Supplementary information

Discovery of modulator for PD-1/PD-L1 interaction by molecular simulation and bioassay

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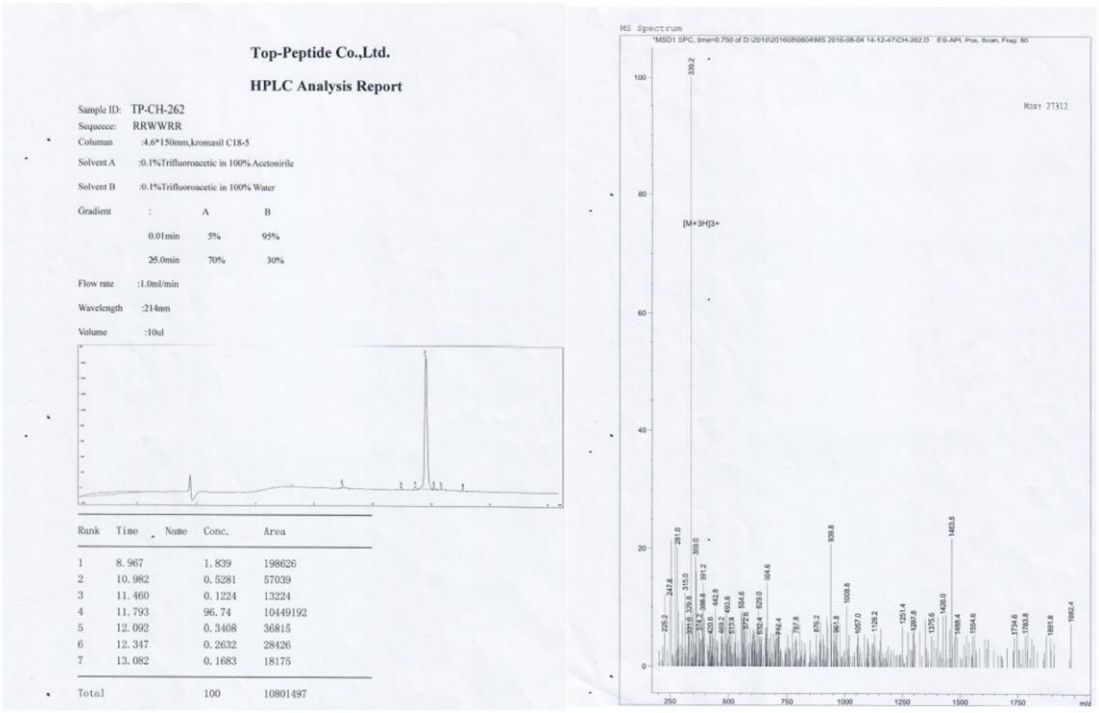
New Journal of Chemistry

1. The characterization of synthetic novel tripeptides



Top-Peptide Co.,Ltd.

