## Supplementary Tables

**S3 Table. *C. tulipa* peptides reported in literature and their evidence from the proteome investigation**. Information has been provided from the LC-MS and LC-ESI-MS/MS analysis conducted on crude and enzyme digested duct segments. All except μ-TIIIA and TVIIA were analysed from the venom duct proteome.

| Peptide name | Literature mass (Da) | Experimental mass (Da) | MS/MS evidence | [1]Duct segment |
|---|---|---|---|---|
| ρ-TIA | 2389.14 | 2390.5351<br>2389.2206 | - | DC<br>PC |
| μ-TIIIA | 2455.97 | - | - | - |
| TVIA | 2844.05 | - | Yes | PC |
| TVIIA | 3209.276 | - | - | - |
| Conantokin-T | 2682.21 | 2682.3514 | Yes | D |
| Conopressin-T | 1107.53 | 1107.5675 | Yes | P and PC |
| T1.1 | 1904.68 | 1904.2497 | - | P and PC |
| T1.2 | 1953.78 | 1953.2469 | Yes | D |
| T6.1 | 3731.64 | - | Yes | PC |

[1]*Distal (D), Distal Central (DC), Proximal Central (PC) and Proximal (P).*

**S4 Table. List of the major gene superfamilies expressed in the venom duct transcriptome of S1 and S2**. The total (T) number of precursors for each superfamily (SF) / specimen (S1/S2), the number of common (C) precursors and representative major precursor information for each superfamily has been detailed out. Additionally, novel precursor information from minor superfamilies has been provided.

| SF | T | | C | Signal sequence | Mature sequence | Framework | Closest known precursor | [1]Known/Predicted pharmacology | Ref |
|---|---|---|---|---|---|---|---|---|---|
| | S1 | S2 | | | | | | | |
| B1 | 208 | 191 | 29 | MHLYTYLYLLVPLVTFHLILGTG | GEEEYQKMLENLKRKQES | N/A | Con-T | *NMDA antagonist | [1] |
| B2 | 24 | 11 | 2 | MLRLIIAAVLASACLAY | GEELEERSHHSKFNGDSDNSPFQSEDGLENFMDFMKDNSNE NLPLQQR | N/A | G066_VD | n.d | [2] |
| O1 | 90 | 22 | 11 | MKLTCVVIVTVLLLTAC | CLSPGSSCSPTSYNCCRSCNPYSRKCR | VI/VII | TVIA | *ω /voltage-gated calcium channel | [3] |
| | | | | MKLTCVVIVAVLLLTAC | QVSWWCGKPEATCGKLYLKCCSGRCNKANWKCL | VI/VII | T6.1 | ω /voltage-gated calcium channel | This study |
| | | | | MKLTCVLIIAVLFLMAC | SRSCSGRDSRCPPVCCMGLMCSRGKCVSIYGEK | VI/VII | TVIIA | Sodium channel | [4] |
| | | | | MKLTSALIVAVLFLTA | NCFPNGKFCGFPKVGKPCCSGVCLFACT | VI/VII | T6.2 | ω /voltage-gated calcium channel | This study |
| O3 | 68 | 17 | 6 | MSGLGIMVLTLLLLVSMA | SRPKTKECERYCELEEKHCCCIRSNGPKCSRICIFKFWC | n.d | T6.3 | voltage-gated calcium/sodium channel | This study |
| | | | | MSGLGIMVLTLLLLVLMTTSH | CEMQCEQKKKHCCRVREERIQCAPKCWGIEW | VI/VII | T6.4 | ω /Voltage-gated calcium channel | This study |
| A | 42 | 19 | 8 | MGMRMMFTVFLFVVLA | FNWRCCLIPACRRNHKKFC | I | TIA | *$\alpha_{1B}$-noradrenergic | [5] |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | receptor antagonist | |
| | | | | MGMRMMFTVFLLVALA | GCCSHPACSGNNPEFCRQ | I | T1.1 | α/nAChR | This study |
| | | | | MGMRMMFTVFLLVVL | GCCSNPACAGNNPHVCRQ | I | T1.2 | α/nAChR | This study |
| | | | | MGMRMMFTVFLLVVLA | GEPVPTTIINFGECCRDPSCWVKVKDFKC | I | T1.3 | α/nAChR | This study |
| Con-ikot-ikot | 29 | 21 | 8 | MAMNMSMTLSTFVMVVVAAT | TPPPHNDCCKMKMCCAIKTEECLKTHSDQQHVYITICYQEA SHTCGQYNEIVGCCYGYRNCMLINVQQLGLRQAQQTCSNRN CLNPCQ | n.d | Con-ikot-ikot-G2 | *AMPA receptor | [6] |
| Conopressin | 24 | 6 | 4 | MTRSVMQMGRLTLVLCLLLLLLL TTQ | CYIQNCLRV | n.d | Conopressins-T | *Vasopressin-oxytocin receptor | [7] |
| S | 4 | 2 | 1 | MMSKMGAMFVLLLLFTLASSQ | GCTGNCDWTCSGDCSCQGTSDSCHCIPPKSIGNRCRCQC | VIII | T8.1 | Serotonin receptor | This study |
| M | 1 | 2 | 1 | MMSKLGVLLTICLLLFPLTAL | HGCCKGPKGCSSRECRPQHCC | III | TIIIA | *μ/Sodium channel | [8] |

