK RLKLPIMK RLKLPIMK RLKLPIMK RLKLPIMK RILLRIKLR RLKCPFYGK RILGPIEVF RIAGKALKK REFEATPAL RIMGRESK RILGPIEVF RIAGKALKK RRHCRSYNG RICHPOPL REFEATPAL REFEATPAL REFEATPAL RIAGKALKK RRHCRSYR RIAGKALKK RRHCRSYNG RIAGKALKK RRHCRSYNG RIAGKALKK RRHCPPVPL RRHCRSYNG RIAGKALKK RRFLHROPL RRHCRSYNG RRH		TLYSPRGE K		ARWTA <u>F</u> FGV		
RLMFFRPIK SLYLKIHLK SLYLKIHLK SLYLKIHLK SLYLKIHLK SLYLKIHLK SLYLKIHLK SLYLKIHLK SLYRAGTFY YLFFIGGYK TTYSPIGEK RLYKLILWR AS KTYPCKIFY SLOPRGSFK KVINLSPFK KVINLSPFK KVINLSPFK SLOPRGSFK KVINLSPFK KVINLSPFK RLKLILGR CLFFGIPWK KGFSAMALK A4 RLFLGLAIK KLKLPIIMK LLINRGFSK RLKCPFYGK KVMTDPSRK A5 RIAGKALKK B5 FRFATPAL LRFSIEEF KLYGCNECK A1 RMLRRAQK TLYSPRGEK AMYORAKLK A1 RMLRRAQK TLYSPRGEK AMYORAKLK A2 SLYLKIH RLKCFFYTK ANYORAKLK A3 FRETATPAL A1 RMLRRAQK TLYSPGEK AMYORAKLK B2 ARFAVNLRL WRNSFLLRY WRNSFLRY WRNSFLLRY WRNSFLRRY RFRFTTRKSL POOL 7 RRHCRSYNR KRRLLILGR TTYSPIGEK RLYKLILWR ARLFLGLAI WRNSFLRRY RRHCRSYNR KRRLLILGR FROSLYLKI RRHCRSYNR KRHLLLGR FROSLYLKI RRHCR		amyqrak <u>l</u> k		GRWALHSA <u>F</u>		
A2 SLYLKIHLK KIYAAGTFY WRNSELLRY YLFFIGGYK YRIYDIPPK TTYSPIGEK ARLFLGLAI RLYKLILWR AS FRFFTRKSL POOL 3 SLOPRGSFK RKINLILGR FROSLYLKI ROFSAMALK RIFLGLAIK LLINGFSK RILKLILGR FROSLYLKI RLKLPJIMK LLINGFSK RRHCRSYMR KKMTDPSRK RILKLILGR FROSLYLKI RLKLPFYGK KRTLLILGR FRICPIFVF POOL 4 KLKLPJIMK LLINGFSK RRHCRYPMK A5 RIAGKALKK B5 FRFATPAL POOL 5 KLYMTDPSRK RKMKNFFFTK RKMKNFFFTK RKMKNFFFTK RKMKNFFFTK RMMANGALK YRIYDIPPK A1 RMLRRRAQK B2 ARFAVNLRL POOL 6 TLYSPRGEK AMYQRAKLK YRIYDIPPK AMYQRAKLK SLLTPPSTK ARLFLGLAI YRIYDIPPK AMYQRAKLK SLLTPPSTK RRHCRSYMR RRTGORYFMK RRLLILLGR FROSLYLKI RRHCRSYMR RRTGORYFMK RRTLLILLGR FROSLYLKI RRTGORYFMK RRTLLILLGR FROSLYLKI RRTGORYFMK RRTLLILLGR FROSLYLKI RRTGORYFMK RRTGORYFMK RRTGORYFMK RRTGORYFMK FRICPIFVF POOL 8 KVINLSPFK LRILBIRLR RRTGORYFMK RRHCRSYMR KRHLLILLGR FRICPIFVF POOL 8 KVINLSPFK LRILBIRLR RRTGORYFMK RRTGORYF		SLLTPP S TK		-		
