Proteomic characterisation of toxins isolated from nematocysts of the South Atlantic jellyfish *Olindias sambaquiensis*


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**Article info**

**Article history:**
Received 14 March 2013
Received in revised form 24 April 2013
Accepted 1 May 2013
Available online 18 May 2013

**Keywords:**
Cnidaria
Jellyfish
Nematocyst
Proteomics
Venom

**Abstract**

Surprisingly little is known of the toxic arsenal of cnidarian nematocysts compared to other venomous animals. Here we investigate the toxins of nematocysts isolated from the jellyfish *Olindias sambaquiensis*. A total of 29 unique ms/ms events were annotated as potential toxins homologous to the toxic proteins from diverse animal phyla, including conesnails, snakes, spiders, scorpions, wasp, bee, parasitic worm and other Cnidaria. Biological activities of these potential toxins include cytolysins, neurotoxins, phospholipases and toxic peptidases. The presence of several toxic enzymes is intriguing, such as sphingomyelin phosphodiesterase B (SMase B) that has only been described in certain spider venoms, and a prepro-haystatin P-IIId snake venom metalloproteinase (SVMP) that activates coagulation factor X, which is very rare even in snake venoms. Our annotation reveals sequence orthologs to many representatives of the most important superfamilies of peptide venoms suggesting that their origins in higher organisms arise from deep eumetazoan innovations. Accordingly, cnidarian venoms may possess unique biological properties that might generate new leads in the discovery of novel pharmacologically active drugs.

**1. Introduction**

Cnidaria is a diverse phylum of basal metazoans comprising over 10,000 species, predominately marine organisms (Daly et al., 2007; Zhang, 2011). The phylum has two major lineages: Anthozoa (sea anemones and corals) which live as sessile polyps, and the Medusozoa (jellyfishes and *Hydra*), comprising the classes Cubozoa, Hydrozoa, Scyphozoa and Staurozoa. Species of these four classes have either a free-swimming or attached medusa stage and many retain the ancestral stage of sessile polyps during their life cycles. Cnidarians have external radial symmetry, although many species are either asymmetric or bilateral in their internal anatomy (Marques and Collins, 2004). Cnidarian polyps and medusae have a single body opening...
that acts as both mouth and anus and is generally surrounded by tentacles bearing stinging cells. The nematocysts (stinging cells), sometimes called cnidocytes, are a special type of cnidae and constitute the defining synapomorphy of the phylum Cnidaria (Marques and Collins, 2004). Cnidarians are toxin-producing animals and, having existed since the Cambrian (Cartwright et al., 2007) or even Pre-Cambrian (Van Iten et al., 2013), is possibly the oldest lineage of animals to have evolved means to inject toxins into prey. While they do not have the macromorphological apparatus such as the fangs of snakes to deliver its venomous substances, cnidarians have unique secretory organelles (nematocysts) within their stinging cells. There have been numerous studies characterising the venoms and toxins of many poisonous animals such as cone-snails, scorpions, snakes and spiders, but by comparison very few cnidarian venoms and toxins have been examined in detail (Turk and Kem, 2009). This is surprising because, although most cnidarians do not have harmful nematocysts that are able to penetrate human skin, contact with certain cubozoans, such as Chironex fleckeri (the Pacific Sea Wasp), Carukia barnesi and Malo kingi (the latter two are both commonly called Irukandji Jellyfish) can be fatal (Fenner and Harrisson, 2000). Other medusozoan taxa, species of both planktonic (Haddad et al., 2002) and benthic animals (Marques et al., 2002), are also involved in human envenomation.

