

Clone#	Peptide Sequence
1	CPGKGLPSC
2	CPGKGLPSC
3	CPFPAKILC
4	CTKPAKALC
5	CIHAPYAKC
6	CPGKGLPSC
7	CPFPALELC
8	CPAKIGQEC
9	<i>ND</i>
10	CKHAPYALC

Supplemental Table 1: Peptide Sequences of Isolated Phage Clones. Sequences of displayed peptides from enriched individual phage clones evaluated in **Fig. 1A**. *ND* = not determined.

	CPFPALC:Fab	CPGKGLPSC:Fab
Data collection		
Space group	C 1 2 1	P 21 21 21
Cell dimensions		
a, b, c (Å)	130.18, 55.23, 73.86	72.43, 203.51, 225.92
α, β, γ (°)	90, 118.696, 90	90, 90, 90
Resolution (Å)	24.46 - 1.8 (1.864 - 1.8)	20.0 – 3.0 (3.107 – 3.0)
R_{merge}	0.06451 (0.4702)	0.2699 (0.8219)
$I / \sigma I$	21.67 (2.05)	4.08 (1.63)
$CC_{1/2}$	0.999 (0.848)	0.963 (0.534)
Completeness (%)	96.99 (79.61)	97.83 (99.21)
Multiplicity	8.3 (2.8)	3.3 (3.3)
Refinement		
Resolution (Å)		
Number of reflections	41567	66291
R_{work} / R_{free} (%)	18.6 / 22.5	23.89 / 28.82
Number of atoms		
macromolecules	3348	19964
ligands	13	0
solvent	541	0
R.M.S. deviations		
Bond lengths (Å)	0.010	0.003
Bond angles (°)	1.282	0.542
Ramachandran		
Favored / allowed / disallowed	98.6 / 1.2 / 0.23	96.29 / 3.60 / 0.12
PDB Code	8G2M	8G8N

Supplemental Table 2: Crystallographic analysis and refinement statistics for peptide:aCTLA4 crystal structures.

Protease	k_{cat}/K_m ($\text{M}^{-1} \cdot \text{s}^{-1}$)	SD ($\text{M}^{-1} \cdot \text{s}^{-1}$)
MMP-1	1.4E+04	5.0E+02
MMP-2	3.1E+04	3.5E+03
MMP-7	2.2E+04	2.0E+03
MMP-9	4.6E+04	4.5E+03
MMP-10	1.2E+03	0
MMP-14	2.4E+03	1.0E+02

Supplemental Table 3: Catalytic efficiency for activation of XTX101 with recombinant human MMPs. SD was calculated from 2 independent experiments.

Group	Treatment	Dose (mg/kg)	Tumor Volume (mm ³) ^a on Day 16	TGI (%) ^b	Complete Responses	p value ^c
1	Isotype Control	10	2220 ± 161	-	0/8	-
2	Ipilimumab analog	1	773 ± 158	65.2	0/8	0.0002
3	Ipilimumab analog	3	227 ± 57	89.8	2/8	<0.0001
4	XTX100	1	213 ± 50	90.4	3/8	<0.0001
5	XTX100	3	135 ± 23	93.9	6/8	<0.0001
6	XTX100	10	134 ± 32	94	4/8	<0.0001
7	XTX101	1	434 ± 140	80.5	2/8	<0.0001
8	XTX101	3	194 ± 32	91.2	3/8	<0.0001
9	XTX101	10	133 ± 31	94	5/8	<0.0001

Supplemental Table 4: Results from XTX101 in MB49 Model Study. Tumor volume measurements, TGI calculations, and complete responses from MB49 tumor model study. ^aMean ± SEM. ^bTumor Growth Inhibition (TGI) = (1-T/C) × 100%; T and C are mean tumor volumes of treatment and vehicle control groups respectively on Day 16. ^cA 2-way repeated measures analysis of variance (ANOVA) with Bonferroni's post-hoc test was performed to determine the statistical significance of treatment versus isotype control. Day 16 results were tabulated.

Group	Treatment	Tumor Volume (mm ³) ^a on Day 14	TGI (%) ^b	p value ^c
1	Isotype control 10 mg/kg	1446 ± 132	-	-
2	XTX101 0.3 mg/kg	1000 ± 109	34.22	0.8354
3	RMP1-14 10 mg/kg	931 ± 171	39.56	0.3722
4	XTX101 0.3 mg/kg + RMP1-14 10 mg/kg	374 ± 125	82.34	0.0002

Supplemental Table 5: Results from XTX101 + anti-PD-1 Combination Therapy in MC38 Tumor Model Study.

Tumor volume measurements and TGI calculations from MC38 tumor model study. ^aMean ± SEM. ^bTumor Growth Inhibition (TGI) = (1-T/C) × 100%; T and C are mean tumor volumes of treatment and vehicle control groups respectively on Day 14.

^cCompared to isotype control (Group 1) by Kruskal-Wallis test with Dunn's multiple comparison test on day 14 post-treatment.