KIYAAGTEY YLEFIQGYK YLEFIQGYK YLEFIQGYK TTYSPIGEK RLYKLILWR A3 KTYPCKIEY SLOPRGSFK KVINLSPFK CLFEGIPWK KOFSAMALK A4 RLFLGLAIK KLKLPIIMK LLIMFGFSK RLKMTDPSRK A5 RIAGKALKK B5 FRFFTAM A6 RIAGKALKK B5 FRFFATAL A1 RMLRRAQK B6 KWNSFLRY KWMNFFETK A1 RMLRRAQK AMYQRAKLK AMYQRAKLK AMYQRAKLK AMYQRAKLK B3 FRFFTRSD A2 SLYLKIHLK B3 FRFFTRSD ARFAVNLRL B4 FRICEICH CLFFGIPWF AMYQRAKLK AMYQRAKLK B5 FRFFTRSD ARFAVNLRL A1 RMLRRAQK B2 ARFAVNLRL B4 FRICEICH CLFFGIPWF AMYQRAKLK AMYQRAKLK AMYQRAKLK AMYQRAKLK B5 FRFFTRSD ARLFLGLAI A1 RLMFFRPIK ARLFLGLAI AMYGRAKLK AMYQRAKLK AMYQRAKLK B6 FRFFTRSD ARLFLGLAI AMYGRAKLK AMYQRAKLK ARLFLGLAI ARLFLGLAI ARLFLGLAI ARLFLGLAI ARRHCRSYNR ARLFLLILGR ARRHCRSYNR ARLFLLILGR ARRHCRSYNR ARLFLLILGR ARRHCRSYNR ARLFLGLAI ARRHCRSYNR ARLFLLILGR ARTHROLLILGR ARTHROLL	40	RLM <u>F</u> FRPIK		KRF <u>L</u> HRQPL		
TTYSPIGEK RLYKLILWR AS KTYPCKIFY BS FRFFTRKSL SLQPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK RLLILGR RLLINGFSK RLLILIGR RTGYFMK KLKLPIIMK LLINGFSK RLKOFFYGK KWMTDPSRK AS RIAGKALKK RRLLILGR RRTQYFMK RLKLPFYGK KWMTDPSRK AS RIAGKALKK RRHCPVPL RYMTDPSRK AS RIAGKALKK BS FRFFATPAL RMLRRRAOK SRVILFSPL KIFNFYPRK KMKNFFFTK ANYQRAKLK AMYQRAKLK AMYQRAKLK RLLINFSFIK ANYQRAKLK RRHCPVPL AMYGRAKLK REFTREN ANYQRAKLK RRHCPVPR AMYQRAKLK RRHCPVPR AMYQRAKLK RRHCPVPR RRHCRSYNR R	A2	SLYL K IHLK	B2	A <u>R</u> FAVNLRL	Pool 2	
TTYSPIGEK RLYKLILWR RLYKLILWR RLYPCKIFY SLOPRGSFK KYINLSPFK RVINLSPFK CLFFGIPWK KVINLSPFK KVINLSPFK CLFFGIPWK KRRLLILGR RTRORYFMK KRTHVGILK RRTORYFMK KKLKLPIIMK LLINRGFSK RLKCPFYGK RLKCPFYGK RLKOPFYGK RIAGKALKK B5 FRFFATPAL LRFSIEEF RLYGONECK KIMKNFFFTK A1 RMLRRRAQK TLYSPRGEK AMYORAKLK SLLTPPSTK RLMFRPIK RLMFRPIK RLMFRPIK RLMFRFIK RLMFRFRIK RLMFRFRIK RLMFRFRIK RLMFRRIK RRHCRSYNR R	A2	KI <u>Y</u> AAGTFY				
RLYKLILWR A3 KTYPCKIFY SLOPRGSFK KVINLSPFK KVINLSPFK KVINLSPFK KVINLSPFK KOFSAMALK A4 RLFLGLAIK KLKLPIMK LLINRGFSK RRKCHEVPVPL KVMTDPSRK A5 RIAGKALKK B5 FRFFATPAL A1 RMLRRRAQK TLYSPRGEK AMYORAKLK AMYORAKLK B2 ARFAVNLRL B3 FRFFTRKSL Pool 3 Pool 4 RFILLIGR Pool 4 RFILLIGR Pool 4 RFILEPVPVPL RRIFFTRY RRIFTRY RRIFFTRY RRIFTRY RRIFTRY RRIFFTRY RRIFTRY RRIFFTRY RRIFTRY RRIFTR		YL <u>F</u> FIQGYK		YR <u>I</u> YDIPPK		
A3 KTYPCKIFY SLOPRGSFK KVINLSPFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK KLKLPIIMK LLINRGFSK RILKCPFYGK KVMTDPSRK A5 RIAGKALKK B5 FRFFATPAL A1 RMLRRAQK TLYSPRGEK AMYQRAKLK AWYQRAKLK B2 ARFAVNLRL A4 RLMFFFTK A1 RLMFFRIK A5 RIAGKALKK B5 FRFFATPAL A6 RILLTPSTK A7 RMLRRAQK A7 RLMFFRIK A8 SLYLKIHLK A9 SLYLKIHLK A1 RLMFFRIK A1 RLMFFRIK A1 RLMFFRIK A2 SLYLKIHLK B3 FRFFTKSL RIYAGTFY YLFFIQGYK