S1 Table. Prediction of potential amino acid residues in *Cs*RDL interacting with fluralaner

Transmembrane domain	Position on *Cs*RDL	WT	Mutation	Binding energy				
				WT	Mutation			**No.**
TMD1	258 (228)	I	T	4.5215(I)	4.5902(T)			**1**
	260 (230)	I	L/M	4.2084(I)	5.3753(L)	4.6323(M)		**2**
	262 (232)	S	C	4.4730(S)	4.4480(C)			**3**
	263 (233)	G	I	4.7443(G)	5.4000(I)			**4**
	264 (234)	L	M	3.9282(L)	3.6924(M)			**5**
	265 (235)	I	T	3.7468(I)	4.8598(M)			**6**
	268 (238)	I	L	4.8808(I)	4.2732(L)			**7**
	275 (245)	L	I	1.4511(L)	3.6435(I)			**8**
TMD2	284 (254)	V	T	3.5264(V)	4.1300(T)			**9**
	288 (258)	V	I	5.4886(V)	2.9646(I)			**10**
	298 (268)	M	S/N	5.4843(M)	4.6268(S)	4.4541(N)		**11**
	299 (269)	S	I/T	6.1474(S)	5.4397(I)	5.7228(T)		**12**
	301 (271)	T	A/L	6.6488(T)	6.2552(A)	5.8912(L)		**13**
	302 (272)	N	R	3.9210(N)	5.0899(R)			**14**
	303 (273)	A	N/E/K	4.9935(A)	3.7599(N)	4.1328(E)	4.5773(K)	**15**
	304 (274)	A	S/T	4.8820(A)	3.7685(S)	4.8886(T)		**16**
TMD3	317 (287)	Y	F	4.8300(Y)	7.2348(F)			**17**
	318 (288)	L	I/V	3.7757(L)	5.4566(I)	4.8602(V)		**18**
	319 (289)	G	A/M/S	5.0231(G)	4.8663(A)	5.6859(M)	7.5320(S)	**19**
	320 (290)	T	V/G	4.4847(T)	4.9667(V)	4.6417(G)		**20**
	323 (293)	V	A	4.2857(V)	3.8009(A)			**21**
	324 (294)	M	F	4.4061(M)	5.2403(F)			**22**
	327 (297)	A	S	3.5754(A)	2.5077(S)			**23**
	328 (298)	S	A	1.9168(S)	2.0141(A)			**24**
	330 (300)	L	I/M	4.1681(L)	3.5937(I)	3.9840(M)		**25**
	336 (306)	G	N	4.3093(G)	5.1995(N)			**26**
	338 (308)	M	I	4.4562(M)	5.0653(I)			**27**
	339 (309)	A	F	5.7805(A)	5.8155(F)			**28**
TMD4	462 (325)	V	F	4.7601(V)	4.6287(F)			**29**
	466 (329)	C	T	3.0400(C)	4.7353(T)			**30**
	468 (331)	V	S	3.8259(V)	3.4912(S)			**31**
	469 (332)	C	F/L	3.6769(C)	4.1046(F)	5.1194(L)		**32**
	473 (336)	M	V	3.3124(M)	6.2653(V)			**33**
	474 (337)	Y	S	4.8024(Y)	5.5412(S)			**34**
	477 (340)	I	D/Y	6.0092(I)	2.9393(D)	4.8363(Y)		**35**

Note, amino acid residues in red were selected for functional expression studies.