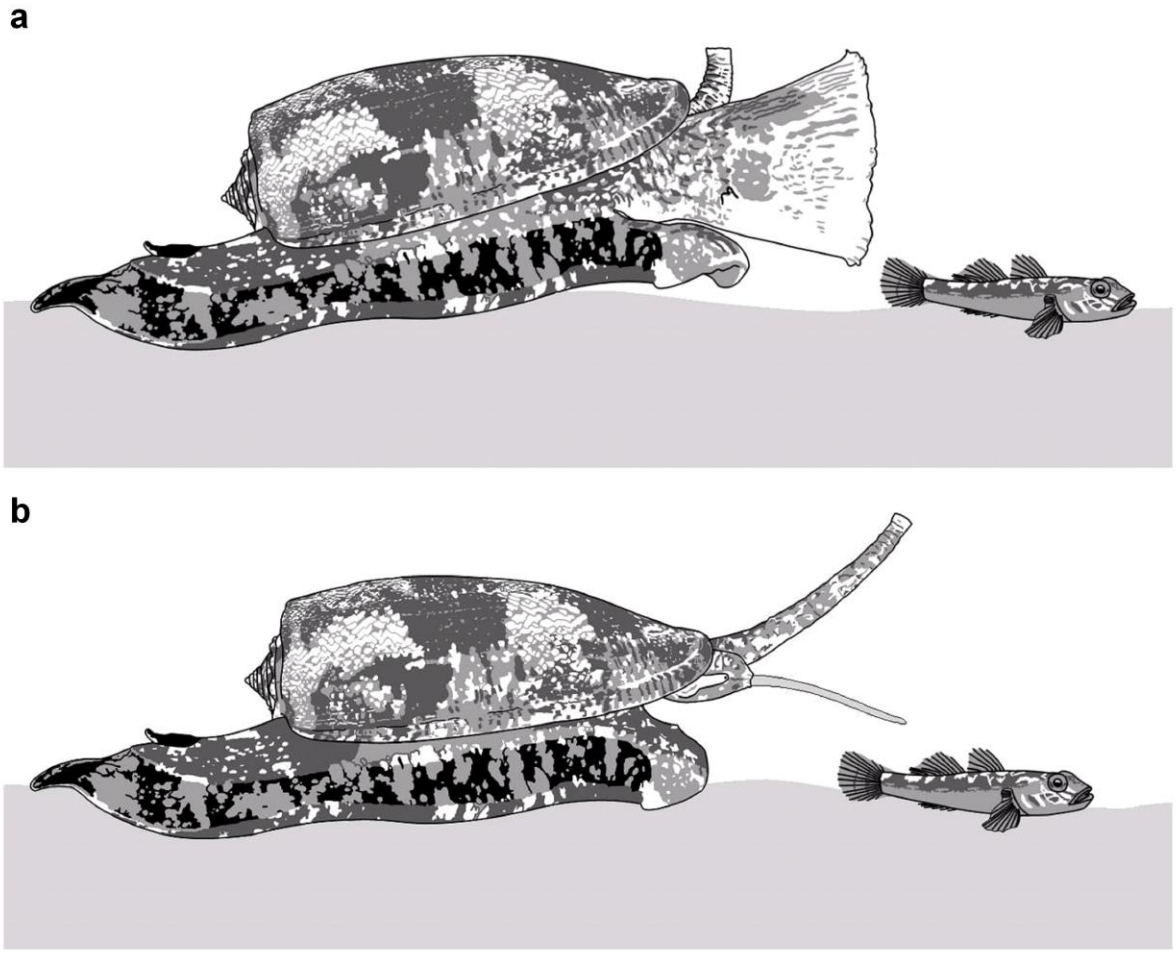
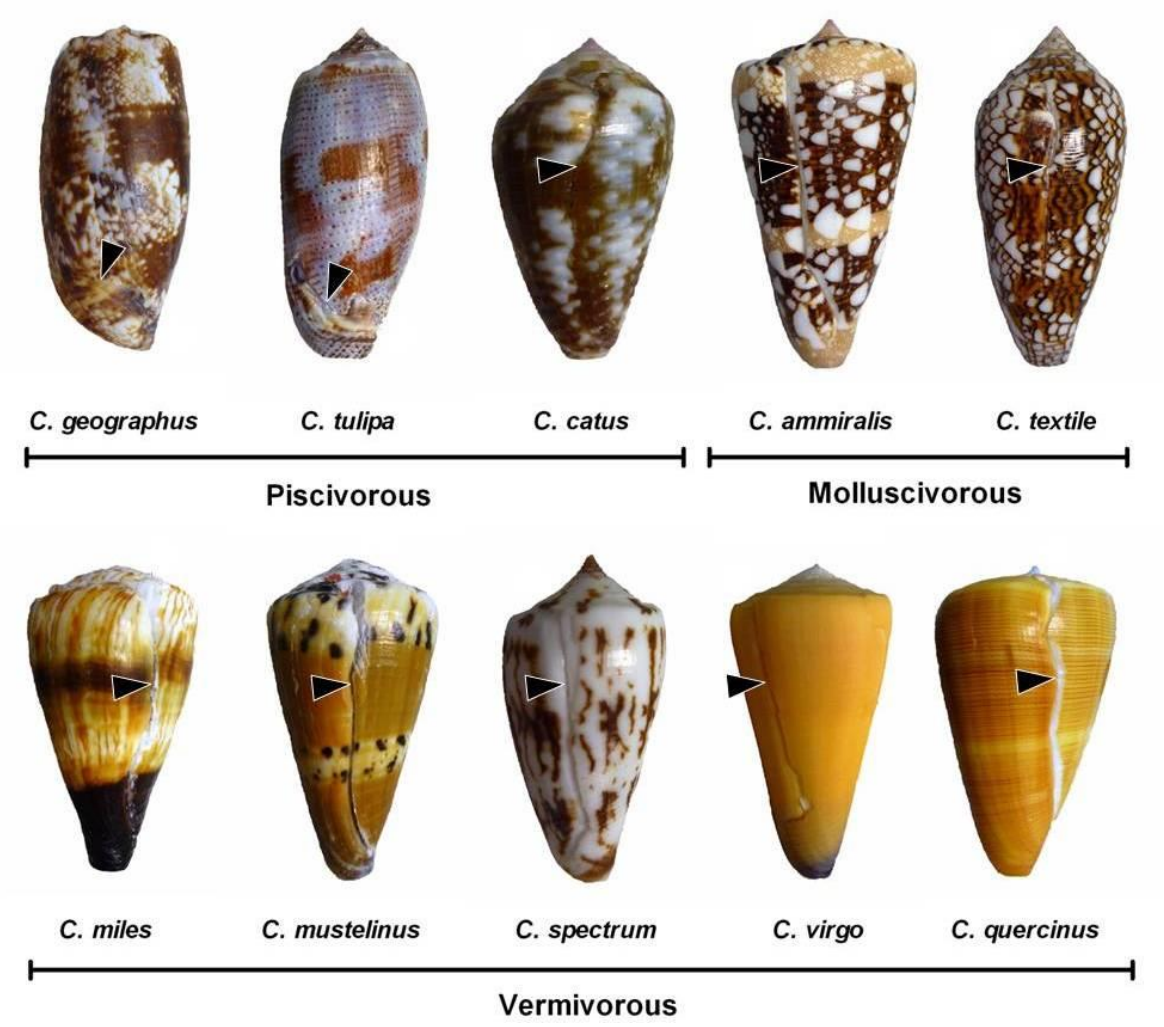