RTYSPIGEK RLYKLILWR A3 KTYPCKIFY SLOPRGSFK KVINLSPFK CLFFGIPWK KVINLSPFK CLFFGIPWK KVINLSPFK CLFFGIPWK KVRFFFTVAM A4 RLFLGLAIK KVRLLILGR FROSLYLKI RRTYCKIFY RRTYCKIFY RRTYCKIFY B4 FRICPIFVF Pool 8 KRTNVGILK LRILLIGR RRTYCKIFY RRTYCKIFY RRTYCKIFY B4 FRICPIFVF Pool 8 KRTNVGILK LRILLIGR RRTYCKIFY RRTYCKIFY SLOPRGSFK KRTNVGILK LRILLIGR RRTYCKIFY RRTYCKIFY SLOPRGSFK KRTNVGILK LRILRIKLR CLFFGIPWK KOFSAMALK RLFLGLAIK KLKLPIIMK B5 FRFFATPAL Pool 9 LRFSIEEF	<u> </u>					
SLQPRGSFK KVINLSPFK KVINLSPFK CLFFGJPWK KQFSAMALK ARTQRYFMK KQFSAMALK RIFLGLAIK KLKLPJIMK LLINRGFSK RLKCPFYGK KVMTDPSRK RIAGKALKK B5 RIAGKALKK B5 RIAGKALKK B5 RIAGKALKK B5 RIFFFATPAL LRFSJIEEF KLYQCNECK KMKNFFFTK A1 RMLRRRAQK TLYSPRGEK AMYQRAKLK SLLTPPSTK AMYQRAKLK SLLTPPSTK RLMFFRPIK A2 SLYLKIHLK B3 FRFFTRKSL RLMFFRPIK A2 SLYLKIHLK RIFFRPIK A3 KTYPCKIFY SLQPRGSFK KVINLSPFK RLYKLILWR A3 KTYPCKIFY SLQPRGSFK KVINLSPFK KRRLLILGR FROSLYLKI RRLMFKPPK RTORYFMK KRRLLILGR FROSLYLKI RRTORYFMK KRRLLILGR FROSLYLKI RRTORYFMK RRTORY	A3					
KVINLSPFK CLFFGIPWK KQFSAMALK RGFSAMALK RLFLGLAIK RLKLPIIMK LLINGFSK RLKCPFYGK KVMTDPSRK A5 RIAGKALKK B5 RIAGKALKK B5 RIAGKALKK RMHEVPVPL RMHRARAOK RMHEVPVPL RMHEVBEFF RMHRARAOK RMHEVPVPL RMHEVBEFF RMHRARAOK RMHEVPVPL RMHEVFFR RMHRARAOK RMHEVPVPL RMHEVPFR RMHEVPFR RMHERRAOK RMHEVPVPL RMHERRAOK RRHILIGR RTTYSPIGEK RLYKLIUWR RRTQRYFMK RRHCRSYNR RHCRSYNR RHCRSYNR RHCRSYNR RRTQRYFMK RRHLILGR RTTYSPIGEK RLYKLIUWR RRTQRYFMK RRTQRYFMK RTROPIFVF RRHCRSYNC RRHC			В3	FRFFTR <u>K</u> SL	Pool 3	
CLFFGIPWK KQF\$AMALK RRTQRYFMK RRHEPVPVL RRHEPVPVL RRFFFVAM RRYFFFVAM RRHSRACK RRHEPVPVL RRHEPVPRK RMKNFFFTK RMKNFFFTK RMKNFFFTK RMRRRAQK RTLYSPRGEK RMRNAGEK RLHPGPL RRHCRSYNR RRTQRYFMK R	<u> </u>			RRHCRSY <u>N</u> R		
A4 RIFLGLAIK B4 FRICPIFVF Pool 4 KIKLPJIMK LLINRGFSK LRILRIKLR RLKCPFYGK KMTDPSRK HRYFFFVAM A5 RIAGKALKK B5 FRFATPAL Pool 5 KLYQCNECK SRVILFSPL A1 RMLRRAQK B2 ARAVNLRL Pool 6 TLYSPRGEK WRNSFLLRY YRIYDIPPK AMYORAKLK B3 FRFFTKSL ARLFLGLAI YRHLFKVFR RLMFFRPIK ARLFRAVK YRIYDIPPK SLLTPPSTK ARLFLGLAI YRHLFKVFR RLMFRAGK B3 FRFFTRKSL Pool 7 KIYAAGTFY RRHCRSYNR KRRLLILGR TTYSPIGEK FROSLYLKI RRTYPCHICK RTTYPCHICK RRTYPCHICK RTTYPCHICK RTTYPCHICK RRTYPCHICK RTTYPCHICK						