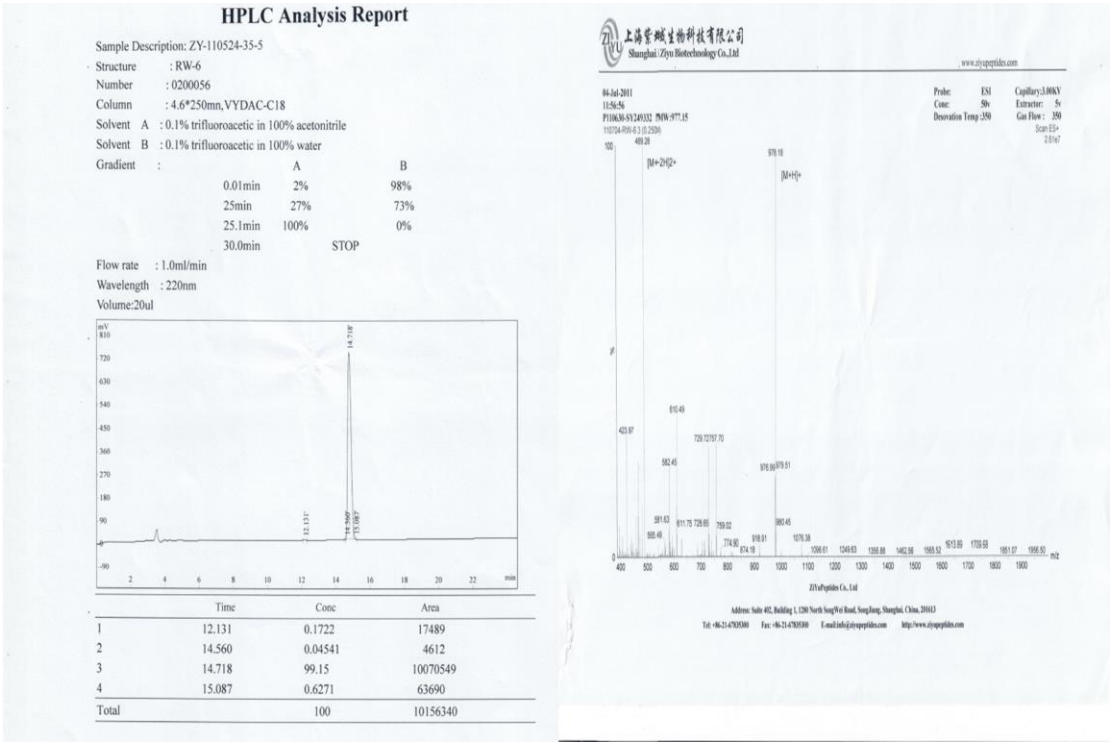
HPLC Analysis Report

Sample ID: TP-CH-262
Sequence: RRWWRR
Column :4.6*150mm,kromasil C18-5
Solvent A :0.1%Trifluoroacetic in 100% Acetonirile
Solvent B :0.1%Trifluoroacetic in 100% Water
Gradient : A B
0.01min 5% 95%
25.0min 70% 30%
Flow rate :1.0ml/min
Wavelength :214nm
Volume :10ul

Rank	Time	Name	Conc.	Area
1	8.967		1.839	198626
2	10.982		0.5281	57039
3	11.460		0.1224	13224
4	11.793		96.74	10449192
5	12.092		0.3408	36815
6	12.347		0.2632	28426
7	13.082		0.1683	18175
Total			100	10801497

MS Spectrum

Figure S1. Characterization of RRWWRR-NH2 by analytical HPLC chromatogram and MS Spectrum.



HPLC Analysis Report

Sample Description: ZY-110524-35-5
Structure : RW-6
Number : 0200056
Column : 4.6*250mn,VYDAC-C18
Solvent A : 0.1% trifluoroacetic in 100% acetonitrile
Solvent B : 0.1% trifluoroacetic in 100% water
Gradient : A B
0.01min 2% 98%
25min 27% 73%
25.1min 100% 0%
30.0min STOP
Flow rate : 1.0ml/min
Wavelength : 220nm
Volume:20ul

	Time	Conc	Area
1	12.131	0.1722	17489
2	14.560	0.04541	4612
3	14.718	99.15	10070549
4	15.087	0.6271	63690
Total		100	10156340

Figure S2. Characterization of RRQWFW-NH2 by analytical HPLC chromatogram and MS Spectrum.

2. Energy decomposition analysis (EDA) of complex PD-1/peptide

Table S1. Energy decomposition analysis (EDA) of complex RRWWRR-NH_2

Name	van der waals	Electrostatic	Polar	MMGBSA
VAL64	-0.6829	0.6142	-0.4514	-0.64686
ASN66	-0.55035	0.3973	0.2983	0.123476
TYR68	-1.92275	-0.6625	-0.13515	-2.84923
ASN74	-0.21315	-1.4625	1.8569	0.171361
GLN75	-1.72905	-1.48805	2.2508	-1.10114
THR76	-2.0394	-12.4872	8.93625	-5.97625
ASP77	-0.72905	-75.9729	73.3841	-3.42004
LYS78	-2.214	70.65795	-68.9956	-0.94493
ASP85	-1.44435	-101.452	99.2522	-3.90088
SER87	-1.3786	3.688	-3.5116	-1.47547
ILE126	-1.99375	0.7337	-0.96885	-2.4128
LEU128	-0.8119	-1.21145	1.58785	-0.68814
ALA132	-0.7037	-1.3771	1.64475	-0.55279
ILE134	-1.95785	-0.73645	1.7693	-1.1459
GLU136	-0.01895	-91.4497	85.6323	-6.04266