[1]Predicted pharmacology based on the conopeptide class and superfamily.

* Pharmacology has been characterised.

N/A not applicable

n.d not determined.

**S5 Table. List of the ρ-TIA precursor variants analysed from the S1 transcriptome**. The transcript number, signal sequence, mature peptide sequence and cysteine residue information has been detailed out. All the precursors display a tight conservation of the signal sequence region, whereas sequence variation is observed in the C-terminal sequence of mature peptide, with reference to the ρ-TIA peptide. Most TIA variants have retained the N-terminal sequence (FNWR) which comprises of the TIA pharmacophore interacting with the $\alpha_{1B}$-adrenoceptor.

| Transcript Number | Read frequency | Signal sequence | Mature sequence | Cysteine Number |
|---|---|---|---|---|
| Tu052/TIA | 2 | MGMRMMFTVFLFV VLATT | FNWRCCLIPACRRNHKKFC | 4 |
| Tu377 | 3 | MGMRMMFTAFLFV VLATT | FNWRCCLIPACRRNHKSFVADDADAHS CHQNNQDMC | 5 |
| Tu378 | 2 | MGMRMMFTVFLFV VLATT | KCCSIPKCYKNNKKMC | 4 |
| Tu379 | 2 | MGMRMMFTVFLFV VLATT | KCCSIPKCYKKQ | 3 |
| Tu380 | 2 | MGMRMMFTVFLFV VLATT | KCCSIPKCYKNNKNKC | 4 |
| Tu381 | 2 | MGMRMMFTVFLFV VLATT | FNWRCCLIPAYRRNHKKFC | 3 |
| Tu395 | 3 | MGMRMMFTVFLFV VLATT | KCCSIPKCYKNNKKCVADDAGAHSCHQ NNQDMC | 6 |
| Tu393 | 2 | MGMRMMFTVFLFV VLATT | FNWRCCLIPACRRNQLKVC | 4 |
| Tu396 | 3 | MGMRMMFTVFLFV VLATT | FNWRCCLIPACRRNHKKFVADDADAHS CHQNNQDMC | 4 |
| Tu397 | 4 | MGMRMMFTVFLFV VLATT | FNWRCCLIPACRRNHKKFCDSYDADAH SCHQNNQDMC | 5 |
| Tu400 | 4 | MGMRMMFTVFLFV VLATT | FNWRCCLIPACRRNHKKFVADDADAHS CHQNKTFCDSYDRQE | 4 |
| Tu403 | 4 | MGMRMMFTVFLFV VLATT | FNWRCCLIPACRRNHKKFCGLTTLMLI PVIRTIKTCVA | 4 |

**S6 Table. Venom duct transcriptome expression of gene superfamilies in *C. tulipa* and *C. geographus***. Transcriptomic data for both specimens retrieved from 454 pyrosequencing [2]. ✓denotes gene superfamily is present.

| Gene superfamily | *C. tulipa* S1 | *C. tulipa* S2 | *C. geographus* |
|---|---|---|---|
| A | ✓ | ✓ | ✓ |
| B1(conantokins) | ✓ | ✓ | ✓ |
| B2 | ✓ | ✓ | ✓ |
| O1 | ✓ | ✓ | ✓ |
| O2 | | ✓ | ✓ |
| O3 | ✓ | ✓ | ✓ |
| M | ✓ | ✓ | ✓ |
| S | ✓ | ✓ | ✓ |
| I1 | ✓ | ✓ | ✓ |
| I3 | | | ✓ |
| H | ✓ | ✓ | |
| J | | | ✓ |
| T | | ✓ | ✓ |
| Con-ikot ikot | ✓ | ✓ | ✓ |
| conkunitzin | ✓ | ✓ | ✓ |
| Conopressin-conophysin | ✓ | ✓ | ✓ |
| contryphan | | | ✓ |
| contulakin | | | ✓ |
| Newgeo 1 | ✓ | ✓ | ✓ |
| Newgeo2 | | | ✓ |
| Newgeo 3 | ✓ | ✓ | ✓ |
| NewGeo 4 | | | ✓ |

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