Supplemental Information

SI Table 1. Sample descriptions and HLA typings of 12 samples from which we isolated HLA peptides and phosphopeptides, including 9 BLCLs, 1 heathy B cell, and 2 AMLs treated with either DMSO or decitabine.

Sample Name	Sample Description	Class I HLA
BLCL HD1	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A11:01,HLA-A02:01,HLA-B27:04,HLA-B40:01,HLA-C07:02,HLA-C08:01
BLCL HD2	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A02:01,HLA-A11:01,HLA-B07:02,HLA-C07:02
Healthy B cells HD3	CD19+ B cells from peripheral blood of healthy donor	HLA-A11:01,HLA-A26:01,HLA-B38:02,HLA-B56:01,HLA-C07:02,HLA-C01:02
BLCL HD4	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A24:02,HLA-B35:02,HLA-C04:01
BLCL HD5	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A02:01,HLA-B37:01,HLA-B51:01,HLA-C06:06,HLA-C15:02
BLCL HD3	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A11:01,HLA-A26:01,HLA-B38:02,HLA-B56:01,HLA-C07:02,HLA-C01:02
EBV-LPD1	EBV+ lymphoma from EBV-PTLD patient	HLA-A11:01,HLA-A29:02,HLA-B44:03,HLA-B35:02,HLA-C04:01,HLA-C16:01
BLCL HD6	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A03:01,HLA-A24:02,HLA-B07:02,HLA-B18:01,HLA-C07:02,HLA-C07:01
BLCL HD7	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A02:01,HLA-B44:02,HLA-B13:02,HLA-C05:01,HLA-C06:02
BLCL HD8	EBV B95.8-transformed B lymphoblastoid cell line from healthy donor	HLA-A02:01,HLA-A11:01,HLA-B08:01,HLA-B15:01,HLA-C07:01,HLA-C03:03
OCI-AML2_DMSO	OCI-AML2 cell line (RRID:CVCL_1619) treated with DMSO	HLA-A02:01,HLA-B15:01,HLA-B18:01,HLA-C03:03,HLA-C07:01
OCI-AML2_DCB	OCI-AML2 cell line (RRID:CVCL_1619) treated with decitabine	HLA-A02:01,HLA-B15:01,HLA-B18:01,HLA-C03:03,HLA-C07:01
AML14_DMSO	AML14 cell line (RRID:CVCL_8286) treated with DMSO	HLA-A02:01,HLA-A32:01,HLA-B44:02,HLA-B51:01,HLA-C05:01,HLA-C14:02
AML14_DCB	AML14 cell line (RRID:CVCL_8286) treated with decitabine	HLA-A02:01,HLA-A32:01,HLA-B44:02,HLA-B51:01,HLA-C05:01,HLA-C14:02

SI Table 2. Phosphopeptides shared between healthy B cells and EBV-BLCL from HD3. Predicted affinities for each peptide and class I allele expressed by HD3 were computed by NetMHCpan4 based on the peptide's unmodified sequence. Predicted affinities are expressed in nM. Affinity values with the highest affinity (lowest nM value) of all predicted HLA allotypes in the same row are indicated in boldface.

Protein	Peptide	('affinity', 'HLA-A*11:01')	('affinity', 'HLA-C*07:02')	('affinity', 'HLA-A*26:01')	('affinity', 'HLA-B*38:02')	('affinity', 'HLA-B*56:01')	('affinity', 'HLA-C*01:02')

HIPK2	AISsPQRSK	**103.1**	32094.4	37861	46988.2	39612.7	37750.6
SRRM2	ATAsPPRQK	**51**	30260.2	31972.4	47055.8	39826.7	37717.5
GPATCH8	GSGsPAPPR	**248.4**	36269.2	39943.2	46585.2	42231.6	40021.5
TRA2B	RPHtPTPGI	32655.2	13780.2	37088.6	26534	**2317.6**	11705.7
FAM21C	RPTsFADEL	32714.6	13044.7	37727.7	10572.1	**3991.8**	10121
POLL	RPVsPPQKA	38495.9	31389.4	41729.7	40007.2	**1623**	31209.2
PPP1CB	RPVtPPRTA	38114.6	24741.7	41651.2	37283.8	**941.7**	24474.1
RCSD1	SPKsPGLKA	36512.9	30029	37156.1	41452.1	**935**	31314.4
SRSF5	SVSRsPVPEK	**20.4**	29960.8	31655.4	46047	34732.2	39368.7
MGA	SVSsPVKSK	**34.2**	25252.3	25526.4	45669.4	34245.2	34320.5

