

Supplementary Materials: New Insights into the Type II Toxins from the Sea Anemone *Heteractis crispa*

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Table S1. Hot spots of δ -SHTX-Hcr1f interchain non-covalent interactions with rNav1.2.

Type ¹	δ -SHTX-Hcr1f	rNav1.2	Energy contribution, kcal/mol	rNav1.2 region
DIH	Lys46	Asp317	-28.909	E α 1a-E α 1b linker
DIH	Lys48	Lys355	-27.764	E β 1b
DIH	Glu31	Lys355	-26.446	E β 1b
DIH	Asp7	Lys355	-23.855	E β 1b
DIH	Lys48	Asp317	-23.828	E α 1a-E α 1b linker
DIH	Lys48	Glu318	-19.798	E α 1b
DIH	Lys46	Glu318	-13.38	E α 1b
DH	Lys32	Glu1616	-8.574	S3 VSD-IV
DH	Lys47	Cys353	-8.414	E β 1b
DH	Asp7	Asn340	-6.453	E α 1b-E β 1b linker
DH	Lys32	Ser1621	-5.907	S4 VSD-IV
DH	Arg45	Asn285	-5.338	E α 1a-E α 1b linker
DH	Asn25	Glu1616	-4.618	S3 VSD-IV
DH	Val21	Asn303	-4.282	E α 1a-E α 1b linker
DH	Asn25	Glu1613	-3.713	S3 VSD-IV
DH	Lys46	Trp316	-2.845	E α 1a-E α 1b linker
D	Asp8	Ile352	-2.838	E β 1b
D	Arg45	Trp316	-2.784	E α 1a-E α 1b linker
DH	Asp11	Asn340	-2.194	E α 1b-E β 1b linker
DH	Glu28	Val311	-2.139	E α 1a-E α 1b linker
DH	Arg13	Val1620	-2.127	S3-S4 linker, VSD-IV
DH	Ser2	Leu300	-1.981	E α 1a
D	Trp30	Trp302	-1.515	E α 1a
D	Val36	Lys1617	-1.492	S3 VSD-IV
D	Trp24	Trp1565	-1.47	S2 VSD-IV
D	Asp6	Val1620	-1.238	S3-S4 linker, VSD-IV
DH	Asp8	Cys353	-1.199	E β 1b

¹H - hydrogen bonds, I - ionic, D - distance (hydrophobic, van der Waals).

Table S2. δ -SHTX-Hcr1f residue Arg13 non-covalent interchain with phospholipid, adjacent to VSD-IV helix S4.

Non-covalent interaction type ¹	δ -SHTX-Hcr1f Arg13 atoms	DPPC atoms	Energy contribution, kcal/mol
Hbond	NH1	O13	-8.1
Hbond	NH2	O13	-7.3
Ionic	NH2	O13	-6.707
Ionic	NH1	O13	-6.152
Ionic	NH1	O14	-2.119
Distance	NH2	P	-0.361
Distance	CG	C13	-0.316
Distance	CG	C15	-0.272
Distance	CZ	P	-0.171
Distance	CZ	C15	-0.16
Distance	NH2	NC3	-0.151

Distance	OD2	C15	-0.112
Distance	CZ	O14	-0.07
Distance	OD2	C13	-0.053
Distance	OD2	NC3	-0.017
Distance	OD1	C13	-0.016

¹ HBond - hydrogen bonds, Distance (hydrophobic, van der Waals).