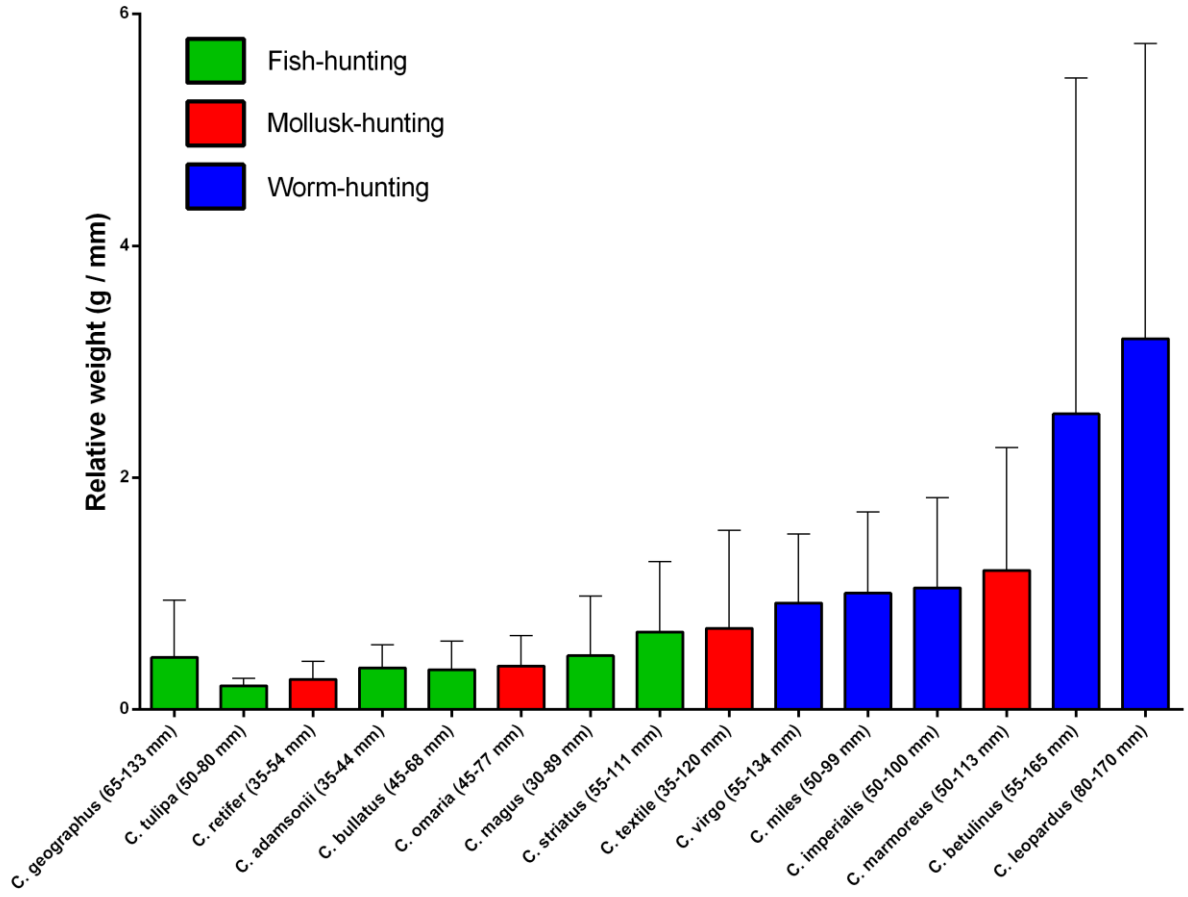
Supplementary Figure 1. *Conus geographus* prey-capture strategies.

a, While most piscivorous cone snails rely on the injection of venom to capture fish, *C. geographus* has evolved a different predatory strategy, using its distended rostrum as a "net" to capture fish sedated by a "nirvana cabal" released into the water. Observations on the feeding behaviour of *C. geographus* suggest that venom may be injected once the fish is securely imprisoned in its false mouth, however, this has never been directly proven. **b**, On occasions some *C. geographus* specimens use their proboscis to directly inject fish with venom, providing the opportunity to collect the predation-evoked venom as demonstrated in this study.

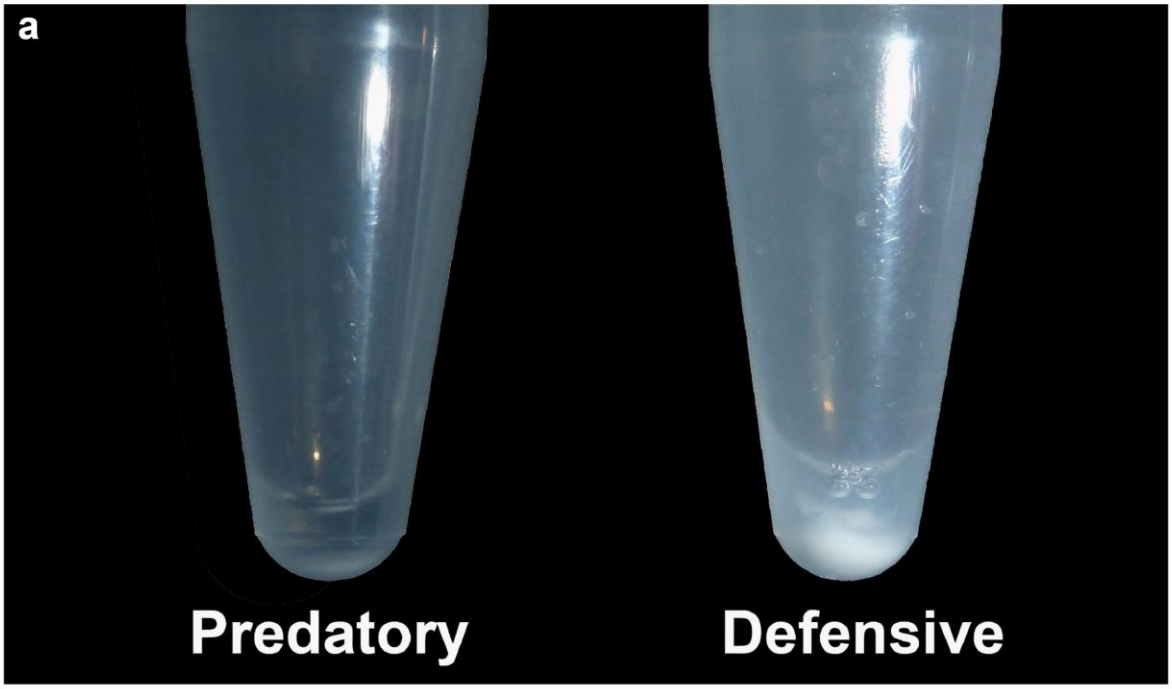


Supplementary Figure 2. Evidence of shell damage on cone snails.

It is relatively common to observe scars on the shell of living cone snails (indicated by arrows). All species appear to be affected, regardless of their size, thickness of shell or feeding habits (piscivorous, molluscivorous or vermivorous). The initial damage can result from wave actions in rocky areas, storm activity (cyclone) and predation. In particular, octopi, crabs and fish are the main predators of cone snails capable of breaking their protective shell. The scars suggest that cone snails can survive these damaging attacks, possibly by using their venom defensively.