A4 RLF_GLAIK KLKLPIMK LLINRGFSK LLINRGFSK RLKCPFYGK KVMTDPSRK A5 RIAGKALKK B5 FRFATPAL LRFSIIEEF KLYQCNECK KIFNFYPRK KMKNFFFTK A1 RMLRRRAQK AMYQRAKLK B2 ARFAVNLRL TLYSPRGEK AMYQRAKLK B3 FRFFTK ARLFRPSTK RLMFFRPIK A2 SLYLKIHLK KIYAAGTFY YLFFIQGYK KIYAAGTFY YLFFIQGYK RLYKLILWR A3 KTYPCKIFY SLQPRGSFK KVINLSPFK CLFFGIPWK KVINLSPFK CLFFGATPAL Pool 5 FRFLHRQPL ARFAVNLRL Pool 6 FRFFTRKSL Pool 7 RRHCRSYNR FRFTRKSL POOl 7 RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK KRTNVGILK LRILIGR FRICPIFVF Pool 8 KRTNVGILK LRILIGR RRTQRYFMK KRTNVGILK KRTNVGILK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK KRTNVGILK LRFSIEEF						
KLKLPIIMK LLINRGFSK LRILRIKLR RLKCPFYGK KVMTDPSRK RIAGKALKK B5 FRFEATPAL LRFSIIEEF KLYQCNECK KIFNFYPRK KMKNFFFTK RMLRRRAQK AMYQRAKLK AMYQRAKLK RLTYSPRGEK RLTYSPRGEK RLTYSPRGEK AMYQRAKLK RLTPSTK RLMFRPIK RLMFRPIK A2 SLYLKIHLK RLMFREROK RLYAAGTFY YLFFIQGYK TTYSPIGEK RLYKLILUGR RLYKLILUGR TTYSPIGEK RLYKLILUGR TTYSPIGEK RLYKLILUGR TTYSPIGEK RTYPCKIFY LRILLIGR TRICPIFVF RRTQRYFMK RRTQRYFMK KYINLSPFK LRILLILIGR FRICPIFVF Pool 8 KRTNVGILK KVINLSPFK LRILRIKLR CLFFGIPWK KQFSAMALK HRYFFFVAM RLFFFEATPAL Pool 9						
LLINRGFSK RLKCPFYGK KVMTDPSRK RIAGKALKK B5 RIAGKALKK B5 RIFFATPAL RFSIEEF KLYQCNECK KIFNFYPRK KMKNFFFTK A1 RMLRRRAQK TLYSPRGEK AMYQRAKLK B2 RLMFFRPIK AMYQRAKLK B3 RLMFFRPIK RLMFFRPIK RLMFFRPIK B3 RLMFFRPIK RIVFFTRKSL RLMFRRAY RRHCRSYNR YRHCRVFR RRHCRSYNR YLFFIQGYK RRHCRSYNR RLYKLILWR RLYKLILWR RLYKLILWR A3 KTYPCKIFY SLQPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK RRHCRSYNR RRTQRYFWK RRTQRYFWK RRTNVGILK RRTNVGILK RRTNVGILK RRHCRSYNP Pool 8 KRTNVGILK RRTNVGILK RRTNVGILK RRHCRSYNP RRHCRSYNR RRTQRYFMK RRTQRYFMK RRTNVGILK RRTNVGILK RRHCRSYNP Pool 9 RRTNVGILK RRHCRSYNP RRHCRSYNR R	A4		B4		Pool 4	
RLKCPFYGK KVMTDPSRK RIAGKALKK B5 RIAGKALKK B5 RIAGKALKK B5 RFFFATPAL RFSIEEF KLYQCNECK KIFNEYPRK KMKNFFFTK A1 RMLRRRAQK TLYSPRGEK AMYQRAKLK B2 RLMFFRPIK AMYQRAKLK RLMFFRPIK B3 RLMFFRPIK RLMFFRPIK RLYFIQGYK RIYAAGTFY YLFFIQGYK TTYSPIGEK RLYKILLUR RLYKLILWR A3 KTYPCKIFY SLOPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK RLFLGLAIK RRHCRSYNR RRH						
