# 17th World Congress of the International Society on Toxinology

**Animal, Plant and Microbial Toxins**

**&**

# Venom Week 2012

**4th International Scientific Symposium on All Things Venomous**

## Honolulu, Hawaii, USA, July 8 – 13, 2012

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**Introduction**

Welcome to the 17th World Congress of the International Society on Toxinology (IST), held jointly with Venom Week 2012, 4th International Scientific Symposium on All Things Venomous, in Honolulu, Hawaii, USA, July 8 – 13, 2012. This is a supplement to the special issue of Toxicon. It contains the abstracts that were submitted too late for inclusion there, as well as a complete program agenda of the meeting, as well as other materials. At the time of this printing, we had 344 scientific abstracts scheduled for presentation and over 300 attendees from all over the planet.

The World Congress of IST is held every three years, most recently in Recife, Brazil in March 2009. The IST World Congress is the primary international meeting bringing together scientists and physicians from around the world to discuss the most recent advances in the structure and function of natural toxins occurring in venomous animals, plants, or microorganisms, in medical, public health, and policy approaches to prevent or treat envenomations, and in the development of new toxin-derived drugs. The Venom Week Symposiums, previously held in 2005, 2007 and 2009, are held in the USA with an international faculty and focus, and present the most recent advances in terrestrial and marine envenomations of medical and veterinary importance, in venom and antivenom basic science, in the handling and breeding of venomous animals in zoos and aquaria, in venomous animal science, and in regulatory issues. As both meetings were scheduled to be held in the summer of 2012 in the USA, the two organizations decided to hold a joint meeting in Honolulu.

The program of the meeting is characterized by two parallel tracks, basic sciences and clinical sciences, thereby providing venues for presenting advances in these two broad areas of toxinology research as well as translational aspects that bridge these two components. Some sessions on important topics are organized by eminent scientists in their field, whereas other sessions were developed from the approximately 300 abstracts submitted to the meeting.

The joint meeting of the 17th World Congress of the IST and Venom Week 2012 is intended to be a forum of scientific exchange among the members of the toxinology communities from around the globe. It is hoped that the unique location of Hawaii enhances the meeting experience. Hawaii is indeed a very special place. The most northern part of Polynesia, it is the most isolated land mass in the world with a sizable population. It is characterized by an unparalleled cultural diversity, where the East meets the West, and where the host culture is Hawaiian. Although part of the United States, it is a fitting place to serve as host for the Asia-Pacific Region of the IST for its World Congress. Oahu, the island on which Honolulu is located, is a Hawaiian name and means “Gathering Place.” Appropriately, it will be the gathering place for the world toxinology community in 2012.

Many thanks go to the Executive of IST, President Dr. Ponnampalam Gopalakrishnakone (Singapore), Secretary/Treasurer Dr. Julian White (Australia), and President-Elect Dr. Alan Harvey (United Kingdom), to the members of both the international Scientific Organizing Committee, the Local Organizing Committee, and to the many sponsors for helping to make the 17th IST World Congress / Venom Week 2012 Meeting a reality and success.

**Meeting Co-Chairs**

Steven A. Seifert, MD (USA)
Carl-Wilhelm Vogel, MD, PhD (USA)

**Members of the Scientific Organizing Committee**

Alejandro Alagon (MEXICO)
Greta Binford (USA)
Leslie V. Boyer (USA)
Sean P. Bush (USA)
Juan J. Calvete (SPAIN)
Jean-Philippe Chippaux (BENIN)
Yara Cury (BRAZIL)
Richard C. Dart (USA)
P Gopalakrishnakone (SINGAPORE)
Eugene Grishin (RUSSIA)
Michael Gurevitz (ISRAEL)
José María Gutiérrez (COSTA RICA)
Abdulrazaq G. Habib (NIGERIA)
Alan Harvey (UK)
Dan E. Keyler (USA)
Glenn King (AUSTRALIA)
Jessi Krebs (USA)
Stephen P. Mackessy (USA)
Ashis k. Mukherjee (INDIA)
Manjunatha R. Kini (SINGAPORE)
Cesare Montecucco (ITALY)
Dietrich Mebs (GERMANY)
Tarek R. Rahmy (EGYPT)
Karen Seibold (USA)
Steven A. Seifert (USA)
Denis Servent (FRANCE)
Reto Stöcklin (SWITZERLAND)
Denise V. Tambourgi (BRAZIL)
Toru Tamiya (JAPAN)
Jan Tytgat (BELGIUM)
Carl-Wilhelm Vogel (USA)
Julian White (AUSTRALIA)

