

Figure S1. The alignment of highly homologous sequences in Table 2 reported from other *Conus* species.



Figure S2. Bayesian tree based on a concatenation of the COI, 16S and 12S genes for the reduced dataset of 326 specimens cited from reference 5. *Conus* species with red frame may generate a few same conopeptide sequences compare to *C. literatus*.

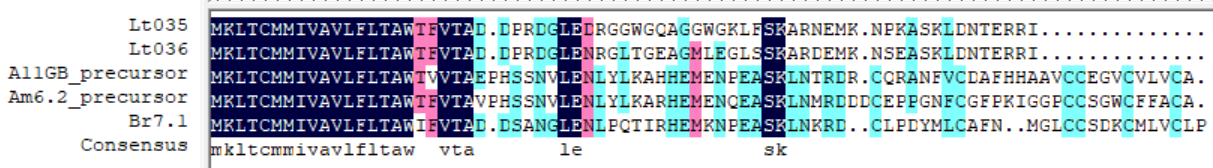


Figure S3. Alignment of O1-superfamily conotoxins with or without rich cysteines.

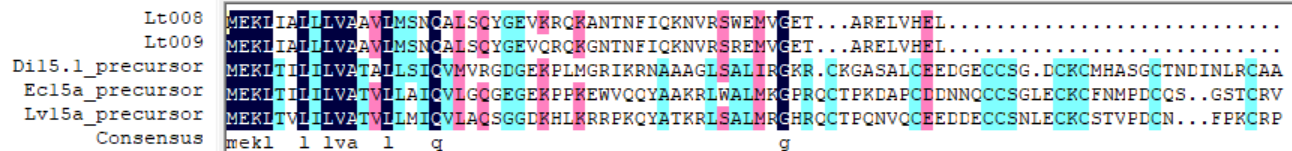


Figure S4. Alignment of O2-superfamily conotoxins with or without rich cysteines.



Figure S5. Codon usage for cysteine in the O1-superfamily conotoxin genes.

M 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 C

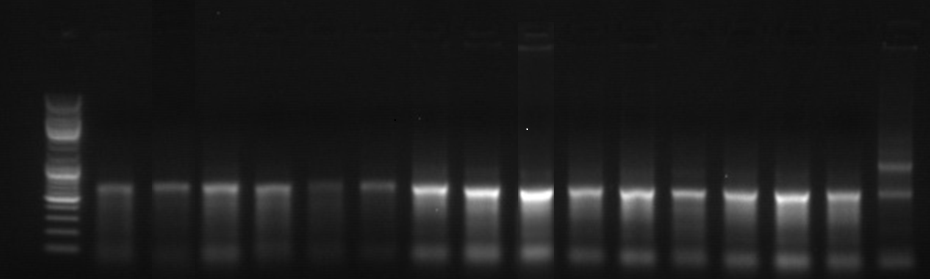
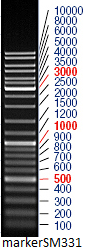
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Figure S6. Total RNAs of each venom ducts were extracted from different individuals of *C. litteratus.* M: RNA Marker, 1-5: Small size cone snail; 6-10: Medium size cone snail; 11-15: Big size cone snail; C: Positive control.

Table S1. Total RNA concentrations for 15 specimens.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| Conc.  (ng/μl) | 476 | 117 | 726 | 628 | 308 | 658 | 1160 | 1600 | 514 | 1120 | 1320 | 1080 | 1800 | 1140 | 1380 |

Table S2. Final RNA concentration of mixed samples of each group.

|  |  |
| --- | --- |
| Group | Conc. (ng/μl) |
| Small size cone snail (Figure S5, 1-5) | 258 |
| Medium size cone snail (Figure S5, 6-10) | 335 |
| Big size cone snail (Figure S5, 11-15) | 300 |

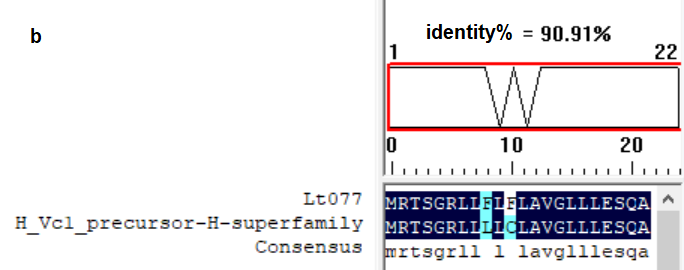
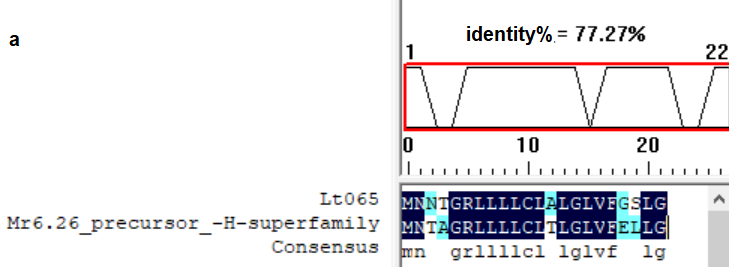


Figure S7. Alignment of the signal region of Lt065, Lt077 with the reported conotoxin belonging to H-superfamily in Conosever.

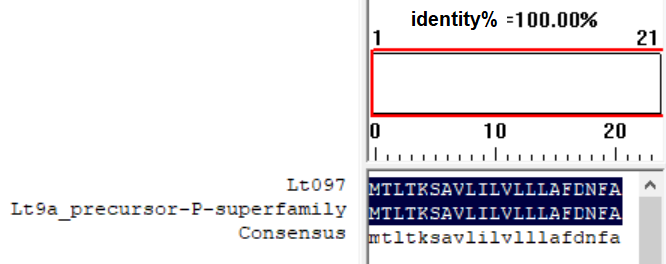


Figure S8. Alignment of the signal region of Lt097 with the reported conotoxin belonging to P-superfamily in Conosever.

Generally, when the identity between two signal sequences is >75%, it is designated as members of the same gene superfamily according to Conoserver classification rules. Signal region of Lt065 shared 77.27% identity with known Mr6.26 precursor. Signal region of Lt077 shared 90.91% identity with known H\_Vc1 precursor. Both Mr6.26 and H\_Vc1 precursors belong to H-superfamily members reported inConoserver. So, Lt065 and Lt077 should be included in H-superfamily (S10-Figure S6). Signal sequence of Lt097 shared 100% identity with known Lt9a precursor, which belongs to P-superfamily in Conoserver. Then Lt097 should be included in the P-superfamily too (S10-Figure S7).