Characterisation of the lethal components of Cubozoa and Scyphozoa venoms has been elusive because it was thought that these toxins are large polypeptides that are unstable. Two haemolysins toxins designated cfTX-1 and cfTX-2 from C. fleckeri have been examined by cDNA cloning, protein expression and recent proteomic analysis (Brinkman and Burnell, 2009; Brinkman et al., 2012). Tentacle extracts of C. fleckeri have phospholipase A2 (PLA2) activity, as demonstrated in tissue extracts in species from four classes of Cnidaria that include hydroidan fire corals (Millepora spp.), the scleractinian coral Pocillopora damicornis and the sea anemones Adamsia carciino-pados (Nevalainen et al., 2004) and Urticina crassicornis (Razpotnik et al., 2010).

Most anthozoan toxins are neurotoxic, ion-channel modulating peptides, for examples the potassium ion channel blocking toxin AeK isolated from Actinia equina (Minagawa et al., 1998) and the toxin ShK isolated from Stichodactyla helianthus (Castañeda et al., 1995). Sea anemone neurotoxins and cytolytic enzymes have also been examined for cardiotonic properties (Suput et al., 2001), which includes the peptide hK2a isolated from Anthopleura sp. (Ouyang et al., 2005) and the actinoporins Anthopleura oEb2.01 (reviewed in A. equina (the latter two are both commonly called Irukandji Jellyfish) can be fatal (Fenner and Harrisson, 2000). Other medusozoan taxa, species of both planktonic (Haddad et al., 2002) and benthic animals (Marques et al., 2002), are also involved in human envenomation.

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2. Materials and methods

2.1. Nematocyst isolation

Animals were collected during a jellyfish monitoring project along the central coast of São Paulo state (Guarujá County). Animals were captured through bottom shrimp trawls (2 cm mesh size) dragged at Enseada beach (24°59′52″S 46°13′26″W) at 10 m depth, with each trawl lasting 10 min on May 7th 2012. The collected animals measured 4–6 cm in bell diameter. After capture, the animals were transferred into plastic buckets containing seawater and transported live to the marine laboratory at the Instituto de Biociências, Universidade de São Paulo. The animals were identified as O. sambaqiuensis (Fig. 1) based on general morphological characters (gonads on radial canals; number of radial and centripetal canals per quadrant; tentacles of two types with and without adhesive pads) according to the descriptions of Vanniucci (1951) and Bouillon (1999). After 2 days held in aquarium conditions (filtered seawater, natural light and at a controlled temperature of 20°C), two animals had their tentacles excised. Intact nematocysts were isolated by modification of the method of Weber et al. (1987). The tentacles were gently homogenized in a pestle and mortar in cold SuFi solution (300 mM sucrose containing 50% v/v Ficoll-Paque Plus, GE Healthcare). This material was kept at 4°C for 30 min and then passed through a 2 mm diameter sieve. The sample was centrifuged for 10 min at 3000 g at 4°C. The supernatant containing debris and cell fragments was removed. The pellet containing intact nematocysts was carefully suspended and washed three times in cold SuFi...
solution. The final material was submitted, after microscopic inspection, for lyophilisation.

2.2. Protein extraction

A volume of 200 ml of 50 mM TEAB was added to two centrifuge tubes containing approximately 25 mg of the freeze dried nematocysts. The reconstituted material was disrupted in a sonic bath (VWR, Lutterworth, UK) for 15 min. The tubes were then centrifuged for 5 min at 10,000 \( \times \) g and 4 °C. The supernatants were decanted and lyophilised before reconstituting in 50 ml TEAB. Both protein extract solutions were pooled and quantified by Nanodrop (Thermo Scientific, Wilmington, DE, USA) spectrophotometry.