A5 RIAGKALKK B5 FRFFATPAL Pool 5 KLYQCNECK SRVILFSPL KIFNFYPRK KMKNFFFTK KRFLHRQPL A1 RMLRRAQK YRIYDIPPK ARLFLGLAI YRHLFKVFR FRFFTRKSL POOl 7 KIYAAGTFY RRHCRSYNR KRRLLILGR TTYSPIGEK RLYKLILWR RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK KVINLSPFK LRILRIKLR CLFFGIPWK KVINLSPFK LRILRIKLR CLFFGIPWK KQFSAMALK HRYFFFVAM RAFFATPAL POOl 9 KLKLPIMK B5 FRFFATPAL POOl 9 KLKLPIMK B5 FRFFATPAL POOl 9						
A5 RIAGKALKK B5 FRFFATPAL LRFSIEEF KLYQCNECK SRVILFSPL KIFNFYPRK KMKNFFFTK KMKNFFFTK KMKNFFFTK KMKNFFETK WRNSFLLRY A1 RMLRRRAQK B2 ARFAVNLRL Pool 6 TLYSPRGEK WRNSFLLRY AMYQRAKLK YRIYDIPPK SLLTPPSTK ARLFLGLAI RLMFFRPIK YRHLFKVFR KRFLLILGR RLMFFRPIK KIYAAGTFY KRRLLILGR TTYSPIGEK RLYKLILWR A3 KTYPCKIFY B4 FRICPIFVF Pool 8 KYINLSPFK KVINLSPFK KRTNVGILK KVINLSPFK KRILLIGR CLFFGIPWK KRRLLILGR A4 RLFLGLAIK B5 FRFFATPAL Pool 9 KLKLPIIMK						
LRFSIEEF SRVILFSPL			B5			
KLYQCNECK SRVILFSPL	A5	RIAGKA <u>L</u> KK			Pool 5	
KIFNEYPRK KMKNFFETK A1 RMLRRRAQK TLYSPRGEK AMYQRAKLK AMYQRAKLK SLTPPSTK RLMFFRPIK A2 SLYLKIHLK KIYAAGTFY YLFFIQGYK RLYSPIGEK RLYKLILWR A3 KTYPCKIFY B4 FRICPIFVF SLQPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK B5 FRFTRKSL Pool 7 RRHCRSYNR RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTUPIFVF Pool 8 KRTNVGILK RRTUPIFVF RRHCRSYNR RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTUPIFVF Pool 8 KRTNVGILK RRTUPIFVF RRHCRSYNR RRTQRYFMK RRTQRYFMK RRTUPIFVF Pool 8 KRTNVGILK RRHCPVPVL RRHCPVPVL RRHCPVPVL RRHCPVPVL RRHCPFVAM RRHCFFVAM R		-	-			
KMKNFFFTK RMLRRRAQK B2 ARFAVNLRL Pool 6		K <u>L</u> YQCNECK		SRVILF <u>S</u> PL		
A1 RMLRRRAQK B2 ARFAVNLRL Pool 6 TLYSPRGEK WRNSFLLRY AMYQRAKLK YRIYDIPPK SLLTPPSTK ARLFLGLAI RLMFFRPIK YRHLFKVFR A2 SLYLKIHLK B3 FRFFTRKSL Pool 7 KIYAAGTFY KRRLLILGR TTYSPIGEK FRQSLYLKI RLYKLILWR AS KTYPCKIEY B4 FRICPIFVF Pool 8 SLQPRGSFK KRINLSPFK LRILRIKLR CLFFGIPWK KRELLILGR CLFFGIPWK KRTNVGILK KQFSAMALK B5 FRFEATPAL Pool 9 KLKLPIMK		KIFN <u>F</u> YPRK	J	-		
TLYSPRGEK AMYQRAKLK YRIYDIPPK SLLTPPSTK RLMFFRPIK AS SLYLKIHLK SLYLKI SLYLKI SLYLKI SLYLKI SLYLKI SLYLKI SLYRGSFK KRTOPIFVF SLOPRGSFK KRTNVGILK KVINLSPFK CLFFGIPWK KQFSAMALK SLYKLILGR SLYLKI SLOPRGSFK KRTNVGILK SLYRKIHLKI SLYRKIHL SLYRKIH SL		KMKNFF <u>F</u> TK		KRF <u>L</u> HRQPL		
AMYQRAKLK SLTPPSTK RLMFFRPIK A2 SLYLKIHLK KIYAAGTFY YLFFIQGYK A3 KTYPCKIFY SLQPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK YRHLFKVFR YRHLFKVFR POOI 7 RRHCRSYNR KRRLLILGR FRQSLYLKI RRTQRYFMK RRTQRYFMK KRTNVGILK LRILRIKLR KRHEVPVPL KQFSAMALK B5 FRFFATPAL POOI 9 LRFSIIEEF	A1	RMLRRRAQ K	B2	A <u>R</u> FAVNLRL	Pool 6	