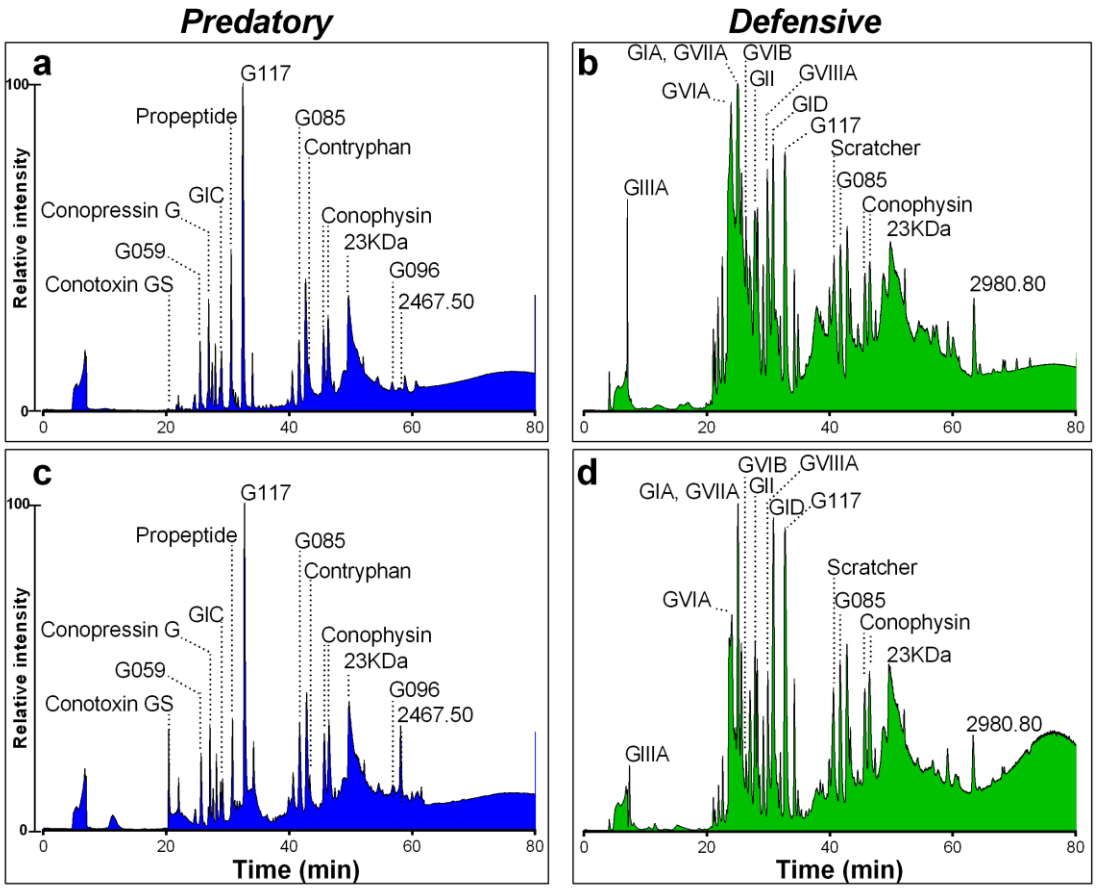
Supplementary Figure 3. Relative weight of *Conus* species. Relative weight (weight of shell/size of shell) provides a convenient estimate of shell thickness, reflecting the relative level of protection offered. Interestingly, *C. geographus* is the most dangerous cone snail but possesses one of the thinnest and lightest shells, with the largest aperture of all *Conus* species. We hypothesize that *C. geographus* evolved an aggressive behaviour and potent defensive venom to compensate for reduced shell protection. In support of this hypothesis, the second species thought to be dangerous to human is *C. tulipa*, which belongs to the same phylogenetic clade, and displays similar aggressive behaviour, shell characteristics and potent venom on vertebrate receptors. In contrast, *Conus* species with strong heavy shell such as *C. leopardus* have less potent venom on vertebrates and less diverse venom peptides compared to other species. Therefore, less potent venom may correlate with reduced dependence on defensive venom. (data from the Manual of the Living Conidae[1], are presented as a range of measurements, usually from at least 10 specimens).



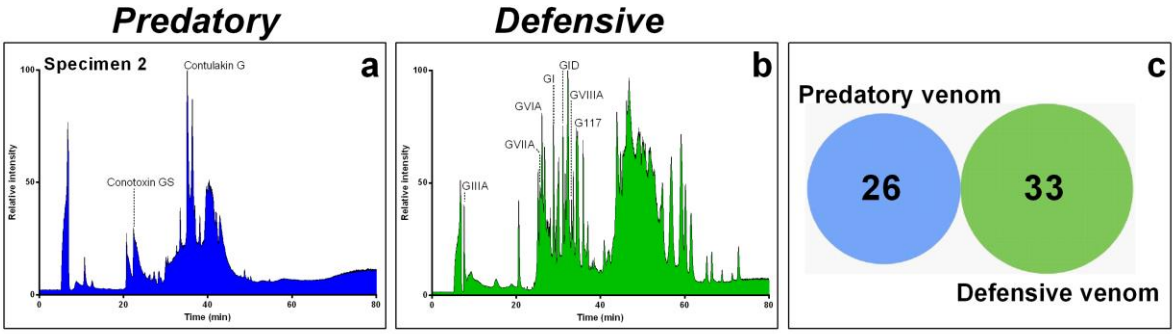
b

Specimen Size (mm)	Predatory Volume (μl)	Defensive Volume (μl)	P / D ratio
1 (92.5)	29	54	0.53
2 (95.5)	34	61	0.55
3 (94)	26	51	0.51
4 (112)	33	66	0.50

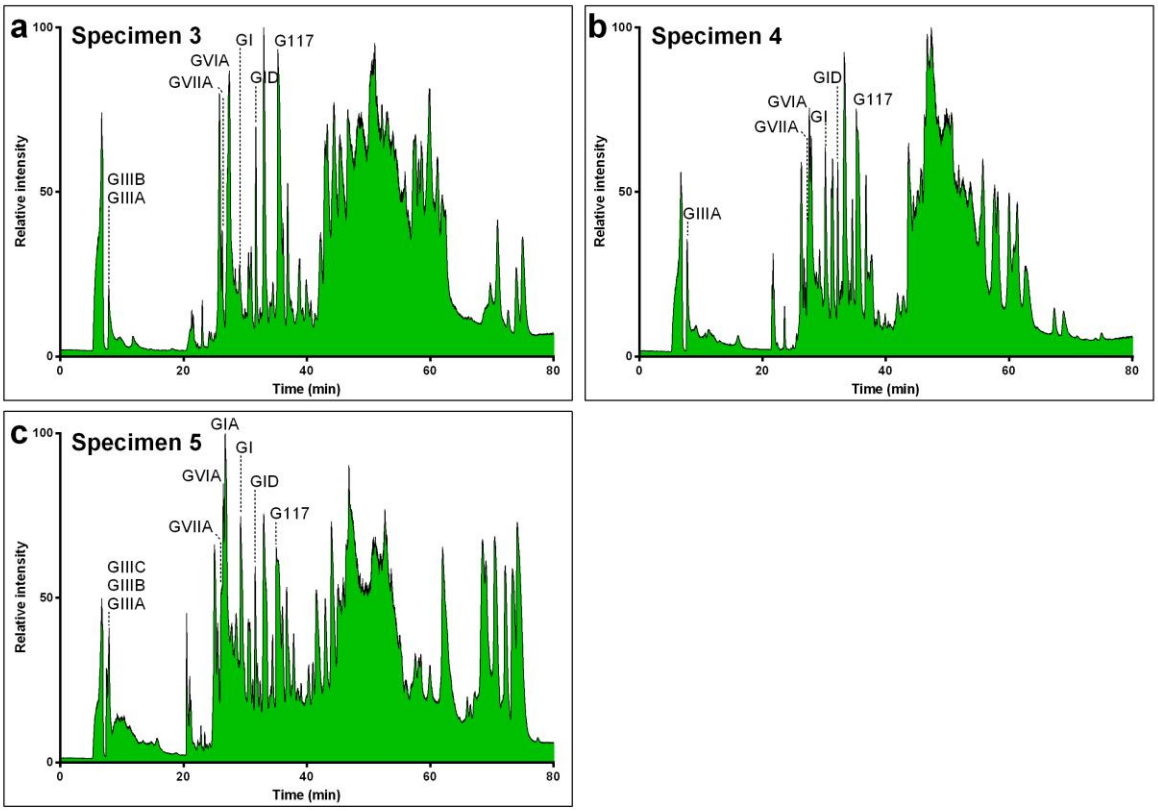
Supplementary Figure 4. Predation- and defence-evoked venoms of *C. geographus.* a, The predatory venom of *C. geographus* appears translucent, whereas the defensive venom from the same specimen contains insoluble material comprising white secretory granules that quickly settles to the bottom. **b**, The volume of predatory venom injected is consistently ~50% the volume of defensive venom injected (predatory/defensive venom volume ratio 0.50–0.55).



