Peptide Pool	Peptide Number	Amino Acid Sequence
Pool 1: E6-1	1	MHQKRTAMFQDPQERPRKLPQL
	2	DPQERPRKLPQLCTELQTTIHD
	3	QLCTELQTTIHDIILECVYCKQ
	4	HDIILECVYCKQQLLRREVYDF
	5	KQQLLRREVYDFAFRDLCIVYR
	6	DFAFRDLCIVYRDGNPYAVCDK
	7	YRDGNPYAVCDKCLKFYSKISE
	8	DKCLKFYSKISEYRHYCYSLYG
Pool 2: E6-2	9	SEYRHYCYSLYGTTLEQQYNKP
	10	YGTTLEQQYNKPLCDLLIRCIN
	11	KPLCDLLIRCINCQKPLCPEEK
	12	INCQKPLCPEEKQRHLDKKQRF
	13	EKQRHLDKKQRFHNIRGRWTGR
	14	RFHNIRGRWTGRCMSCCRSSRT
	15	GRWTGRCMSCCRSSRTRRETQL
Pool 3: E7	16	MHGDTPTLHEYMLDLQPETTDL
	17	YMLDLQPETTDLYCYEQLNDSS
	18	DLYCYEQLNDSSEEEDEIDGPA
	19	SSEEEDEIDGPAGQAEPDRAHY
	20	PAGQAEPDRAHYNIVTFCCKCD
	21	HYNIVTFCCKCDSTLRLCVQST
	22	CDSTLRLCVQSTHVDIRTLEDL
	23	STHVDIRTLEDLLMGTLGIVCP

	24	RTLEDLLMGTLGIVCPICSQKP
Pool 4: Potential epitopes that may have arisen as a consequence of shuffling the protein domains.	25	TDLYCICSQKPKCDSTLRL
	26	GTLGIVCPYEQLNDSS
	27	YNIVTFCCQPETTDLY
	28	HDIILECVNCQKPLCP
	29	GRWTGRCMKCLKFYSK
	30	CDLLIRCIYCKQQLLR
	31	GNPYAVCDSCCRSSRT
	32	RTRRETQLQLCTELQT

Supplementary table 1: Overview of peptide pools used in the ex vivo reactivity screens, and the amino acid sequence of each peptide.

Target + Fluorochrome	**Clone**	**Details**	**Vendor**
CD3-APC-H7	Clone SK7	Mouse IgG1	BD Biosciences
CD14-Pacific Blue	Clone TùK4	Mouse IgG2a	Invitrogen
CD16-Pacific Blue	Clone 3G8	Mouse IgG1	Invitrogen
CD19-Pacific Blue	Clone SJ25-C1	Mouse IgG1	Invitrogen
CD4-PE	Clone S3.5	Mouse IgG2a	Invitrogen
CD8-PerCP-Cy5.5	Clone SK1	Mouse IgG1	BioLegend
CCR7-PE-CF594	Clone 150503	Mouse IgG2a	BD Biosciences
CD45RA-PE-Cy5.5	Clone MEM-56	Mouse IgG2b	Invitrogen
PD-1-eVolve 655	Clone J105	Mouse IgG1	eBiosciences
IFNɣ-FITC	Clone B27	Mouse IgG1	BD Biosciences
IL-2-APC	Clone MQ1-17H12	Rat IgG2a	BD Biosciences
TNFα-PE-Cy7	Clone MAb11	Mouse IgG1	BD Biosciences
CD107a-Alexa Fluor 700	Clone H4A3	Mouse IgG1	BD Biosciences
Fixable Violet Dead Cell Stain Kit, 405 nm	Fluorescent reactive dye + DMSO		Invitrogen

Supplementary table 2: Antibody panel used for ex vivo reactivity screens.

SUPPLEMENTARY FIGURE LEGENDS

Supplementary figure 1: Gating strategy example of phenotypic characterization and cytokine production of CD4 and CD8 T cells.

Supplementary figure 2: Phenotypic characterization of circulating T cells. **a)** Frequency of PD-1 positive CD4 and CD8 T cells over time. **b)** Differentiation state of CD4 and CD8 T cells defined by CD45RA and CCR7 surface marker expression. CD45RA+ CCR7+: naïve T cells, CD45RA- CCR7+: central memory T cells, CD45RA- CCR7-: effector memory T cells and CD45RA+ CCR7-: effector T cells. Responding patients are colored red and non-responding patients are colored blue.

Supplementary figure 3: Depicted are the frequencies of single, double and triple cytokine producing CD4 and CD8 T cells, with and without co-expression of degranulation marker CD107a (LAMP-1), determined using Boolean gating. Depicted are immunologically responding patients **a** patient 1, **b** patient 2, **c** patient 4, **d** patient 7 and **e** patient 8.

Supplementary figure 4: Time course graphs showing the IFNγ, TNFα, IL-2 and CD107a responses against E6-1, E6-2 and E7 peptide pool for each patient. No peptides indicate that T cells were co-cultured with unloaded APCs to access background or aspecific reactivity. The green boxes highlight the patients with an immunological response.

Supplementary figure 5: Reactivity against the peptides that arose as a consequence of shuffling the E6 and E7 coding sequences. Boxes highlight responding patients.

Supplementary figure 6: Reactivity against ICE peptide pool at day 0. On the left, patient responses are depicted and on the right four healthy controls are depicted for the matched cytokines or LAMP-1. The black boxes on the x-axis highlight responding patients.