NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

SEMINAR

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Hosted by Professor R M Kini

Innovation in Toxinology:

Ant peptidomes as new discovery frontier







By Pierre Escoubas

VenomeTech, Valbonne, France

Animal venoms are large combinatorial libraries of biologically active peptides that encompass a wide variety of structures and pharmacological activities. They represent an immense and largely untapped resource of novel therapeutics and drug models. Exploration of the pharmacology and molecular diversity of venoms has resulted in the development of several innovative drugs but the full potential of venom biodiversity remains largely unexplored to date.

Although numerous snake, spider, scorpion or cone snail venoms have been explored, surprisingly, the full extent of animal venom biodiversity has not yet been investigated, with entire zoological groups remaining uncharted territory. Thus innovation in toxinology is both possible an desirable in the 21st century, as the search for novel drugs and molecular tools has gained increasing momentum due to the progress of pharmacological knowledge at the cellular and receptor levels.

Ants use their venoms for predation and defense, and their proteinaceous components have scarcely been studied with only ca 40 peptides described at the start of this project. Ants are amongst the most widespread and abundant organisms on Earth, accounting for ca. 15% of the total animal biomass. And ca 10,000 species possess stinging abilities and peptidic venoms out of more than 15,000 described ant species. Nevertheless, although they represent an enormous potential diversity of new peptides, ant venoms have remained mostly unexplored so far, due to the minute venom amounts produced by individuals as well as complex taxonomic issues.

We first developed a novel chemotaxonomic method based on venom fingerprinting by MALDI-TOF mass spectrometry to image venom peptidomes and clarify taxonomic issues. Following successful application to hundreds of neotropical ant venom samples, we further applied the methodology as well as proteomics methods, to the identification of various structural types of peptides in the venoms. Our studies revealed the presence not only of linear peptides but also of numerous disulfide-linked peptides including homo- and heterodimeric peptides. Overall, we demonstrated that ant venoms encompass a much higher structural complexity than previously thought and that such complexity could be linked to the putative presence of a complex pharmacological diversity. Further work on selected venoms led to the isolation of specific disulfide-linked peptides, and full characterization permitted the identification of novel molecular scaffolds as well as activity on calcium ion channels.

Our exploratory work has thus revealed the immense and unsuspected molecular diversity of ant venoms and has opened a new research avenue for toxinology. As more ant venoms will be dissected using cutting-edge technologies such as transcriptome analysis, a larger repertoire of ant peptides will become available to drug discovery programs. This novel and original molecular biodiversity will most certainly be of great importance in the development of novel drugs, biopesticides and molecular tools.

Artwork by Ann Nee, DBS, NUS