2.3. Protein preparation

One microlitre of protein extract (equivalent to 88.65 \( \mu \)g of protein determined by Nanodrop analysis) was amended to 20 \( \mu \)l in TEAB before adding 20 \( \mu \)l of Laemmli buffer, heated for 10 min at 90 °C and loaded onto a 4–20% polyacrylamide gel for separation by SDS-PAGE electrophoresis. Electrophoresis was performed using Tris-Glycine buffer (Sigma, Dorset, UK) at 200 V for approximately 30 min. The gel was fixed, stained with Coomassie Blue, visualised with ImageQuant (GE Healthcare, Buckinghamshire, UK) and then de-stained. The stacked gel was then divided into bands and each band excised. In-gel reduction, alkylation, and proteolytic digestion with trypsin were performed for each band prior to liquid chromatographic separation and mass spectrometric analysis (Schevchenko et al., 1996) as follows. Briefly, cysteine residues were reduced with 10 mM dithiothreitol and alkylated with 55 mM iodoacetamide in 100 mM ammonium bicarbonate to form stable carbamidomethyl derivatives. Trypsin digestion of the section was carried out overnight at 37 °C in 50 mM ammonium carbonate buffer and the supernatant was retained. Peptides were extracted from the excised gel portion by two washes with 50 mM ammonium bicarbonate and acetonitrile. Each wash involved shaking gel sections for 15 min before collecting the peptide-containing extract. The extract was pooled with the initial digestion supernatant and then lyophilised. The extract residue was reconstituted in 50 \( \mu \)l of 50 mM ammonium bicarbonate prior to LC-MS/MS analysis with 5 \( \mu \)l of the sample injected.

2.4. LC-MS/MS

Samples were analysed on a Thermo Scientific Orbitrap Velos Pro mass spectrometer coupled to an EASY-nLC II (Proxeon) nano LC system. Samples were trapped on a 0.1 \( \times \) 20 mm Easy-column (Fisher Scientific, Loughborough, UK) packed with ReproSil-Pur C18, 5 \( \mu \)m. After loading and washing of the adsorbed samples the separation was run on a 0.075 \( \times \) 100 mm Easy-column packed with ReproSil-Pur C18, 3 \( \mu \)m (Fisher Scientific) for 60 min using a gradient ranging from 5% to 40% of 99.9% acetonitrile: 0.1% formic acid (buffer B) against 0.1 % formic acid in 99 % H2O (buffer A) at a flow rate of 300 nL/min for 40 min. Then the gradient was changed from 40% to 80% of buffer B for 10 min followed by 10 min at 80% B. Mass spectra ranging from 400 to 1800 Da (m/z) were acquired from proteins in the Orbitrap at a resolution of 30,000 and the 20 most intense ions were subjected to MS/MS by CID fragmentation in the ion trap using a threshold of 5000 counts. The isolation width of precursor selection was 2 units and the normalized collision energy for peptides was 35. Automatic gain control settings for FTMS survey scans were 10^6 counts and for FT MS/MS scans 10^4 counts. Maximum acquisition time was 500 ms for survey scans and 250 ms for MS/MS scans. Charge-unassigned and +1 charged ions were excluded for MS/MS.

2.5. Data analysis

Rawfile data from mass spectrometry analysis were processed for database spectral matching using Proteome Discoverer (Thermo Scientific) software. Mascot was used as the search algorithm with the following variable modifications: methionine oxidation, phosphorylation on S/T/Y, deamidation on N/D. Carbamidomethyl cysteine was selected as a fixed modification. A digestion enzyme of trypsin was set allowing up to two missed cleavages. The numerous MS/MS spectra relating to these peptide mixtures were analysed using a two-step process. Firstly, a profile was created...
by searching against three databases 1/ against all entries in the uniprot_sprot_110118 database (524420 entries), 2/ a custom database created from Uniprot entries retrieved from separate keyword searches for ‘toxin’ and ‘venom’, and 3/ a custom database created from entries retrieved from the annotated UniProtKB/Swiss-Prot Tox-Prot program (Jungo et al., 2012). All database search results were reviewed by loading the MASCOT result files into Scaffold 3.5.1 (Proteome Software). Peptides where two or more spectral counts were obtained were retained for further analysis. When single spectra where matched to regions of identical sequence within species homologues contained in the database(s), a 95% confidence score was required for the spectra to be retained for further analysis. Secondly, the three profiles were merged, duplicates removed and the peptides manually annotated to select only peptides thought to originate from known toxins or venoms. Spectra for these toxins and venoms were manually validated and only those that contained an unbroken series of overlapping b-type and y-type sequence-specific fragment ions with neutral losses consistent with the sequence were considered as valid. Proteins that contained similar peptides that could not be differentiated by MS/MS analysis alone were grouped to satisfy the principles of parsimony.