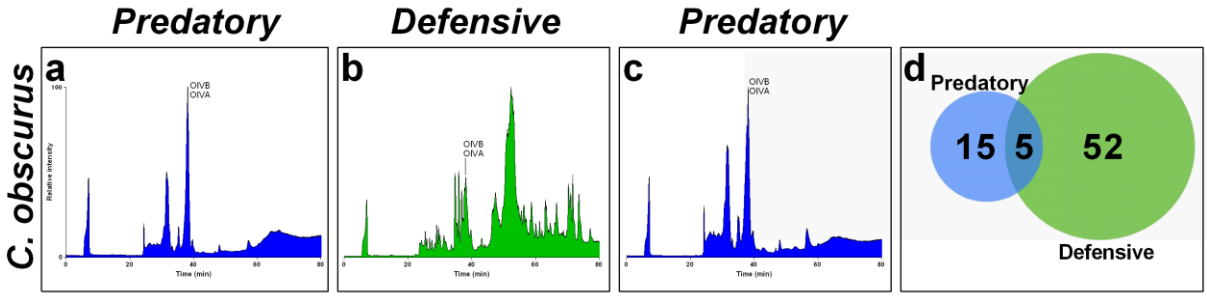
Supplementary Figure 5. Predation- and defence-evoked venoms of *C. geographus* can be generated reproducibly over time. a and **c**, Shown are LC-MS profiles and composition for two independent predatory stings collected from the same specimen 8 days apart (and interrupted by a defensive sting in **b**), and (**b** and **d**) two defensive stings also collected 8 days apart. This experiment demonstrates that discrete sets of toxins can be generated in response to predatory or defensive stimuli and remain unaltered by the type of sting previously deployed.



Supplementary Figure 6. Predation- and defence-evoked venoms from a second *C. geographus* specimen. a, Consistent with results obtained for the *C. geographus* specimen shown in Fig. 1 and Fig. S5, predation-evoked venom from a second *C. geographus* specimen again show a simple LC-MS trace, where the fish-specific conotoxin GS is a major conotoxin, together with the NMDA antagonist conantokin G. **b**, The defence-evoked venom in contrast is highly complex and similar to the *C. geographus* specimen shown in Fig. 1 and Fig. S5, again with paralytic peptides such as GI, GVI, GVIIA and GIIIA dominating. **c**, Remarkably for this specimen, the two venoms show no overlap for the major peptide masses detected, supporting the independent release of distinct sets of conotoxins upon predatory or defensive stimuli.

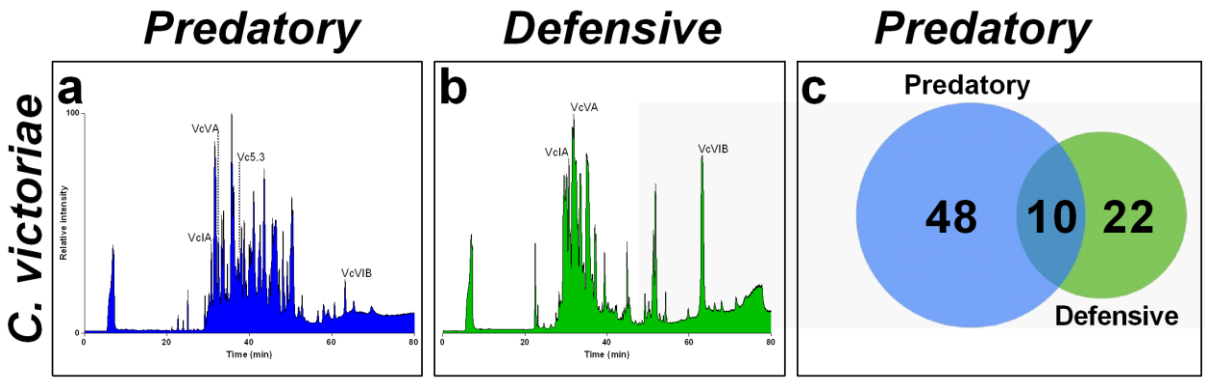


Supplementary Figure 7. Defence-evoked venoms from three specimens of *C. geographus.* a-c, The defence-evoked venom was collected from three other specimens of *C. geographus*. While minor intraspecific variations (particularly variations in the intensity level of specific toxins) are observed, especially for the most hydrophobic peptides, the composition remains consistent across all specimens examined, with paralytic toxins such as GI, GVIA, GVIIA and GIIIA dominating in this venom.



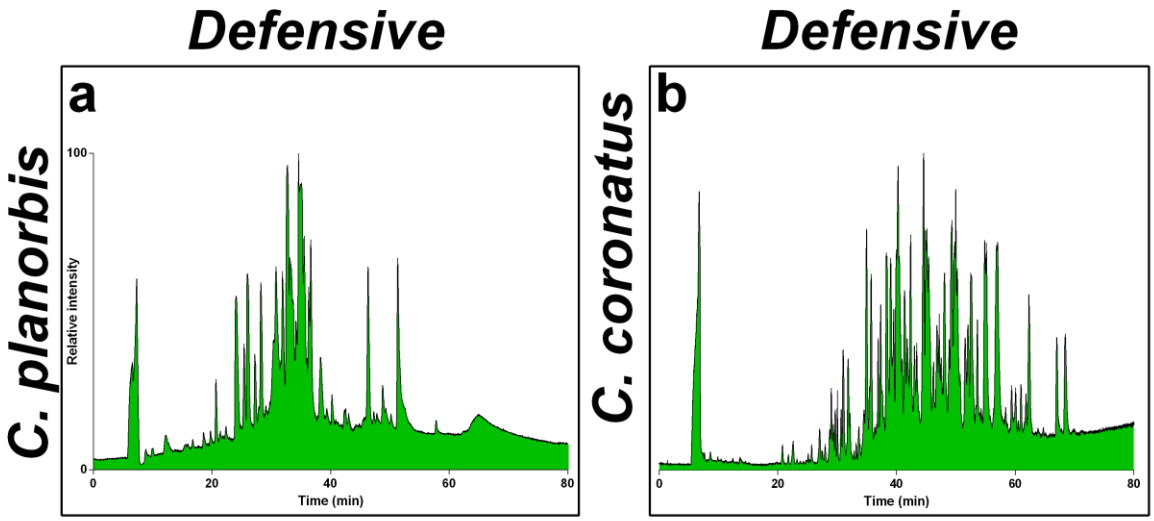
Supplementary Figure 8. LC-MS profiles of predation- and defence-evoked venoms of *C. obscurus*.

C. obscurus is also a piscivorous species like *C. geographus*, but belongs to a different phylogenetic clade (Protostrioconus) and uses a "hook-and-line" prey capture strategy rather than a net strategy (see supplementary Movie 6). Predation- and defence-evoked venoms were collected from the same individual at 2–7 days intervals (**a-c**). Again, the predation-evoked venom appears relatively simple in composition (20 major masses detected), and largely dominated by two characterised peptides, OIVA and OIVB. These excitatory toxins are part of the lightning-strike cabal, and induce a fast immobilisation of fish. The predation-evoked venom of *C. obscurus* resembles other hook-and-line piscivorous cones snails including *C. striatus* and *C. consors*. In contrast, the defence-evoked venom of *C. obscurus* is more complex (57 major masses detected) and comprises mostly unknown toxins, with only 5 of the predatory venom masses (20%) identified as being common to the defensive venom, including the previously identified αA-conotoxins OIVA and OIVB (**d**).



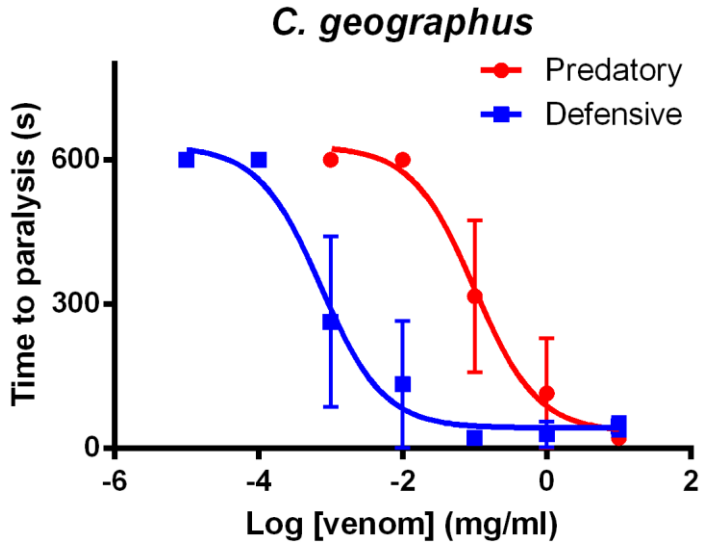
Supplementary Figure 9. LC-MS profiles of predation- and defence-evoked venoms of *C. victoriae.*

Predation- and defence-evoked venoms were also collected from *C. victoriae* (**a** and **b**), a mollusc-hunting cone snail like *C. marmoreus* (*Conus* Clade) but which belongs the Cylinder clade. Surprisingly, the predatory venom of *C. victoriae* (58 major masses detected) was more complex than its defensive venom (32 major masses detected) in contrast to other species examined. However, only 20% of the predation-evoked toxins were also present in the defensive-evoked venom (**c**). A number of minor predatory venom peptides were seen as major component in the defensive venom, including the conotoxins VcVIB, VcVA and VcIA.