**Members of the Local Organizing Committee**

Brian E. Hew (Black Ivory Biotech, Aiea, Hawaii)
Ben Okimoto (Honolulu Zoo, Hawaii)
John M. Pezzuto (University of Hawaii at Hilo)
Andrew Rossiter (Waikiki Aquarium, Hawaii)
Steven A. Seifert (University of New Mexico)
Carl-Wilhelm Vogel (University of Hawaii at Manoa)
Julian White (Women's and Children's Hospital, Adelaide)
Catherine Wood (University of New Mexico)

**Sponsors**

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Atheris Laboratories, Switzerland
International Society on Toxinology
College of Pharmacy, University of Hawaii at Hilo
University of New Mexico Health Sciences Center
Midwest Tongs
Waikiki Aquarium
Honolulu Zoo
Organization for the Prohibition of Chemical Weapons (OPCW)

**Meeting Organizers / Co-Chairs**

Carl-Wilhelm Vogel, MD, PhD
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*MSC09 5080*
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**UNM School of Medicine, CME Conference Planners:**

Catherine Wood
Dorrie Murray

# A MESSAGE FROM THE PRESIDENT OF I.S.T.

Dear Fellow Toxinologists and Friends,

The 17th World Congress on Animal, Plant and Microbial Toxin of the International Society on Toxinology will be held in Hilton Village, Hawaii from July 8 -13, 2012. This time we are combining the world Congress with the venom week 2012. Over the years there have been concerns that the Society and the meetings have not given sufficient attention to clinical toxinology. This world congress will be well balanced between basic toxinology research and clinical toxinology. The congress programme is well organized with many experts from various parts of the world participating. There will be a special plenary session including "Biotoxins and bioterrorism". "Drug discovery from natural toxins". The local organizing committee led by Carl and Steve as well as other members are not leaving any stones unturned to make this remarkable congress a memorable one. We also hope to invite many clinical toxinologists from Asia and Africa to highlight the problems of envenomations which has been described as the "Disease of the poor". While we bring frontier research as basic toxinology we also look into the possibility of the basic research turned into application by translation research with particular reference to human treatment. There will be also discussion on the initiatives of the IST, such as Nomenclature Committee, Global Snake Bite Initiative, Clinical Toxinology Group, etc. We are also encouraging the young toxinologists and research students to attend the World Congress. If there is sufficient number of students we will be able to organize a "Student Forum".

Hawaii is well known for its tourist attractions, fabulous sea beaches, volcanoes as well as exotic delicious food and also a melting pot of culture.

As President of the International Society on Toxinology, I warmly welcome you all to Hawaii to attend the World Congress. I guarantee a very good scientific program and a memorable social event which will remain in your memory for a long time.

WITH BEST WISHES,

Gopal.
Prof.P.GOPALAKRISHNAKONE,
MBBS,PHD,FAMS,DSc

# A Message from the Organizer of Venom Week Symposiums, and Meeting Co-Organizer and Co-Chair

Venom Week 2012, is the 4th International Scientific Symposium on all things venomous, and will be held in conjunction with the 17th World Congress of the International Society on Toxinology (IST), July 8 – 13, 2012, in Honolulu, Hawaii.

Venom Week meetings have been held periodically since 2005. They have been North American-based scientific meetings with an international faculty and focus. They have been a unique collaboration among those with an interest in venomous animals, their venoms and the management of envenomations, bringing together basic and clinical scientists, zoo and collections management personnel, veterinarians, venomous animal scientists and more.

Since the IST World Congress was scheduled to be held in the U.S. at the same time as the 2012 Venom Week meeting, and there was both overlap and unique aspects to each, it seemed appropriate to combine these meetings to obtain the benefits of shared interests and the opportunities for new collaborations. It is clear from the outstanding participant list and the submitted scientific abstracts that an exciting meeting is in store, with over 300 scientific presentations in a wide diversity of toxinologic subjects.

All of that and Hawaii, too.

As the organizer of the Venom Week Symposiums, I wish to welcome you to Hawaii to attend the combined meeting of Venom Week and the IST World Congress. In concert with my colleague, Dr. Gopalakrishnakone, and in conjunction with my Co-Organizer and Co-Chair of the current meeting, Carl-Wilhelm Vogel, we guarantee a fascinating and productive scientific meeting and a memorable event whose impact on the advancement of the study of natural toxins, venomous animals and related subjects will be global in impact and years in duration.

Steven A. Seifert, MD, FAACT, FACMT

# A Message from the Meeting Co-Organizer and Co-Chair

Dear Toxinologists from Around the World,

It gives me great pleasure to serve as organizer, jointly with Dr. Steven Seifert, on behalf of the International Society on Toxinology (IST) of its 17th World Congress. For the first time, the meeting will be held jointly with the Venom Week Symposium. The meeting will take place in Honolulu, Hawaii, USA, in the Hilton Hawaiian Village in Waikiki, from July 8th through July 13th, 2012.