### 3. Results

*Ollindias sambaquiensis* has three types of tentacles and all contain the same three nematocysts (microbasic mastigophore, pseudostenole, and microbasic euryteles). The use of bottom shrimp trawls inevitably leads to the amputation of tentacles of any great length. For this reason, all remaining tentacles were cut from around the bell margin, ensuring that all three tentacle types were sampled. Light microscopy revealed that greater than 90% of nematocyst capsules were not discharged after processing. The size and shape of the nematocysts indicated that these were microbasic mastigophores, the most common and most often associated with envenomation (AC Marques pers. comm.). Total soluble proteins extracted from the nematocyst preparation were first separated by 1D-gel electrophoresis and then 15 gel slices covering molecular masses up to 200 kDa were analysed by LC-MS/MS following in-gel trypic digestion. Since LC/MS/MS experiments are capable of generating MS/MS spectra for large numbers of peptides within complex mixtures of proteins, we needed a way to extract information for numerous novel jellyfish proteins in a timely manner. We avoided extensive *de novo* sequencing by adopting an approach which involved the matching of peptides representing identical regions of sequence to related homologues already contained with the database. Hence, in this way only a few matching peptides were required to identify, with good confidence, a number of species specific homologues for particular toxic proteins or venoms. Manual validation of ms/ms spectra leading to the annotation of the putative toxins given in Table 1 is shown in Supplemental File 1. Our two step analysis of the soluble nematocyst proteome of *O. sambaquiensis* revealed 29 probable toxins similar to venom proteins from diverse phyla (Table 1). Biological activities of these venoms include hypothetical cytolysins, neurotoxins, phospholipases and toxic peptidases. Several major families of lytic enzymes are represented with metalloproteases being the most prominent. Other enzyme classes include lipid hydrolytic enzymes that cause membrane dysfunction.

### 4. Discussion

Identification of toxic peptides in cnidarians is limited to a small number of toxins (mainly from sea anemones) which have been identified by traditional protein analytical methods, and the identification of these toxins is still under-represented taxonomically. 29 Putative toxins were identified in this study which used a high throughput proteomics platform to characterise the nematocyst proteome of a jellyfish, *O. sambaquiensis* (Table 1). Representatives from all of the important protein superfamilies of toxins were identified. The most ancient toxic device of venom elaboration is the ability to interfere with ion-channels by acting as blockers or activators. Ion-channels are effective targets to subdue prey and predators, and most toxins that act on these channels result in neurotoxic or paralysing effects on the target organism. Toxins that interfere with ion-channels are found in diverse venomous animals that include molluscs, spiders and scorpions, and perhaps the best studied examples are from the very large family of *Conus* peptide toxins. More than a 100 different conotoxins have been described, and a great majority of these peptides selectively target a specific-type ion-channel receptor (Terlau and Olivera, 2004). Because conotoxins discriminate between closely related subtypes of ion-channels they are widely used as molecular probes (agonists or antagonists) in ion-channel research, several have direct diagnostic and therapeutic potential, and the synthetic derivative of the io-conotoxin peptide SNX-111 (Ziconotide marketed as Prialt®) was the first to be approved in 2004 for clinical use by the USA Food and Drug Administration as a non-opioid analgesic (McGivern, 2007).

