Batrachotoxin, Pyrethroids and BTG 502 Share Overlapping Binding Sites On Insect Sodium Channels

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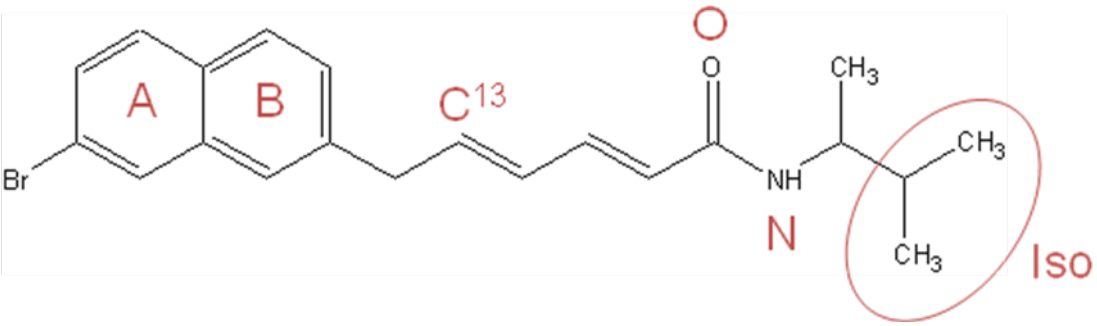
Table S1. Distance constraints that were used for BTG 502 docking to impose proximity of experimentally determined BTG 502 sensing residues with indicated BTG 502 moieties.



Binding Mode	BTG sensing residue						
	I^{3i12}	G^{3i14}	S^{3i15}	F^{3i16}	F^{3i17}	L^{3i19}	F^{4i15}
1	Iso						
2	A						
3	B						
4				Iso			
5				A			
6				B			
7					A		
8					B		
9							A
10							B
11						C13	
12	Iso						A
13	Iso						B
14	Iso				A		
15			N				
16			O				
17			N		A		
18			O				A
19	Iso		O				
20	Iso		N				
21	Iso					C13	
22						Iso	
23				A		Iso	
24	A					Iso	
25	A		O				
26				A		C13	
27							Iso

28			A	Iso
29	A			Iso
30	A		Iso	

There are too many combinations by which BTG 502 moieties could be constrained to BTG 502-sensing residues Therefore, we used a knowledge-based, heuristic approach to dock BTG 502.
We have chosen 30 combinations in which six BTG 502 moieties (indicated at structural formulae above) were constrained to side chains of the seven experimentally determined BTG 502 sensing residues. For example, binding mode 1 was obtained by constraining the "ISO" group to I^{3i12} and MC-minimizing the complex with this biased contact. In binding mode 18 was obtained by constraining the oxygen from the amide group (O) to S^{3i15} and the first aromatic ring (A) to F^{4i15}.

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TABLE S2. Effect of mutations on the action of BTX, deltamethrin and BTG 502

Residue	BTX agonism	Deltamethrin agonism	BTG 502 agonism	BTG 502 antagonism of deltamethrin action
I^{3i12}		+	+	–
G^{3i14}	+	+	+	–
S^{3i15}	+		+	+
F^{3i16}	+	+	+	–
F^{3i17}		+	+	+
L^{3i19}	+		+	+
N^{3i20}		+	–	–
F^{4i15}	+		+	+

+, Mutation affects the ligand action

- , Mutation does not affect the ligand action

Each colour encodes a group of residues whose mutations have similar effects. For example, red "+" indicate residues whose mutations affect agonism of BTX, agonism of BTG 502, and antagonism of BTG 502 on the deltamethrin-induced current.

The residues in Figure S2 are colored according to the Table