Although Hawaii is part of the USA, we will be the host for the IST World Congress for IST's Asia Pacific regional section, given Hawaii's mid-Pacific location, in line with IST's cycle of the World Meeting through its three regions (Pan America, Europe, Asia Pacific). The Hawaii meeting will follow the 16th World IST Meeting in Recife, Brazil in 2009 (Pan American Section) and the 15th World IST Meeting in Glasgow, Scotland in 2006 (European Section).

We have received over 340 abstracts for presentation at the meting. We are pleased to offer separate session tracks in the clinical sciences and basic sciences to highlight IST's growing commitment to the clinical aspects of envenomations. In addition, we will have timely sessions on the potential use of biological toxins as agents of bioterrorism, toxins as lead compounds for new drug development, including translational aspects.

The approximately 300 abstracts received by the abstract submission deadline will be published in a special issue of Toxicon, made available to all meeting attendants. Late breaking abstracts will be included in the meeting supplement.

We also plan an exiting social program to highlight the multicultural aspects of Hawaii. In addition, we hope that all meting attendants will take advantage of the many leisure activities that Honolulu, the island of Oahu, and all of the Hawaiian Islands offer, from world class beaches, to world class shopping, and unmatched natural beauty.

With Warmest Aloha
Carl-Wilhelm Vogel, MD, PhD, FCAP, FASCP

# A Message from the Incoming President of the I.S.T.

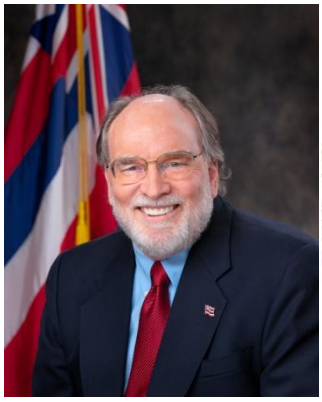
Dear Colleagues

As the incoming president of the International Society on Toxinology, I am very happy to add my welcome to you to this Congress. It is a great occasion to have the IST's international congress together with Venom Week, and I hope that this will stimulate many new ideas and collaborations.

I would like to thank the organisers for putting together a challenging and exciting programme and for hosting us in such a beautiful location. I am sure that we all benefit professionally and socially from the coming days.

Best wishes,

Alan Harvey



*Special Message from Governor Neil Abercrombie*

*In Recognition of the*

## 17th World Congress of the International Society on Toxinology & Venom Week 2012, 4th International Scientific Symposium

July 8-13, 2012

On behalf of the people of Hawai'i, I extend a heartfelt *aloha* to the participants of the **17th World Congress of the International Society on Toxinology (IST)** and **Venom Week 2012, 4th International Scientific Symposium** at the Hilton Hawaiian Village in beautiful Honolulu, Hawai'i.

This year's IST World Congress on Animal, Plant and Microbial Toxins will be combined with Venom Week 2012, a scientific symposium on all things venomous. I am certain there will be special interest in the plenary sessions on "Biotoxins and Bioterrorism" and "Drug discoveries from Natural Toxins."

The State of Hawai'i has made significant investments in biomedical research through the University of Hawai'i – Mānoa (UHM) John A. Burns School of Medicine, Cancer Research Center and the University of Hawai'i – Hilo College of Pharmacy. We are supportive of the advances that biomedical and biotechnological research can offer and are hopeful that the study of natural toxins will lead to new therapies and the development of new pharmaceutical drugs. We are pleased that you have selected Hawai'i as your meeting site. We hope that symposium participants are able to spend some time enjoying the spectacular, natural wonders of the Hawaiian Islands and take advantage of our local, ethnic culinary delights.

A special *mahalo* (thank you) to Dr. Carl-Wilhelm Vogel of UHM Cancer Research Center, and Dr. Steven Seifert of the University of New Mexico, Co-Chairs of the meeting; and to all those who have worked to make this an interesting and productive gathering.

To the **World Congress of the International Society on Toxinology**, and **Venom Week 2012**, I share my best wishes for a memorable conference and continued success.

*Aloha,*
**NEIL ABERCROMBIE**
Governor, State of Hawai'i

PETER B. CARLISLE
MAYOR

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CITY AND COUNTY OF HONOLULU
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DOUGLAS S. CHIN
MANAGING DIRECTOR

CHRYSTN K. A. EADS
DEPUTY MANAGING DIRECTOR

## MESSAGE FROM MAYOR PETER B. CARLISLE

It gives me great pleasure to send my warmest aloha to those attending the 17th World Congress of the International Society on Toxinology and the Venom Week 2012, 4th International Scientific Symposium.

We appreciate Honolulu being chosen to host this event and are pleased to provide the support of the Honolulu Zoo.

This gathering will enable productive scientific exchange on important topics such as preventing and treating snake bites in countries around the world, the development of novel drugs from toxins, and the potential use of toxins as bioterrorism agents.