SI Figure 1: IRS2 Ser1100 phosphorylation levels in CPTAC colorectal cancer (Vasaikar et al. *Cell.* (2019)) samples profiled for mutations in PPP1CA, encoding the PP1A phosphatase. Data accessed in cBioPortal.


PPP1CA | Not mutated | Gain | Diploid
PPP1CA | Shallow Deletion | Deep Deletion
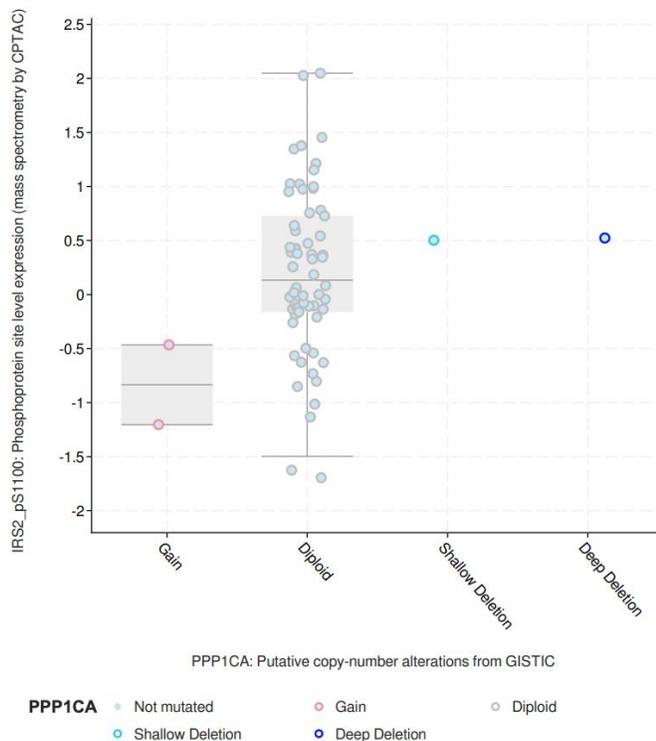
SI Figure 2: Kinases enrichment analysis using KEA3 of parental genes of phosphopeptides represented in HLA-A3/A11+ solid or heme tumors. (A) Kinases enriched in the gene set of phosphopeptides only represented in solid tumors but not heme tumors. (B) Kinases enriched in the gene set of phosphopeptides only in heme, but not solid tumors. Kinases are ranked by their MeanRank, with MeanRank decreasing from bottom to top, and plotted against the sum of their ranks in each of the kinase libraries, which are indicated by color.
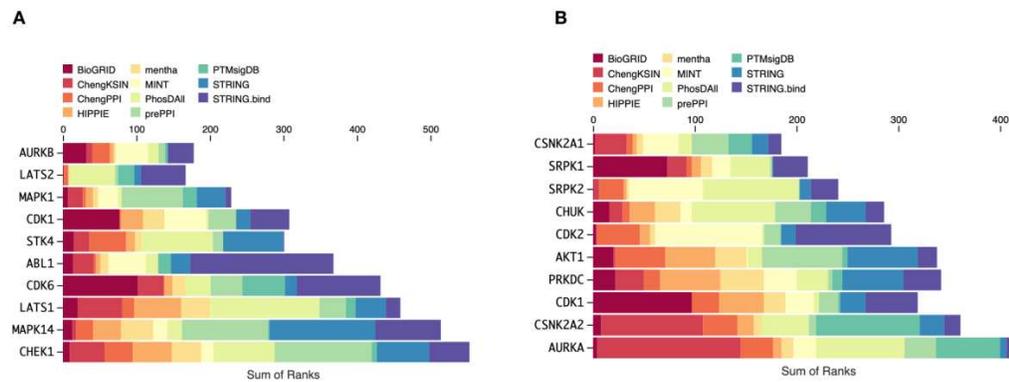
SI Table 3: NetMHCphosPan-1.0-predicted affinities of HLA-A*03:01-binding phosphopeptides. %rank_el indicates percentile rank (%rank). BindLevel indicates binding strength of peptide; strong binders are defined as having %rank<0.5, and weak binders with %rank<2. Peptides were used to evaluate T cell responses in Figures 5A-J.

