DADP: the database of anuran defense peptides

Mario Novković¹, Juraj Simunić¹, Viktor Bojović², Alessandro Tossi³ and Davor Juretić¹,∗
¹Department of Physics, Faculty of Science, University of Split, 21000 Split. ²Centre for Informatics and Computing, Rudjer Bošković Institute, 10000 Zagreb, Croatia and ³Department of Life Sciences, University of Trieste, 34127 Trieste, Italy

Associate Editor: Burkhard Rost

ABSTRACT

Summary: Anuran tissues, and especially skin, are a rich source of bioactive peptides and their precursors. We here present a manually curated database of antimicrobial and other defense peptides with a total of 2571 entries, most of them in the precursor form with demarcated signal peptide (SP), acidic proregion(s) and bioactive moiety(s) corresponding to 1923 non-identical bioactive sequences. Search functions on the corresponding web server facilitate the extraction of six distinct SP classes. The more conserved of these can be used for searching cDNA and UniProtKB databases for potential bioactive peptides, for creating PROSITE search patterns, and for phylogenetic analysis.

Availability: DADP is accessible at http://split4.pmfst.hr/dadp/

Supplementary information: Supplementary data are available at Bioinformatics online.

Received on December 6, 2011; revised on March 2, 2012; accepted on March 20, 2012

1 INTRODUCTION

With the growing problem of pathogens developing resistance to conventional antibiotics, there is a great interest in antimicrobial peptides (AMPs) as substitute therapeutics (Hancock and Sahl, 2012). However, these databases tend to focus on the antimicrobial activities, with AMPs being in the majority (Supplementary Table S3). Missing activities field denotes unknown function. Phylogenetic analysis and classification in six classes, based on signal peptide (SP) similarity (Supplementary Fig. S1), was constructed using MEGA software version 5 (Tamura et al., 2007). Activity and cytotoxicity data were extracted from published papers where the minimal inhibitory concentration (MIC, μM) based on microdilution assays was reported for Escherichia coli and/or Staphylococcus aureus. HC50 refers to peptide concentration, also micromolar, required for 50% haemolysis of red blood cells. MIC data are available for 921 peptide sequences.

3 IMPLEMENTATION

DADP is hosted on a 64 bit Linux server using Apache (http://www.apache.org/) and PHP (http://www.php.net/). All entries are stored in a MySQL (http://www.mysql.com/) database. The application was written in PHP, using the jQuery JavaScript Library (http://jquery.com/) with the DataTables (http://datatables.net/) plug-in for the tables’ implementation, and CSS for web design.

4 WEB INTERFACE

The DADP web interface offers browsing capability for all peptide entries, for SPs and for SP classes in particular. An advanced search option is available for more specific user requests. Each DADP ID entry contains detailed information about peptide names and sequences, tripartite structure, species, SP class, biogeography,
biological function, peptide activity and links to UniProtKB. Search results are presented as tables.

5 DISCUSSION
Bioactive peptides from amphibian species with function, often related to host defense, are a fast growing group in the UniProtKB database and this attempt to collect and order them all can mostly serve to emphasize the incompleteness of our knowledge. For instance, out of 167 species from the DADP, only 28 can be found among 2200 threatened and near threatened anuran species from the IUCN Red List. The DADP focuses on precursors and their conserved SPs and has allowed the individuation of six distinct SP classes (see Supplementary Material and Supplementary Tables S4 and S5). Consensus sequences for the different SP classes are a good foundation for searching protein or DNA databases that might carry precursors with novel AMP sequences, where a direct homology search based on the active region only is unsuccessful (Juretic et al., 2011).

The conservation of SPs in different suborders and families Ranidae, Hylidae, Hyperoliidae and Rhacophoridae. SP classes 1–6 are associated not only with AMPs but also with mature bioactive peptides having other functions.

Precursor structure is informative about origin, function and evolution of mature peptides collected in the DADP, but there are numerous peptides present only as the mature bioactive sequence, where the precursor structure is not reported. The activity data, shown as MIC and HECp values, are available for over 900 sequences. These should, however, be considered critically as both are quite sensitive to assay conditions, which vary from lab to lab (e.g. medium, salt concentrations and the size of inoculum, which should be at least 10^5 cfu/ml for MIC (Resende et al., 2008) and at most 1% erythrocytes for HECp determinations, limits often either not observed or not defined in published papers).

The conservation of SPs in different suborders and families of anurans, whose relatedness follows continental tectonics and corresponding changes in biogeography, is quite impressive (Supplementary Fig. S1 and the DADP web server). This is one of those rare examples when maintenance of the export mechanism, is evolutionarily more conserved than the mature exported polypeptide structure. It may be beneficial for the host to have accelerated co-evolution of the mature defense peptide sequences, to keep up with the constantly shifting microbial biota, allowing to maintain the host-of the mature defense peptide sequences, to keep up with the...

ACKNOWLEDGEMENTS
Funding: Croatian Ministry of Science, Education and Sport (Grant No. 177-1770495-0476).
Conflict of Interest: none declared.
REFERENCES