SLLTPP\$TK	AI	TLYSPRGE K		WRNS <u>F</u> LLRY		
RLMFFRPIK A2 RLMFFRPIK SLYLKIHLK B3 FRFFTRKSL RRHCRSYNR YLFFIQGYK KRRLLILGR TTYSPIGEK RLYKLILWR A3 KTYPCKIFY SLQPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK RS RLMFKVFR RRHCRSYNR KRRLLILGR FRQSLYLKI RRTQRYFMK RRTQRYFMK LRICPIFVF Pool 8 KRTNVGILK LRILRIKLR KRHEVPVPL HRYFFVAM HRYFFFVAM LRFSIIEEF		amyqrak <u>l</u> k		YR <u>I</u> YDIPPK		
A2 SLYLKIHLK B3 FRFFTRKSL Pool 7 KIYAAGTFY RRHCRSYNR YLFFIQGYK KRRLLILGR TTYSPIGEK FRQSLYLKI RLYKLILWR RRTQRYFMK A3 KTYPCKIFY B4 FRICPIFVF Pool 8 SLQPRGSFK KVINLSPFK LRILRIKLR CLFFGIPWK KQFSAMALK A4 RLFLGLAIK B5 FRFEATPAL Pool 9 KLKLPIMK	<u> </u>	SLLTPP S TK		ARLF <u>L</u> GLAI		
KIYAAGTFY		RLM <u>F</u> FRPIK				
YLFFIQGYK TTYSPIGEK RLYKLILWR A3 KTYPCKIFY SLQPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK RRTQRYFMK KRHCPIFVF Pool 8 KRHEVPVPL KRHEVPVPL HRYFFFVAM HRYFFFVAM LRFSIIEEF	A2	SLYL K IHLK	В3	FRFFTR K SL	Pool 7	
TTYSPIGEK						
RLYKLILWR						
A3 KTYPCKIEY B4 FRICPIFVF Pool 8 SLQPRGSFK KVINLSPFK LRILRIKLR CLFFGIPWK KQFSAMALK HRYEFFVAM A4 RLFLGLAIK B5 FRFATPAL Pool 9 KLKLPIMK LRISIEEF						
SLQPRGSFK KVINLSPFK CLFFGIPWK KQFSAMALK A4 RLFLGLAIK B5 FRFEATPAL RLFKLFIMK LRINIKLR KRHEVPVPL HRYFFFVAM FRFEATPAL Pool 9 LRFSIIEEF			<u>.</u>			
KVINLSPFK LRILRIKLR	A3		В4		Pool 8	
CLFFGIPWK KQFSAMALK HRYFFFVAM A4 RLFLGLAIK KLKLPIIMK KRHEVPVPL HRYFFFVAM FRFFATPAL Pool 9 LRFSIIEEF			4 l		4	
A4 RLFLGLAIK B5 FRFATPAL Pool 9 KLKLPIIMK LRFSIIEEF			 			
A4 RLFLGLAIK B5 FRFFATPAL Pool 9 KLKLPIIMK LRFSIIEEF			 		4	
KLKLP <u>I</u> IMK LRFS <u>I</u> IEEF	_{^4}		De l		Pool 0	
	A4		ВЭ		F001 9	
TELINITION STATE			1		1	
RLKCPF Y GK R R FSSLYSF						
KVMTDPSRK RRLLILGRI	 		1		1	
A5 RIAGKALKK B1 FRMFLTQGF Pool 10	Δ5		R1		Pool 10	
- ARWTAFFGV	A5	_	- BI		1 001 10	
KLYQCNECK GRWALHSAF			1			
SLLTPP S TK GRIAF F LKY						
RLM F FRPIK KRF <u>L</u> HRQPL			1		1	
A1 SLYL K IHLK B2 A R FAVNLRL Pool 11	A1	SLYL <u>K</u> IHLK	B2	A <u>R</u> FAVNLRL	Pool 11	
KI <u>Y</u> AAGTFY WRNS <u>F</u> LLRY		KI Y AAGTFY]	WRNS F LLRY		
YL <u>F</u> FIQGYK YR <u>I</u> YDIPPK		YL F FIQGYK		YR I YDIPPK		