Table S2. Energy decomposition analysis (EDA) of complex RRQWFW-NH_2

Name	van der waals	Electrostatic	Polar	MMGBSA
VAL64	-0.3814	0.72345	-0.3671	-0.12618
ASN66	-0.7169	-0.5827	1.1904	-0.16014
TRP67	-0.1043	-0.89945	0.7542	-0.24955
TYR68	-1.28835	-4.16515	3.3758	-2.27494
ASN74	-0.0732	-0.0018	0.196	0.114917
GLN75	-0.1947	-0.10495	0.3794	0.070663
THR76	-1.5031	-1.11715	2.2865	-0.67181
ASP77	-1.22445	-29.377	29.9599	-0.81426
LYS78	-0.00335	0.1404	-0.1474	-0.01035
ASP85	-0.8737	-60.5576	59.2912	-2.32271
SER87	-0.1613	-0.39065	0.53515	-0.071
ILE126	-1.7918	0.41815	-0.19745	-1.77394
LEU128	-0.18705	-0.2162	0.3507	-0.09934
ALA132	-0.0777	1.3128	-1.2784	-0.0434
ILE134	-2.6856	0.4765	-0.1165	-2.60596
GLU136	-0.87365	-30.8354	31.35285	-0.57908

3 SPR measurement of PD-1/peptides to immobilized PD-L1

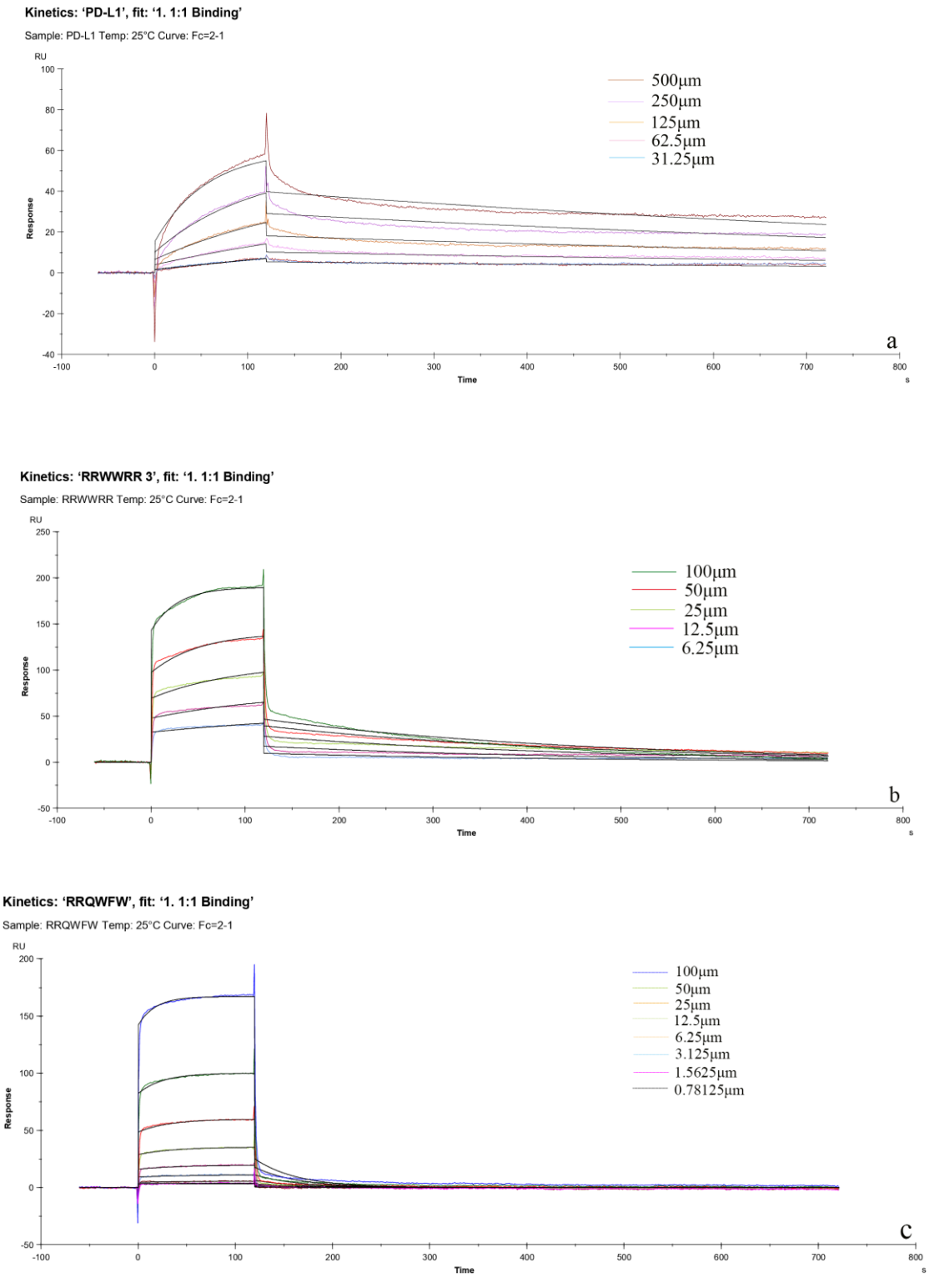


Figure S3. Affinity between PD-1 and peptides (PD-L1(a)/RRWWRR (b) /RRQWFW(c)). A series of concentrations of peptides (PD-L1) were run over PD-1 to obtain the affinity between PD-1 and peptides (PD-L1) by kinetic analysis.

