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ELECTRONIC SUPPLEMENTARY INFORMATION

Blockade of the checkpoint PD-1 by its ligand PD-L1 and the immuno-oncological drugs Pembrolizumab and Nivolumab

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TABLE I. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of PD-1 interacting with Pembrolizumab heavy-chain residues that showed the most significant interaction energies.

Residue PD-1	TIE		Number of Pairs
	ε_{20}	ε_{40}	
V64	-4.30	-4.25	7
N66	-4.54	-4.29	8
Y68	-3.01	-2.85	7
T76	-5.21	-5.13	8
D77	-3.96	-3.38	9
K78	-29.80	-29.06	13
D85	-12.87	-11.84	9
S87	-6.54	-6.12	19
Q88	-5.45	-5.43	21
P89	-17.17	-16.84	25
G90	-10.98	-10.61	12
Q91	-3.26	-3.13	10
I126	-4.09	-4.16	5
L128	-3.32	-3.33	6
K131	-15.51	-13.87	12
A132	-3.90	-3.60	4
I134	-2.45	-2.42	6

TABLE II. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of Pembrolizumab heavy-chain (PEM-HC) interacting with PD-1 residues that showed the most significant interaction energies.

Residue PEM-HC	TIE		Number of Pairs
	ε_{20}	ε_{40}	
Y33	-21.94	-21.48	15
Y35	-5.47	-5.36	8
I51	-2.24	-2.18	5
N52	-8.34	-8.27	10
S54	-3.18	-3.15	10
N55	-2.25	-2.06	12
T58	-5.57	-5.41	5
N59	-5.99	-5.74	6
R99	-5.58	-6.77	15
D100	-2.77	-2.19	14
Y101	-18.49	-18.07	23
R102	-21.58	-20.03	30
F103	-13.91	-13.62	21
D104	-5.84	-5.51	13
M105	-9.67	-9.02	13
D108	-6.56	-4.82	1

TABLE III. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of PD-1 interacting with Pembrolizumab light-chain residues that showed the most significant interaction energies.

Residue PD-1	TIE ε_{20}	TIE ε_{40}	Number of Pairs
S62	9.75	9.75	8
F63	5.05	5.06	4
V64	-2.77	-2.79	7
F82	-3.01	-2.97	4
P83	-5.75	-5.87	9
E84	-1.84	-2.51	8
D85	-2.05	-1.98	8
R86	-11.08	-10.98	16
S87	-10.01	-9.82	12
L128	-4.08	-4.08	13
A129	-4.59	-4.59	8
K131	-17.89	-15.77	13

TABLE IV. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of Pembrolizumab light-chain (PEM-LC) interacting with PD-1 residues that showed the most significant interaction energies.

Residue PEM-LC	TIE ε_{20}	TIE ε_{40}	Number of Pairs
T31	-2.93	-2.91	6
Y34	-4.68	-4.56	19
Y36	-7.41	-7.16	10
Y53	-4.18	-4.07	9
L54	-2.04	-2.00	10
Y57	6.06	6.17	10
E59	-11.69	-9.69	4
S60	-2.71	-2.71	5
S95	-6.99	-6.85	5
R96	-3.66	-4.33	5
L98	-3.42	-3.29	8

TABLE V. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of PD-1 interacting with Nivolumab heavy-chain residues that showed the most significant interaction energies.

Residue PD-1	TIE ε_{20}	TIE ε_{40}	Number of Pairs
D26	-3.39	-2.43	7
P28	-23.27	-22.78	25
D29	-8.93	-8.70	20
R30	-18.03	-16.60	14
P31	-3.84	-3.81	7
T59	5.26	5.28	5
S62	-2.77	-2.75	9
L128	-2.87	-2.95	6
A129	-4.16	-3.70	10
P130	-9.91	-9.60	11
K131	-18.37	-15.20	7

TABLE VI. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of Nivolumab heavy-chain (NIV-HC) interacting with PD-1 residues that showed the most significant interaction energies.

Residue NIV-HC	TIE		Number of Pairs
	ε_{20}	ε_{40}	
T28	-3.39	-3.27	8
N31	-8.43	-7.77	16
S32	-4.27	-4.24	10
W52	-18.94	-18.66	7
Y53	-10.34	-10.49	8
N99	-5.41	-5.21	10
D100	-13.11	-10.71	14
Y102	-8.34	-8.25	10

TABLE VII. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of PD-1 interacting with Nivolumab light-chain residues that showed the most significant interaction energies.

Residue PD-1	TIE		Number of Pairs
	ε_{20}	ε_{40}	
D26	-4.15	-3.00	6
A129	9.66	9.84	7
P130	-8.29	-8.05	13
K131	-22.12	-21.89	22
A132	-5.99	-6.15	11
Q133	-3.05	-3.03	5

TABLE VIII. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of Nivolumab light-chain (NIV-LC) interacting with PD-1 residues that showed the most significant interaction energies.

Residue NIV-LC	TIE		Number of Pairs
	ε_{20}	ε_{40}	
L46	-4.22	-4.38	4
Y49	-14.95	-15.06	8
A55	-4.87	-4.90	6
T56	5.69	6.06	10

TABLE IX. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of PD-1 interacting with PD-L1 residues that showed the most significant interaction energies.

Residue PD-1	TIE		Number of Pairs
	ε_{20}	ε_{40}	
N66	-5.17	-3.08	12
Y68	-11.72	-11.63	12
N74	-2.96	-2.38	8
Q75	-17.20	-16.54	19
T76	-11.43	-11.17	14
D77	-3.43	-2.88	9
K78	-5.62	-11.18	17
E84	-5.79	-5.52	8
I126	-7.11	-7.07	16
L128	-5.50	-4.31	20
K131	-18.24	-14.70	20
Q133	-2.35	-2.15	11
I134	-10.87	-10.41	19
E136	-13.10	-10.26	6

TABLE X. Calculated total interaction energy (TIE), in kcal.mol^{-1}, and the number of the pairs evaluated through the MFCC scheme for the amino-acids of PD-L1 interacting with PD-1 residues that showed the most significant interaction energies.

Residue PD-L1	TIE		Number of Pairs
	ε_{20}	ε_{40}	
ALA18	-3.80	-3.70	7
PHE19	-8.99	-8.62	11
THR20	-6.63	-6.55	10
ASP26	-3.64	-3.37	6
ILE54	-2.88	-2.89	10
TYR56	-6.63	-6.02	9
GLU58	-3.61	-2.47	7
GLN66	-2.53	-2.30	8
VAL76	-2.85	-2.76	5
ARG113	-10.88	-9.62	15
MET115	-5.99	-6.08	17
GLY120	-1.99	-2.09	8
ALA121	-8.67	-8.27	20
ASP122	-1.11	-2.50	17
TYR123	-17.42	-17.13	26
LYS124	-13.95	-13.16	16
ARG125	-15.22	-13.10	15