Only two of the hits revealed the presence of conotoxin homologs (Table 1) that likely have neurotoxic activity (Zhangsun et al., 2006; Biggs et al., 2010). Ion-channel toxins from Cnidaria (Uniprot Q3C258, Beadlet Anemone), spiders (Uniprot Q9XZC0, Mediterranean Black Widow Spider; the theraphotoxins (Uniprot B1P1E7 and B1P1A0, Chinese Earth Tiger Tarantula) and snakes (Uniprot P85061, Australian Death Adder) were also identified. In addition to postsynaptic polypeptide neurotoxins common to venoms of elapid and hydroid snakes, are selective antagonists of nicotinic acetylcholine receptors (Uniprot O12961, Chinese Krait Snake), revealing the great potential of this proteome for screening of pharmacologically active compounds.

Hydrololytic enzymes have also been recruited into the toxic milieu of venoms. For example, phospholipases are commonly found in the venoms of wasps (Pinto et al., 2012), scorpions (Diego-Garcia et al., 2012), sea anemones (Landucci et al., 2012), spiders (Chaim et al., 2011) and snakes (Zychar et al., 2010) where they accelerate the toxic effects of venoms as allergens, inflammatory agents or as tissue and blood cytotoxins. In snake venoms, phospholipases such as phospholipase A2 (PLA2) are often abundant with many acting on the pre-synaptic nerve pathway only a few matching peptides were required to identify, with good confidence, a number of species specific homologues for particular toxic proteins or venoms. Manual validation of ms/ms spectra leading to the annotation of the putative toxins given in Table 1 is shown in Supplemental File 1. Our two step analysis of the soluble nematocyst proteome of *O. sambaquiensis* revealed 29 probable toxins similar to venom proteins from diverse phyla (Table 1). Biological activities of these venoms include hypothetical cytolysins, neurotoxins, phospholipases and toxic peptidases. Several major families of lytic enzymes are represented with metalloproteases being the most prominent. Other enzyme classes include lipid hydrolytic enzymes that cause membrane dysfunction.
dysfunction of the neuromuscular junction (Montecucco et al., 2009; Tedesco et al., 2009; Montecucco and Rossetto, 2000; Montecucco et al., 2009; Tedesco et al., 2009). Proteases are also constituents of the toxic armament of venomous animals and are well represented (Table 1) by serine protease and metalloprotease enzymes in this dataset (for example, Uniprot Q9W7S2, Chinese Sharp Nose Viper; Uniprot P0C7A9, Brazilian Golden Lancehead Viper; Uniprot E9JG55, Burton’s Carpet Viper; Uniprot F8S120, Eastern Diamondback Rattlesnake). These proteases are essentially digestive enzymes that in venom may elicit cytotoxic, hemotoxic, hemorrhagic and myotoxic effects to subdue and kill prey, and these enzymes may additionally assist in subsequent prey digestion (reviewed in Marques et al., 2002). Notable are the pore-forming toxins characterised in this study (Table 1) with similarity to other cnidarian toxins that cause disruption to normal transmembrane ion concentration gradients, some with haemolytic activity, that include Toxin AvTX-60A (Okinawan Sea Anemone) and Toxin PsTX-60A (Night Anemone). Previously, toxins from jellyfish venoms, such as the Box Jellyfish, have only been characterised by use of cDNA cloning and proteomics (Brinkman and Burnell, 2009; Brinkman et al., 2012). Detection of Cubozoa and Scyphozoa toxins by direct proteome analysis coupled with advanced bioinformatic homology searching now offers a new and powerful technique to characterise venoms from these potentially lethal animals, which were thought previously to be too labile to characterise by traditional bioassay-guided chromatographic methods. Of those jellyfish venoms related to spider toxins, the most distinguishable is sphingomyelin phosphodiesterase B (Smase D), which is a highly destructive component in the venom of brown spiders that causes dermonecrosis in mammals and, up to now, Smase D has been described only in Loxosceles, Sicarius and Drimus spider venoms (Binford et al., 2009). The presence of these enzymes in a jellyfish terminal where they hydrolyse plasma membrane phospholipids into lysophospholipids and fatty acids. Such plasma membrane alterations can trigger synaptic vesicle exocytosis causing depletion of synaptic vesicles and increase membrane permeability to calcium ions resulting in degradation of cell organelles such as mitochondria, which are essential for the function of nerve terminals leading to rapid paralysis from permanent membrane dysfunction of the neuromuscular junction (Montecucco and Rossetto, 2000; Montecucco et al., 2009; Tedesco et al., 2009).

