**S1 Fig. Maximum likelihood tree based on concatenation of COI, 16S, and 12S genes from Conus.**The bolded species were included in the venom gland transcriptomes analyzed in this study. The presence and absence of identified DREPs are marked next to the species name. The tree is rooted with *Californiconus californicus*genes.

**S2 Fig. Amino acid identity of doppelganger toxins to prey.**Amino acid identity of doppelganger toxins to prey DREP separated into the signal sequence, peptide/toxin region, and where applicable spacer region(s). Significance is calculated by Wilcoxon rank-sum test and p-values compared to the peptide/toxin regions are shown.

**S3 Fig. Mean doppelganger toxin gene expression in cone snail venom glands**. Dots represent individual data points.

**S4 Fig. Mass spectrometry of doppelganger toxins.** MS (upper) and MS/MS (lower) spectra of Tail and Medial doppelganger toxins. (A) *Conus terebra*Tail doppelganger toxin is C-terminally amidated, (B) *Conus textile*Medial doppelganger toxin 1, (C) *Conus marmoreus*Medial doppelganger toxin 2.

**S5 Fig. DREP transcript expression.**Mean (**A**) Aplysia-DREP, (**B**) Lumbricus-DREP, and (**C**) Doryteuthis-DREP transcript expression in different tissues.

**S6 Fig. BLOSUM62 map of doppelganger toxins and DREPs**. The nodes represent individual precursor sequences, and the edges correspond to the BLASTp p-values linking the ends.

**S7 Fig.** **Evolutionary trace analyses.** Evolutionary trace analyses show different conservation (rate4site) scores in the toxin/peptide regions compared to the signal sequence and spacer region(s). (Left) Position-specific rate4site scores for doppelganger toxin and DREPs. (Right) Wilcoxon rank-sum test shows differences between the toxin region compared to the signal sequence and spacer region. The signal peptide is depicted in light blue, processing sites are in red, and cysteines in yellow. The peptide and toxin regions are shown above the graphs. Spacer regions are defined as the non-signal sequence/peptide/processing site regions.

**S8 Fig. Wilcoxon rank-sum test of rate4site scores of exon1 and exon2 of Triangle doppelganger toxin.**