Supplementary Figure 10. LC-MS profiles of defence-evoked venoms of *C. planorbis* and *C. coronatus.*

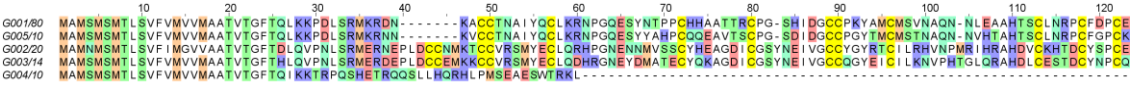
The defence-evoked venoms of two worm-hunting species could also be obtained despite their small radula, which made the milking challenging. Both *C. planorbis* (Vituliconus clade) and *C. coronatus* (Miliariconus clade) generated complex defence-evoked venoms (**a**, and **b**), where the 40-60 min time period appears dramatically different between the two species. These likely reflect the already well known interspecific variations in venom complexity that was demonstrated using dissected venom duct extracts. *C. coronatus* venom contains > 100 major masses, indicating that complex defensive-evoked venom can be generated by fish-, mollusc- but also worm-hunting cone snails.



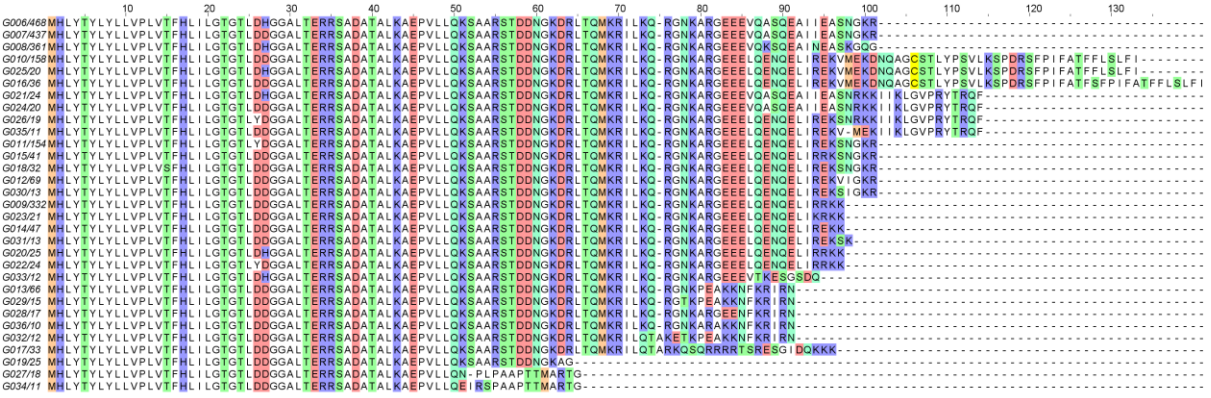
Supplementary Figure 11. Effective dose of *C. geographus* predation- and defence-evoked venoms on adult zebrafish.

Incremental doses of both venoms were injected intramuscularly into adult zebrafish and time of paralysis (see method section) was plotted against venom concentration. The IC_{50} values obtained for the curves were then used to determine the ED_{50}. The IC_{50} for the defence- and predation-evoked venom were 0.0005 mg/ml and 0.175 mg/ml, respectively. Based on the calculated average weight of our adult zebrafish (0.5 g) and quantity effectively injected per fish (5 µl), the defence-evoked venom of *C. geographus* has an ED_{50} of 10 µg/kg, whereas the predation-evoked venom was much less potent, with an ED_{50} of 3.5 mg/kg. These results are consistent with the defence-evoked venom being used to deter much larger predators compared to the usual prey of *C. geographus*.