4. Competitive inhibition of peptide inhibitors on PD-1/PD-L1

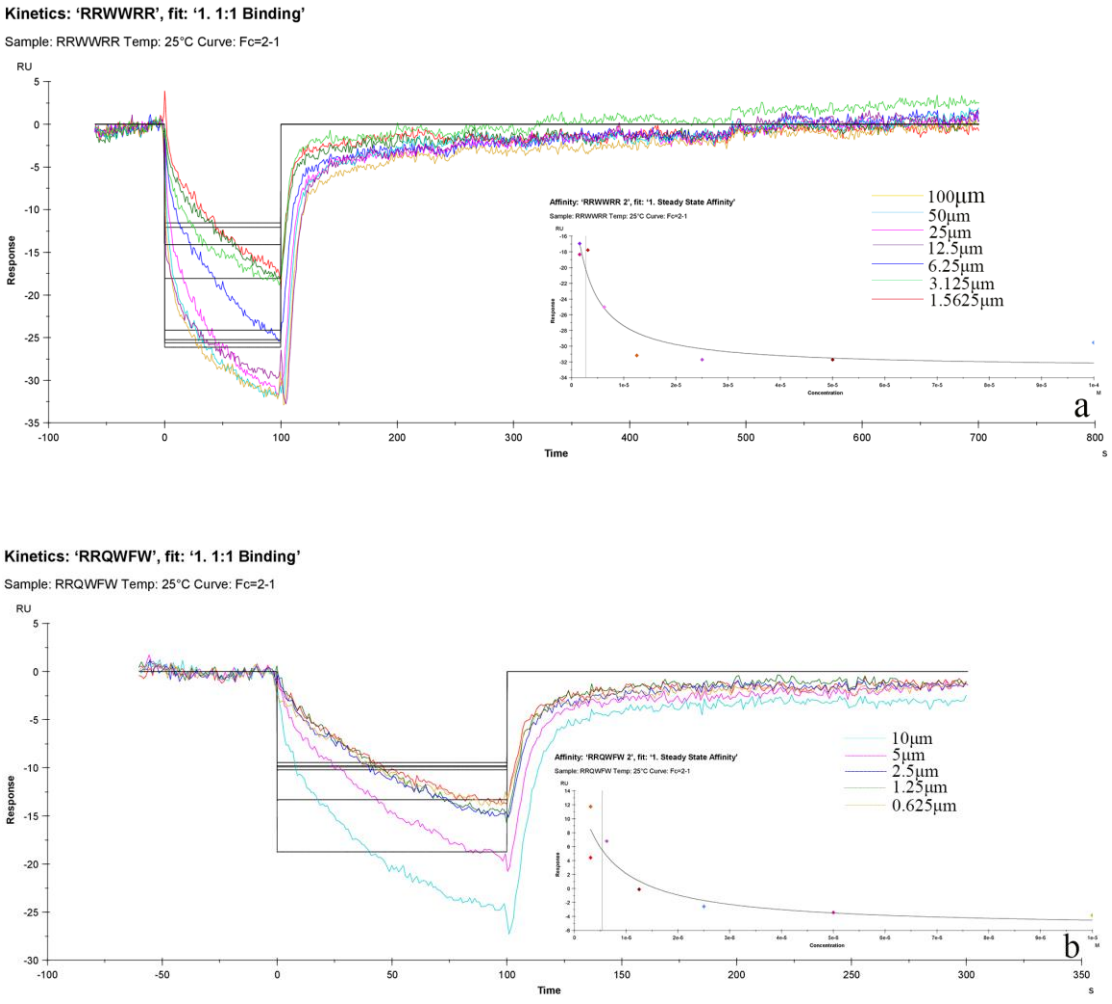


Figure S4. Competitive between PD-1/ PD-L1 and peptides (RRWWRR(a)/RRQWFW(b)).