Name	Sequence	HLA-A03:01 %rank_el	BindLevel
pSRRM1	RTApSPPPPPK	0.0091	Strong Binder
pMGAP	SVSpSPVKSK	0.0038	Strong Binder
pHIF1a	RTApSPNRAGK	0.0038	Strong Binder
pPRDM2	RTApSPPALPK	0.0019	Strong Binder
pMYBBP1a	ATQpSPISKK	0.0032	Strong Binder

SI Figure 3: Baseline levels of HLA-C expressed as geometric mean fluorescence intensity (gMFI) on T2-C*07:01 and T2-C*07:02 cells after performing incubation steps described in methods section without the presence of a peptide but with B2M. Significance assessed by independent t-test.
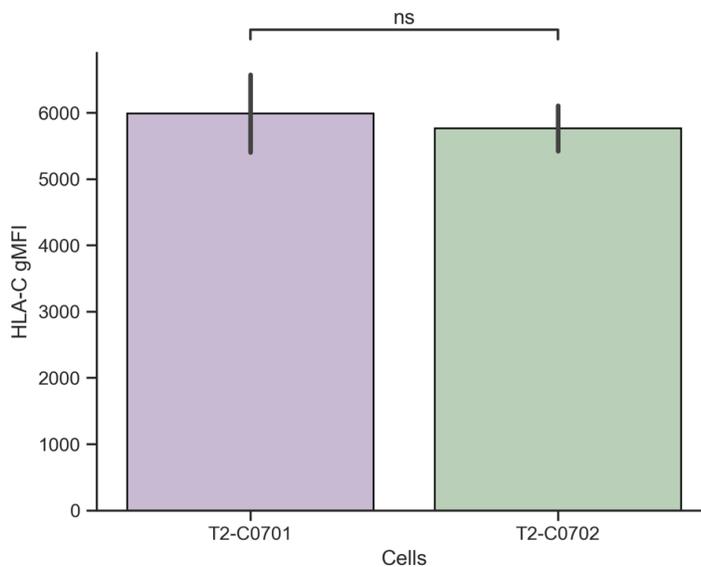
SI Table 4: Hydrogen bond analysis of pNCOR/C0701 and pNCOR/C0702 models. Hbond donor and acceptor residues suffixed with .A indicate residues on HLA and .B indicates residues on peptide. Boldfaced residue pairs indicates hydrogen bonds mutually exclusive to each complex.

Model	Average score of top 10 complexes (REU)	Hbond donor	Hbond acceptor
pNCOR/C0701	-461	ASN 80.A	PHE 9.B
		THR 143.A	PHE 9.B
		LYS 146.A	PHE 9.B
		TYR 159.A	**ARG 1.B**
		ARG 1.B	TYR 7.A
		ARG 1.B	TYR 171.A
		ARG 2.B	GLU 63.A
		ARG 2.B	GLU 63.A
		ARG 2.B	**TYR 99.A**
		ARG 2.B	ASP 9.A
		ARG 2.B	**TYR 99.A**
		LEU 6.B	GLN 70.A
		PHE 9.B	SER 77.A
pNCOR/C0702	-327	**ARG 69.A**	**SEP 4.B**
		ASN 80.A	PHE 9.B
		THR 143.A	PHE 9.B
		LYS 146.A	PHE 9.B
		LYS 146.A	PHE 9.B
		ARG 1.B	TYR 7.A
		ARG 1.B	TYR 171.A
		ARG 1.B	**GLU 63.A**
		ARG 2.B	GLU 63.A
		ARG 2.B	ASP 9.A
		LEU 6.B	GLN 70.A
		PHE 9.B	SER 77.A