Con-ikot-ikot

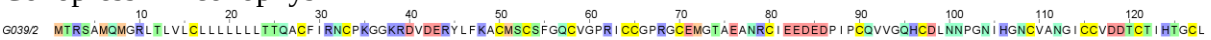


Conantokin

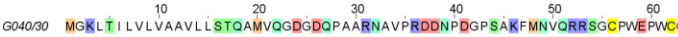


Conkunitzin

Conopressin – conophysin

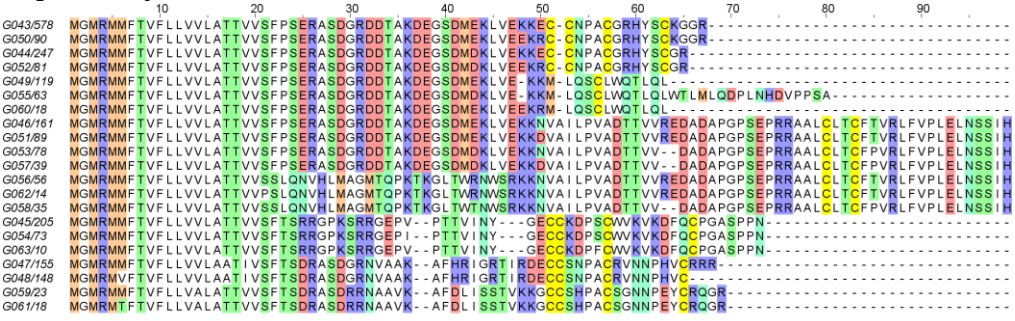


Contryphan

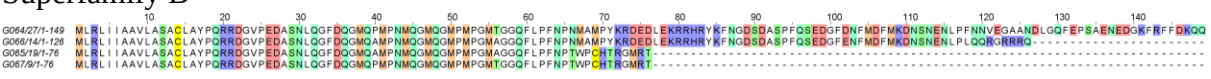


Contulakin

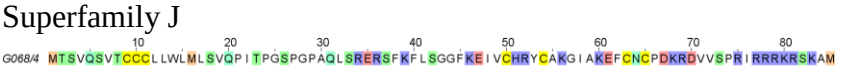
Superfamily A



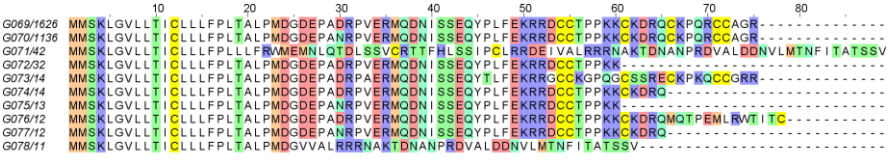
Superfamily B



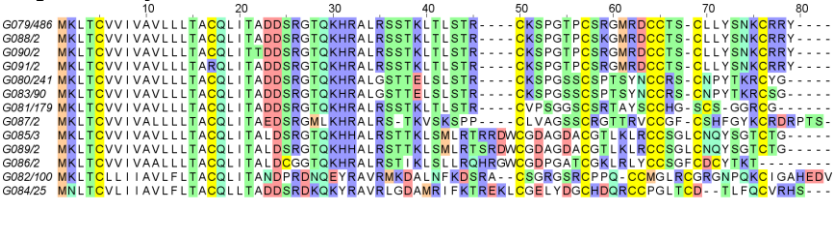
Superfamily J



Superfamily M



Superfamily O1

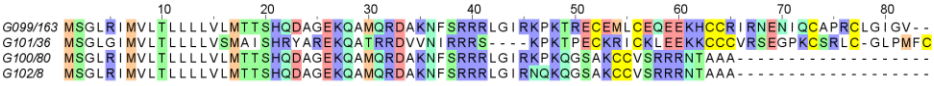


Superfamily O1-variant 1

Superfamily O1-variant 2

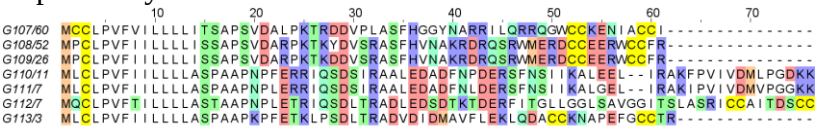
Superfamily O2

Superfamily O3

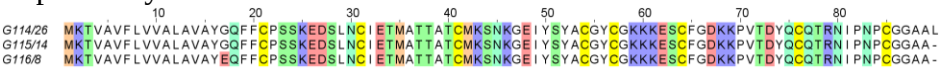


Superfamily S

Superfamily T



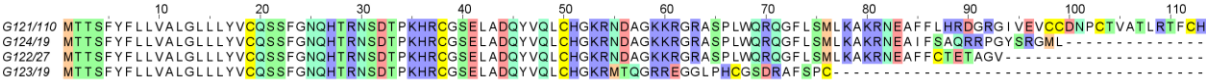
Superfamily I1



Superfamily I3

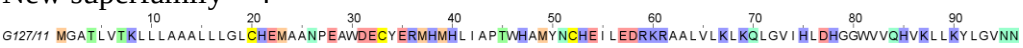
New superfamily – 1

New superfamily - 2

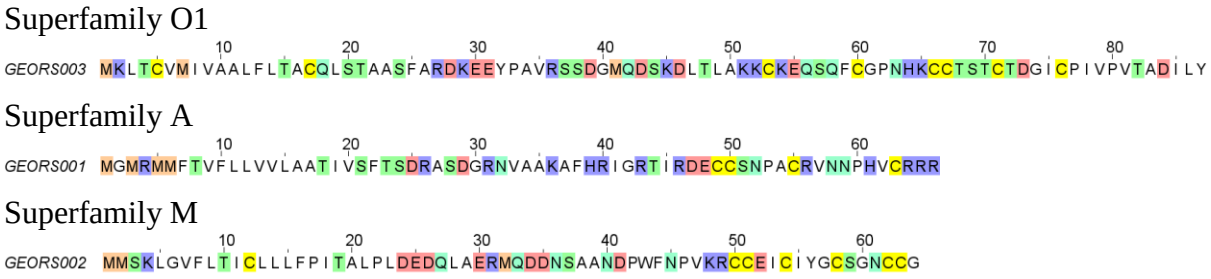


New superfamily – 3

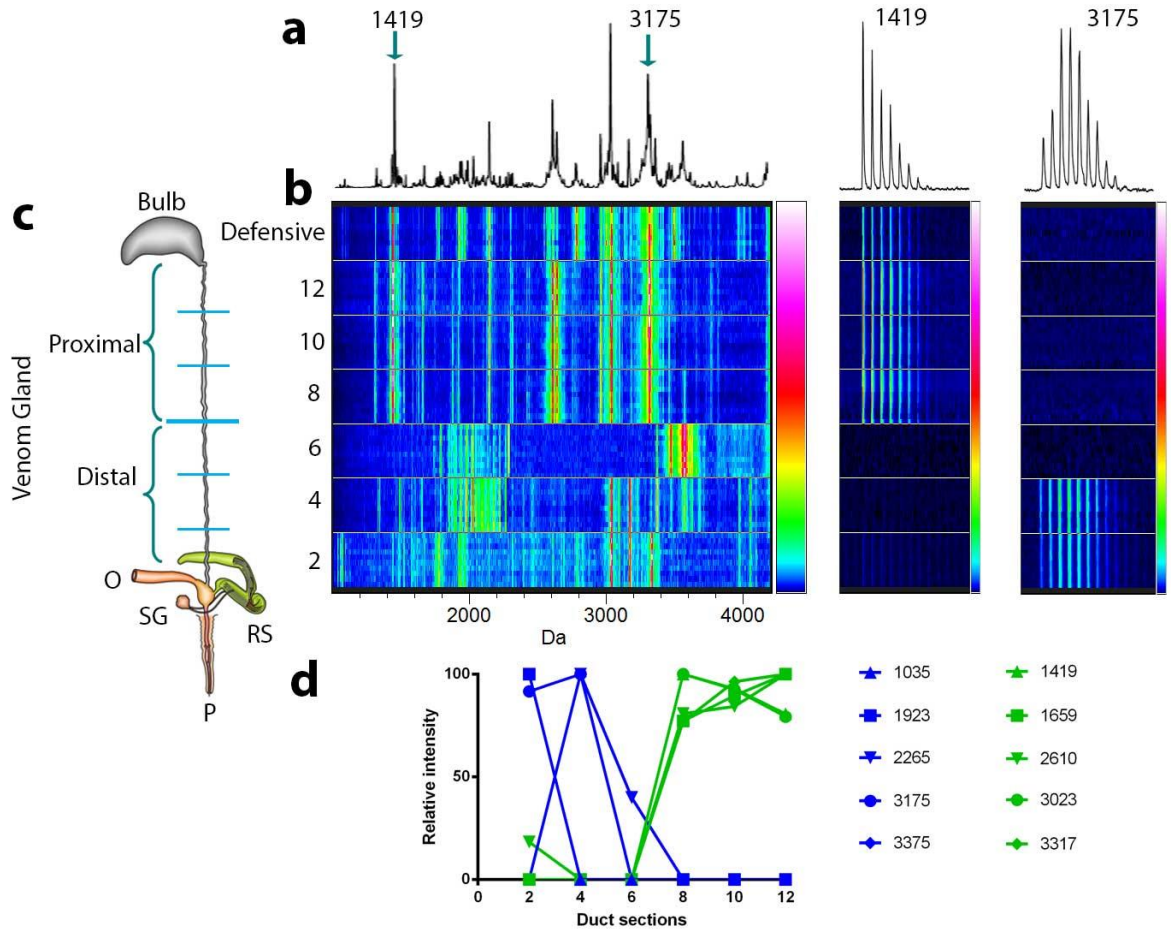
New superfamily – 4



Supplementary Figure 12. Alignment of conotoxin sequences from a *C. geographus* venom duct transcriptome. The 454 sequencing raw data (reads) of the venom duct transcriptome were sorted using Conosorter and conotoxin sequences were classified by gene superfamilies. Each sequence is identified by an identifier number (GXXX), with the number of reads corresponding to the full length precursor indicated by the extension (GXXX/**XX**). The number of reads provides an estimate of the level of expression of a particular sequence at the time of RNA extraction.



Supplementary Figure 13. Conotoxin sequences from a *C. geographus* radular sac transcriptome. Only 3 sequences corresponding to conotoxin precursors were retrieved from the transcriptome of the radular sac, and all were expressed at very low levels (GEORS003 with 6 reads, GEORS002 with 2, and GEORS001 with 1).



Supplementary Figure 14. Distribution of toxins in *C. geographus* venom duct. Extracts from 6 sections of the venom duct (**a**) of a second specimen of *C. geographus* were spotted on MALDI plate together with the defensive venom from the same specimen. **b**, The average spectrum is again highly complex in the range 1000-4000 Da, corresponding to the size of the most common conotoxins. **c**, The gel-view representation shows distinct regionalization of many components, consistent with the data obtained for a separate specimen shown in Fig. 3. **d**, Furthermore, quantification of five selected predatory (including Conopressin G (1035) and Conantokin G (2265)) and defensive toxins (including GII (1419), GIIIA (2610) and GVIIA (3317)) clearly shows a tight correlation between distal duct producing predation-evoked venom peptides and the proximal duct producing defensive-evoked venom peptides.

Supplementary Table 1: MS/MS sequence coverage of conotoxin transcripts.

