

**S5 Table. Potencies of GABA and fluralaner on wild-type or G3'M<sub>TMD3</sub> RDL cRNA from different species expressed in *X. laevis* oocytes.**

cRNA	Fluralaner	GABA	
	IC <sub>50</sub> (95% CI) (nM)	EC <sub>50</sub> (95% CI) (μM)	Hill Slope (95% CI)
wild-type <i>Cs</i> RDL	4.51 (3.00-6.79)	38.32 (34.43-42.66)	1.87 (1.55-2.20)
G3'M <sub>TMD3</sub> <i>Cs</i> RDL	> 10,000*	1306* (1208-1413)	2.40 (1.99-2.81)
wild-type <i>Ls</i> RDL	3.27 (1.90-5.62)	31.95 (27.90-36.60)	1.97 (1.45-2.48)
G3'M <sub>TMD3</sub> <i>Ls</i> RDL	> 10,000*	756.60* (687.20-833.10)	2.30 (1.85-2.75)
wild-type <i>Am</i> RDL	9.38 (6.68-13.17)	13.37 (12.31-14.53)	2.62 (2.13-3.12)
G3'M <sub>TMD3</sub> <i>Am</i> RDL	> 10,000*	267.50* (203.90-351.00)	1.98 (0.939-3.02)
wild-type <i>Dm</i> RDL	6.96 (2.70-17.95)	23.51 (20.88-26.48)	1.95 (1.53-2.36)
G3'M <sub>TMD3</sub> <i>Dm</i> RDL	> 10,000*	234.40* (198.00-277.40)	2.33 (1.48-3.18)
wild-type <i>Tu</i> RDL	2.53 (1.53-4.19)	295.10 (232.70-374.10)	1.51 (1.02-2.00)
G3'M <sub>TMD3</sub> <i>Tu</i> RDL	> 10,000*	2360* (2094-2661)	2.23 (1.67-2.78)

Note, The different species used were *Chilo suppressalis* (*Cs*), *Laodelphax striatellus* (*Ls*), *Apis mellifera* (*Am*), *Drosophila melanogaster* (*Dm*) and *Tetranychus urticae* (*Tu*). CI, confidence interval.

\* indicates significant difference relative to wild-type RDL as determined by the 95% CI without overlapping.