### Table 1

<table>
<thead>
<tr>
<th>Peptide</th>
<th>Mode of action</th>
<th>Uniprot accession number</th>
<th>Organism with closest homology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acrotoxin 9.1</td>
<td>Unknown</td>
<td>P0C7A9</td>
<td>Bothrops jararaca (Brazilian Golden Lancehead Viper)</td>
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<tr>
<td>Acrotoxin 9.1</td>
<td>Pre-synaptic neurotoxin</td>
<td>Q9XZC5</td>
<td>Lanthreductus tredecinguattus (Mediterranean Black Widow Spider)</td>
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<tr>
<td>Metalloprotease</td>
<td>Proteolysis</td>
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<td>Bathus judicus (Israeli Black Scorpion)</td>
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<tr>
<td>Metalloprotease</td>
<td>Hypotensive and vasodepressor activity</td>
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<tr>
<td>Neublin-like protein</td>
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<td>Q5AXY</td>
<td>Oxymus scutellatus (Coastal Taipan)</td>
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<tr>
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<td>Potassium ion channel inhibitor</td>
<td>P0C185</td>
<td>Tityus costatus (Brazilian Scorpion)</td>
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<tr>
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<td>Daboia russelli (Eastern Russell’s Viper)</td>
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<td>Prepro-halystatin</td>
<td>Zinc metalloendopeptidase</td>
<td>Q5Q020</td>
<td>Gloydius halys (Siberian Pit Viper)</td>
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<td>CSJ8C9</td>
<td>Opisthanclus cyanoporum (South American Scorpion)</td>
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<td>Serine protease 8</td>
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<td>Crotalus adamanteus (Eastern Diamondback Rattlesnake)</td>
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<td>Endopeptidase</td>
<td>Q5WVSP</td>
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<td>CQB7S5</td>
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<tr>
<td>U14-Theraphotoxin-Cj1b</td>
<td>Possible ion channel inhibitor</td>
<td>B1P1E7</td>
<td>Chilobrachys jingzhao (Chinese Earth Tiger Tarantula)</td>
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<tr>
<td>k -Theraphotoxin-Cj1b</td>
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<td>B1P1A</td>
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<td>Q76DT2</td>
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<tr>
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<td>G7Y9P2</td>
<td>Clonorchis sinensis (Chinese Liver Fluke)</td>
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<td>Venom dipetidylpeptidase IV</td>
<td>Endopeptidase</td>
<td>A6MJH9</td>
<td>Notechis scutatus (Eastern Tiger Snake)</td>
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<tr>
<td>Venom serine protease 34</td>
<td>Endopeptidase</td>
<td>Q8MQS8</td>
<td>Apis mellifera (European Honey Bee)</td>
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</table>
proteome is therefore intriguing, since tissue necrosis has not been reported in any case of envenomation attributed to O. sambauquisis (Kokej et al., 1993; Haddad et al., 2002).