Superfamily	ID	MS/MS Sequence (in bold)	Sou-rce	PTM
Con-ikot-ikot	G001	MAMSMSMTLSVFVMVVMAATVTGFTQLKKPDLSRMKRDNK***ACCTNAIYQ*** ***CLKRNPGQESYNTPPCHHAATTRCPGSHIDGCCPK***YAMCMSVNAQN NLEAAHTSCLNRPCFDPCE	PEV	O
Con-ikot-ikot	G003	MAMSMSMTLSVFVMVVMAATVTGFTHLQVPNLSRMERDEPLDCCEMKK CCVRSMYECLQDHR***GNEYDMATECYQK***AGDICGSYNEIVGCCQGYEICIL KNVPHTGLQR***AHDLCESTDCYNPCQ***	PEV	
Con-ikot-ikot	G005	MAMSMSMTLSVFVMVVMAATVTGFTQLKKPDLSRMKR***NNKVCCTNAIYQ*** ***CLKRNPGQESYYAHPC***QQEAVTSCPGSDIDGCCPGYTM***CMSTNAQNNV*** ***HTAHTSCLNRPCFGPC***K	PEV	O
Conkunitzin	G037	MEGRRVAAVLIVTICMLALEAGA***LRDPPLCNLLPDTGPC***LAHMERFYFDR FSKECKVFIYGGC***PGNANNFPTAKECYKRCGN***K	DEV	O
Conkunitzin	G038	MEGRRLAVVLIVTSCLSALTVGDTR***SVPDVCLQPMDVGPCER***QLPR***YYFN*** ***AVQVTCKRFDYGGCGGNQNR***FNSKDDCLKKCLYSLT	DEV PEV	
Conophysin_conopressin	G039	MTRSAMQMGRLTLVLCLLLLLLLLTTQACFIRNCPKGGKRDVDER***YLFKAC*** ***FGQCVGPR***ICCGPR***GCEMGTAEANRCIEEDEDPIPCQVVGQHCDL*** ***NNPGNIHGN***CVANGIC***CVDDTCTIHTGCL***	DEV PEV	
Contryphan	G040	MGKLTILVLVAAVLLSTQAMVQGDGDQPAAR***NAVPRDDNPDGPSAKFMN*** ***VQ***RRSGCPWEPWCG	DEV	
Superfamily_A	G044	MGMRMMFTVFLLVVLATTVVSFPSERASDGR***DDTAKDEGSDMDKLVEK***K ***ECCNPACGR***HYSCGR	DEV	
Superfamily_A	G045	MGMRMMFTVFLLVVLATTVVSFTSRRGPKSRRGEPVPTTVINYGECCK***D*** ***PSCWVKVKDFQCPGASPPN***	PEV	O
Superfamily_A	G043	MGMRMMFTVFLLVVLATTVVSFPSERASDGRDDTAKDEGSDMEKLVEK ***KECCNPACGRHYSCKG***GR	DEV	*
Superfamily_A	G059	MGMRMMFTVFLLVALATTVVSFTSDRASDRR**NAAVKAFDLISSTVKKGC** **CSHPACSGNNPEYCRQGR**	PEV	* Y-So4
Superfamily_A	G059	MGMRMMFTVFLLVALATTVVSFTSDRASDRRNAAVKAFDLISSTVKK***GCC*** ***SHPACSGNNPEYCRQ***GR	DEV	*
Superfamily_A	G050	MGMRMMFTVFLLVVLATTVVSFPSERASDGRDDTAKDEGSDMEKLVEEK ***RCCNPACGRHYSCKG***GR	DEV	
Superfamily_A	G047	MGMRMMFTVFLLVVLAATIVSFTSDRASDGRNVAAKAFHRIGRT***IRDECC*** ***SNPACRVNNPHVCR***RR	DEV	O
Superfamily_A	G061	MGMRMTFTVFLLVALATTVVSFTSDRASDRRNAAVK***AFDLISSTVK***K***GCC*** ***SHPACSGNNPEYCR***QGR	DEV	
Superfamily_B	G066	MLRLIIAAVLASACLAYPQRRDGVPEDASN*LQG****FDQGMQAMPNMQGMQ*** ***GMPMPGMAGGQFLPFNPNMAMPY***KRDEDLEKR***RHRYKFNGDSDAS*** ***PFQSEDGFENFMDFMKDNSNENLP***LQQRGRRRQ	DEV	
Superfamily_B	G064	MLRLIIAAVLASACLAYPQRRDGVPEDASNLQ***GFDQGMQPMPNMQGMQ*** ***PMPGMTGGQFLP***FNPNMAMPYKRDEDLEKR***RHRYKFNGDSDASPF*** ***QSEDGFDNFMDFMKDNSNENLPFNNVEGAANDLGQ***FEPSAENEDGKF RFFDKQQ	PEV	
Superfamily_J	G068	MTSVQSVTCCCLLWLMLSVQPITPGSPGPAQLSRER***SFKFLSGGFKEIVC*** ***HRYCAKGIAKEFCNCPD***KRDVVSPRIRRRKRSKAM	DEV	
Superfamily_M	G069	MMSKLGVLLTICLLLFPLTALPMDGDEPADRPVERMQDNISSEQYPLFEKR ***RDCCTPPKKCKDRQCKPQRCCA***GR	DEV	* O
Superfamily_M	G069	MMSKLGVLLTICPLLFPLTA***LPMDGDEPADRPVE***RMQDNISSEQYPLFEKR RDCCTPPKKCKDRQCKPQRCCAGR	DEV	
Superfamily O1	G084	MNLTCVLIIAVLFLTACQLLTADDSRDKQKYRAVRLGDAMRIFKTREK***LCGE*** ***LYDGCHDQRCCPGLTCDTLFQCVR***HS	PEV	
Superfamily O1	G085	MKLTCVVIVAVLLLTACQLITALDSRGTQKHHALRSTTKLSMLRTSR***DWCG*** ***DAGDACGTLKLRCCSGLCNQYSGTCT***G	PEV	* W-Br
Superfamily O1	G081	MKLTCVVIVAVLLLTACQLITADDSRGTQKHRALRSSTKLTLST***RCVPSGG*** ***SCSRTAYSCCHGSCSGGRCG***	DEV	
Superfamily O1	G086	MKLTCVVIVAALLLTACQLITALDCGGTQKHRALRSTIKLSLLRQHR***GWCG*** ***DPGATCGK****LRLYC****CSGFCDCYTK***T	DEV	
Superfamily O1	G087	MKLTCVVIVALLLLTACQLITAEDSRGMLKHRALRSTKVSK***SPPCLVAGSSC*** ***R***GTTRVCCGFCSHFGYKCRDRPTS	DEV	O
Superfamily O1	G089	MKLTCVVIVAVLLLTACQLITALDSRGTQKHHALRSTTKLSMLRTSR***DWCG*** ***DAGDACGTLK***LRCCSGLCNQYSGTCTG	DEV	
Superfamily O1	G091	MKLTCVVIVAVLLLTARQLITADDSRGTQKHRALRSSTKLTLSTRCKSPGTP CSR***GMRDCCTSCLLYSNKCR***RY	DEV	
Superfamily O1	G083	MKLTCVVIVAVLLLTACQLITADDSRGTQKHRALGSTTELSLSTR***CKSPGS*** ***SCSPTSYNCCRSCNPYTKRCSG***	PEV	O