Table S3. Predicted peptide pool arrangement for immunogenicity assessment.

Step	Time (ps)	Restraint atoms	Restraint force constant (kcal mol-1 Å-2)	Initial temperature (K)	Target temperature (K)	Thermodynamic ensemble	Barostat
1	10	all	2.39	0	0	NVT	-
2	50	all	2.39	2.5	5	NVT	-
3	50	all ^a	2.39	5	10	NVT	-
4	50	all ^a	2.39	10	20	NVT	-
5	50	bb	2.39	25	50	NVT	-
6	100	bb	2.39	50	100	NVT	-
7	100	bb	2.39	100	200	NVT	-
8	100	bb ^b	0.24	100	200	NVT	-
9	200	mh-bb ^c	0.24	100	200	NVT	-
10	200	mh-bb ^c	0.24	150	300	NVT	-
11	590	-	-	150	300	NVT	-
12	1500	-	-	150	300	NPT	Berendsen

Table S4. Heat-up parameters used for MD simulations.

All MHC and peptide atoms
Heavy (C,CA,O,N) backbone (bb) atoms of MHC and peptide
Heavy backbone atoms of MHC (mh-bb)
NVT: constant number, volume and temperature; NPT: constant number, pressure and temperature

Name cell line	Alias	HLA-A	HLA-B	HLA-C
HOM2	LCL 01	03:01	27:05:00	01:02
SWEIG007	LCL 02	29:02:00	40:02:00	02:02
AMALA	LCL 03	02:17	15:01	03:03
OZB	LCL 04	02:09/03:01	35:01/38:01	04:01/12:03
RSH	LCL 05	68:02/30:01	42:01:00	17:01
KLO	LCL 06	02:08/01:01	50:01/08:01	07:01/06:02
LWAGS	LCL 07	33:01:00	14:02	08:02
-	LCL 08	02:01	07:02/15:01	30:4/12:03
BM21	LCL 09	01:01	41:01:00	17:01