The most predominant of the jellyfish toxins are family members of snake venom metalloproteinase (SVMP) disintegrins, with homologs identified in the peptide search. SVMPs share ancestral genes with matrix metalloproteinase endogenous enzymes (Moura da Silva et al., 1996) that in the pathology of viper envenomation cause the disruption of capillary vessels and tissues that is manifest by severe inflammation (Moura da Silva et al., 2007). Snake and scorpion venom phospholipases A2 were also identified in the jellyfish proteome (for example, Uniprot Q6H3D0, Chinese Green Tree Viper; Uniprot A8CG84, Eastern Russell's Viper and Uniprot C5J8C9, South American Scorpion). These enzymes disturb blood clotting and cause local tissue damage that frequently occurs in envenomation by viper snakes. These enzymes are not present in the basal milieu of the Toxicofera reptile venom system and were recruited most likely during early differentiation of venomous snakes (Fry et al., 2008). Hemotoxic serine proteases can have both fibrinolytic (coagulant) and fibrinogenolytic (anticoagulant) activities to disrupt hemostasis, and those that elaborate only thrombin-like activity (blood coagulant factor II) cause fibrinogen coagulation. In addition, several hemotoxic serine proteases specifically stimulate protein C inactivation of coagulation factor V to inhibit blood clotting plasminogen to dissolve fibrin blood clots as a necessary cofactor of the mammalian thrombininase complex (reviewed in Crammer and Gale, 2012). Like most serine proteases, venom metalloproteases are also activators of coagulation factor II, and a few have a unique substrate specificity to activate coagulation factor X (Kini, 2006) or act by disrupting the integrity of blood vessels to cause fatal hemorrhagic lesions (Moura da Silva et al., 2007). Moreover, some group II PLA2s or class P-II SVMPs enzymes detected in the jellyfish proteome appear in Toxicofera reptiles only after differentiation between Elapid and Viperid snakes (Fry et al., 2008; Juarez et al., 2008). This evidence raises important questions concerning their identification in the jellyfish proteome suggesting independent evolution of toxic enzymes in these distinct organisms. However, in this case, it is unclear what would be the evolutionary pressure to select such toxins with specific action to mammalian blood clotting or damage to vascular systems, although mature jellyfish are known to prey on juvenile fish (Underwood and Seymour, 2007).

A number of different phospholipases and metalloproteinases were identified by MS/MS peptide sequences corresponding to signal-peptides. The most intriguing was the detection prepro-halystatin from the Siberian Pit Viper Gloydius halys (Uniprot Q90220). This is a RVV-X peptide comprising the signal peptide and the N-terminus of the pro-domain (Takeda et al., 2007) and is a P-IIId representative of SVMPs that activates coagulation factor X and is very rare, even in snake venoms.

Our results demonstrates the effective utility of a high throughput proteomics platform for toxin identification, and for potential bio-discovery these results highlight the urgency of future biochemical assessments for testing in vivo the physiological effects of marine toxins. It is estimated that there are up to 700 species of Conus snails, each possessing around 200 conopeptides in their venom, thus theoretically there are over 50,000 pharmacologically active components to be found in the genus Conus venoms alone (Adams et al., 1999). If the 29 potential toxins presented in Table 1 of our data were extrapolated to all 10,000 species of Cnidaria, 29,000 toxins have yet to be explored as potential therapeutics, novel templates for drug design or diagnostic tools. This predicted magnitude of unique toxins may be realistic given that 55 putative toxins have been described solely in the proteome of H. magnipapillata nematocysts (Balasubramanian et al., 2012) and 23 putative toxins were detected from contaminating nematocysts in the proteome of a symbiont enriched fraction of the coral S. pistillata (Weston et al., 2012). From an evolutionary perspective, the sequence similarities between toxic peptides of the jellyfish O. sambauquisis and that of phylogenetically unrelated metazoans represent an intriguing result. Both the amount of toxins and venoms gathered from a proteome preparation of a single cnidarian species, together with the degree of variation recovered, are remarkable. In the view of these new data, the molecular evolution of super gene families coding for toxins and venoms arising in the Cnidaria should be addressed.

Acknowledgements

The authors thank Prof Robert Hider for his useful comments. This work was funded by a co-operation grant between King’s College London and Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP). Additional funding to support animal collection under SISBIO license 15031-2 was provided from Brazil by FAPESP (grant 2010/50174-7), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ).

Appendix A. Supplementary material

Supplementary material related to this article can be found at http://dx.doi.org/10.1016/j.toxicon.2013.05.002.

Conflict of interest statement

There are no competing interests.

References