Superfamily O1	G080	MKLTCVVIVAVLLLTACQLITADDSRGTQKHRALGSTTELSLSTR***CKSPGS*** ***SCSPTSYNCCRSCNPYTKRCYG***	DEV	O
Superfamily O1	G079	MKLTCVVIVAVLLLTACQLITADDSRGTQKHRALRSSTKLTLSTR***CKSPGTP*** ***CSRGMRDCCTSCLLYSNKCRRY***	DEV	
SF O1-var1	G092	MNLTCVLIIAVLFLTACQLIAADDSRDNQKHRAVRMRDALKNFKDSR***ACSGR*** ***GSRCPPQCCMGLTCGREYPPRCG***	DEV	O
SF O1-var2	G095	MKLACVVIVAVLLLTACQLITALDSR***SPVTKCSDGTHPTLVKHCKATGEYCRRYVTRCCCKCGNNNRCT***	PEV	O
Superfamily O2	G098	MEKLTILLLVAAVLMSTQAMI***QGGGENRPK***KNIKYLSKSQRSAESGIWGECS DFLTGCTSPSQCCSENCETYCRAW	DEV	D-pyr
Superfamily O2	G096	MEKLTILLLVAAVLMSTQAMIQGGGENRPMENIKYLSKSQRSAER***GVWSECSDWLAGCSSPSECCSEKCDTFCRLW***R	PEV	O W-Br
Superfamily O2	G096	MEKLTILLLVAAVLMSTQAMI***QGGGENRPMENIKYLSKSQRSAERGVWSECSDWLAGCSSPSECCSEKCDTFCRLW***R	DEV	O W-Br
Superfamily S	G104	MMSKMGAMFVLLLLFTLASSLQEGDVQARKTRLKSDFYRALARDDR***GCTRTCGGPKCTGTCTCTNSSKCGCRYNVHPSG WGCGCACS***G	PEV	* W-Br
Superfamily T	G111	MLCLPVFIILLLLASPAAPNPLERRIQSDSIRAALEDADFNLDER***SFNSIIKALGELIRAKIPVIVDMVPGG***KK	DEV	*
Superfamily T	G113	MLCLPVFIILLLLASPAAP***KPFETKLPSDLTRADVDIDMAVFLEKLQDACCKNAPEFGCCTR***	DEV	
Superfamily T	G112	MQCLPVFTILLLLASTAAPNPLETRIQSDLTR***ADLEDSDTKTDERFITGLLGGLSAVGGITSLASRICCAITDSCC***	DEV	
Superfamily T	G110	MLCLPVFIILLLLASPAAPNPFERRIQSDSIRAALEDADFNPDE***RSFNSIIKALEELIRAKFPVIVDMLPGD***KK	DEV	
Superfamily I3	G117	MKLFLAIVLILMLQFLSTGAETSDNHASRSTTALRDWLLGPKAKR***CAVTHEKC*** ***SDDYDCCGSLCCVGICAKTIAPCK***	PEV DEV	
New 2	G121	MTTSFYFLLVALGLLLYVCQSSFGNQHTR***NSDTPKHRCGSELADQYVQLCHG***KRNDAGKKRGRASPLWQRQGFLSMLKA KRNEAFFLHRDGR***GIVEVCCDNPCTVATLRTFCH***	PEV	
New 3	G125	MGSMKIYLCLAFLLLLPFTIVDSGLLDKIETIRNWRR***DESKCDGCNCAELR***SSR***CTEAMFCLTPELCTPSVSCPTGECR***CTK FHQSRCTRFEECVPNKCRDA	PEV	
New 3	G126	MGSMKIYLCLAFLLLLPSTIVDSGLLDKIETIRNWRRDESKCDRCNCAELRSSR***CTQAIFCLTPELCTPSISCPTGECR***CTKFH QSRCTRFVECVPNKCTDA	PEV	
New 4	G127	MGATLVTKLLLAAALLLGLCHEMAANPEAWDECYER***MHMHLIAPTWHAMYNCHEILEDR***KR***AALVLK***LKQLGVIHLDHGG WVVQHVKLLKYLGVNN	PEV	

To determine their toxin composition, both predation- and defence-evoked venoms were analysed by LC-MS/MS. Only MS/MS coverage (in bold/italic) of transcriptomic sequences with a confidence value of 99 are reported. Amino acids identified with post-translational modifications (PTMs) are underlined (O, hydroxyproline; Y-So4, sulfotyrosine; *, C-terminal amidation; W-Br, Bromotryptophan; D-pyr, pyroglutamate). Predation-evoked venom (PEV) and defence-evoked venom (DEV) highlighted blue and green, respectively, whereas conotoxins detected in both venom types are shown in pink.

Supplementary Table 2. Molecular evolution of *C. geographus* conotoxin gene superfamilies.

	FUBAR[a]		PAML		MEME[b]	BSR[c]
			M8	M2a		
Con-ikot-ikot	$\omega>1$[d] $\omega<1$[e]	11 2	$\omega>1$[f] $\omega=$	23 (13+10) 2.38	20 (13+7) 2.42	7	5
Conantokin	$\omega>1$[d] $\omega<1$[e]	5 2	$\omega>1$[f] $\omega=$	17 (16+1) 1.26	15 (15+0) 1.20	31	43
Conkunitzin	$\omega>1$[d] $\omega<1$[e]	0 0	$\omega>1$[f] $\omega=$	26 (8+18) 4.39	17 (6+11) 4.38	0	2
Contulakin	$\omega>1$[d] $\omega<1$[e]	1 0	$\omega>1$[f] $\omega=$	0 1.72	0 1.72	0	1
Sumerfamily A	$\omega>1$[d] $\omega<1$[e]	1 0	$\omega>1$[f] $\omega=$	6 (3+3) 1.57	4 (1+3) 1.55	5	1
Sumerfamily M	$\omega>1$[d] $\omega<1$[e]	2 0	$\omega>1$[f] $\omega=$	14 (12+2) 2.80	14 (11+3) 2.87	6	7
Sumerfamily O1	$\omega>1$[d] $\omega<1$[e]	11 1	$\omega>1$[f] $\omega=$	25 (22+3) 7.0	23 (21+2) 6.65	4	5
Sumerfamily O2	$\omega>1$[d] $\omega<1$[e]	0 2	$\omega>1$[f] $\omega=$	0 1.46	0 1.46	0	0
Sumerfamily S	$\omega>1$[d]	4 1	$\omega>1$[f]	30 28+2	30 28+2	1	3

	FUBAR[a]		PAML			MEME[b]	BSR[c]
	ω<1[e]		ω=	28.14	28.26		
Sumerfamily T	ω>1[d] ω<1[e]	0 0	ω>1[f] ω=	3 (0+3) 1.54	1 (0+1) 2.73	1	0

a: Fast, Unconstrained Bayesian Approximation (FUBAR)

b: Sites detected as experiencing episodic diversifying selection (0.05 significance) by the Mixed Effects Model Evolution (MEME)

c: Number of branches detected as episodically diversifying by branch-site REL

d: Number of sites detected by FUBAR as under pervasive diversifying selection at the posterior probability ≥0.9

e: Number of sites detected by FUBAR as under pervasive purifying selection at the posterior probability ≥0.9

f: Number of positively selected sites detected using the Bayes Empirical Bayes approach implemented in M8 and M2a. Sites detected at 0.99 and 0.95 significance are indicated in the parenthesis.

ω**:** mean dN/dS

Supplementary Table 3. Molecular evolution of *C. marmoreus* conotoxin gene superfamilies.

	FUBAR[a]		PAML		MEME[b]	BSR[c]
			M8	M2a		
Sumerfamily H	$\omega>1$[d]	2	$\omega>1$[f]	14 (7+7)	1	2
	$\omega<1$[e]	1	$\omega=$	4.98	4.98	
Sumerfamily I2	$\omega>1$[d]	4	$\omega>1$[f]	16 (11+5)	6	7
	$\omega<1$[e]	1	$\omega=$	2.40	2.0	
Sumerfamily M	$\omega>1$[d]	8	$\omega>1$[f]	10 (9+1)	4	7
	$\omega<1$[e]	4	$\omega=$	2.43	2.38	
Sumerfamily O1	$\omega>1$[d]	8	$\omega>1$[f]	9 (8+1)	6	4
	$\omega<1$[e]	2	$\omega=$	2.23	2.25	
Sumerfamily O2	$\omega>1$[d]	5	$\omega>1$[f]	13 (10+3)	4	3
	$\omega<1$[e]	2	$\omega=$	2.76	2.76	
Sumerfamily T	$\omega>1$[d]	9	$\omega>1$[f]	7 (6+1)	1	8
	$\omega<1$[e]	1	$\omega=$	4.97	4.89	

a: Fast, Unconstrained Bayesian Approximation (FUBAR)

b: Sites detected as experiencing episodic diversifying selection (0.05 significance) by the Mixed Effects Model Evolution (MEME)

c: Number of branches detected as episodically diversifying by branch-site REL

d: Number of sites detected by FUBAR as under pervasive diversifying selection at the posterior probability ≥0.9

e: Number of sites detected by FUBAR as under pervasive purifying selection at the posterior probability ≥0.9

f: Number of positively selected sites detected using the Bayes Empirical Bayes approach implemented in M8 and M2a. Sites detected at 0.99 and 0.95 significance are indicated in the parenthesis.

ω**:** mean dN/dS.

Supplementary References

[1]Rockel, D., Korn, W. and Kohn, A. J. (1995) Manual of the Living Conidae. Volume 1: Indo-Pacific Region. Verlag Christa Hemmen (ed.), Grillparzertr., Germany.