Table S5. HLA-allotypes of lymphoblastoid cell lines

Table S6. Characteristics of neoantigen-specific TCRs.

42F	Specificity	Source	TCR	TRAV	TRAJ	CDR3 alpha	TRBV	TRBJ	TRBD	CDR3 beta
20.0			SYTL4-TIL1	38-2/DV8*01	42*01	CAYRSARGSQGNLIF	7-8*01	2-5*01	2*01	CASSLGNYYQETQYF
)	O) (TL 45363F	TILs	SYTL4-TIL2	35*02	52*01	CAAGGTSYGKLTF	27*01	2-3*01	2*01	CASSWGGAVGDTQYF
	SYTL4 ^{S363F}		SYTL4-PBC1	9-2*02	34*01	CALYTFYNTDKLIF	6-2*01	2-5*01	2*01	CASTIAASGYQETQYF
			SYTL4-PBC2	8-3*01	43*01	CAVGVLRGDMRF	12-3*01	2-3*01	1*01	CASSSRGPTDTQYF
5	P13I	PBMCs	KIF2C-PBC1	14/DV4*02F	31*01F	CAMREQNNNARLMF	7-6*01F	2-1*01F	2*01F	CASSLTRMGDRGEFF
	KIF2C ^{P13L}		KIFC-PBC2	12-2*01F	6*01F	CAVKERASGGSYIPTF	10-3*02F	2-3*01F	1*01F	CAISDTSGGLWTDTQYF
<u> </u>	NCAPG2 ^{P333}		NCAPG2-PBC1	12-2*02	30*01	CPTGGDDKIIF	15*02	1-6*02	1*01	CATSRGDRPLHF

TCR	Recognition motif ^a	Number of antigens b,c
SYTL4-TIL1	X-R-I-A-F-F-X-X-X	6
SYTL4-TIL2	X-R-I-A-F-F-X-X-X	6
SYTL4-PBC1	X-R-I-A-F-F-X-X-X	6
SYTL4-PBC2	X-R-I-A-F-F-X-X-X	6
KIF2C-PBC1	X-X-X-L-X-L-A-I-K	60
KIF2C-PBC2	X-X-X-L-X-L-X-I-K	> 400
NCAPG2-PBC1	K-X-X-L-W-R-X-X-K	4

a) Recognition motifs are defined through T cell IFN-y production in response to alanine/threonine scanned cognate epitopes
b) Number of human proteins containing matching recognition motif according to ScanProSite
c) Results derived from protein sequence database UniprotKB, Swiss-Prot (splice variants included)

Table S7. Number of human proteins potentially identified by neoantigen-specific TCR according to their recognition motif.

TCR	M _{Int} (%)	M _{Int} -LN1 (%)	M _{Int} -LN2 (%)	M _{Lung} (%)	M _{Lung} -LN (%)
SYTL4-TIL1	0.041	0.036	0.012	0.039	0.005
SYTL4-TIL2	0.079	0.022	0.019	0.017	0.026
SYTL4-PBC1	0.152	-	0.019	0.024	0.034
SYTL4-PBC2	0.029	0.014	-	0.020	0.021
KIF2C-PBC1	0.560	0.029	0.037	0.629	0.023
KIF2C-PBC2	0.115	0.007	0.019	0.800	0.070
NCAPG2-PBC1	0.003	0.007	-	-	-

Table S8. Productive frequency (%) of neoantigen-specific clonotypes in tumor metastases and lymph nodes detected by TCR- β sequencing.

TCR	d142 (%)	d546 (%)	d796 (%)	d945 (%)	d1120 (%)	d1519 (%)
SYTL4-TIL1	0.0018	0.0016	0.0022	0.0020	0.0008	0.0010
SYTL4-TIL2	-	•	0.0015	0.0007	0.0008	0.0010
SYTL4-PBC1	0.0053	0.0132	0.0112	0.0099	0.0115	0.0094
SYTL4-PBC2	-	0.0008	0.0015	0.0007	0.0008	-
KIF2C-PBC1	0.1489	0.1672	0.3273	0.5449	0.4715	0.2505
KIF2C-PBC2	0.0132	0.0311	0.0509	0.0365	0.0376	0.0136
NCAPG2-PBC1	0.0247	0.0156	0.0187	0.0205	0.0230	0.0167

Table S9. Productive frequency (%) of neoantigen-specific clonotypes detected by TCR- β sequencing on peripheral blood collected at different time points indicated as days (d) after start of Ipilimumab treatment.