Special thanks to organizers, Carl-Wilhelm Vogel, MD, PhD of the University of Hawaii Cancer Center and Steven A. Seifert, MD of the University of New Mexico Poison and Drug Information Center, along with their team of colleagues and co-workers.

On behalf of the people of the City and County of Honolulu, I extend best wishes for a successful event.

Peter B. Carlisle

Peter B. Carlisle

# Program

## 17th World Congress of the International Society on Toxinology

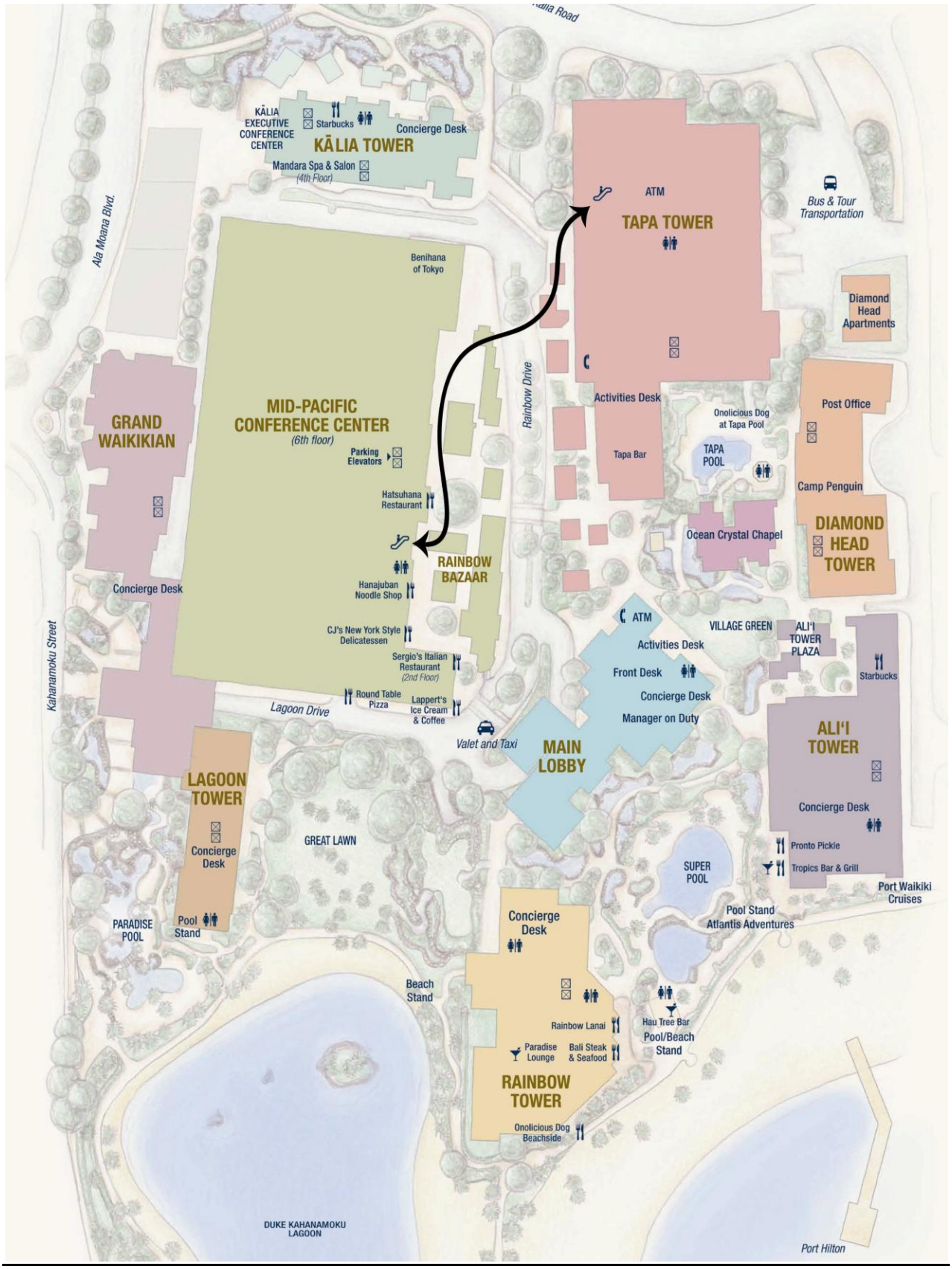
**Animal, Plant and Microbial Toxins**

**&**

## Venom Week 2012

**4th International Scientific Symposium on All Things Venomous**

## Honolulu, Hawaii, USA, July 8 – 13, 2012


KĀLIA EXECUTIVE CONFERENCE CENTER
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Mandara Spa & Salon
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Ala Moana Blvd.
ATM
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GRAND WAIKIKIAN
MID-PACIFIC CONFERENCE CENTER
(6th floor)
Parking Elevators
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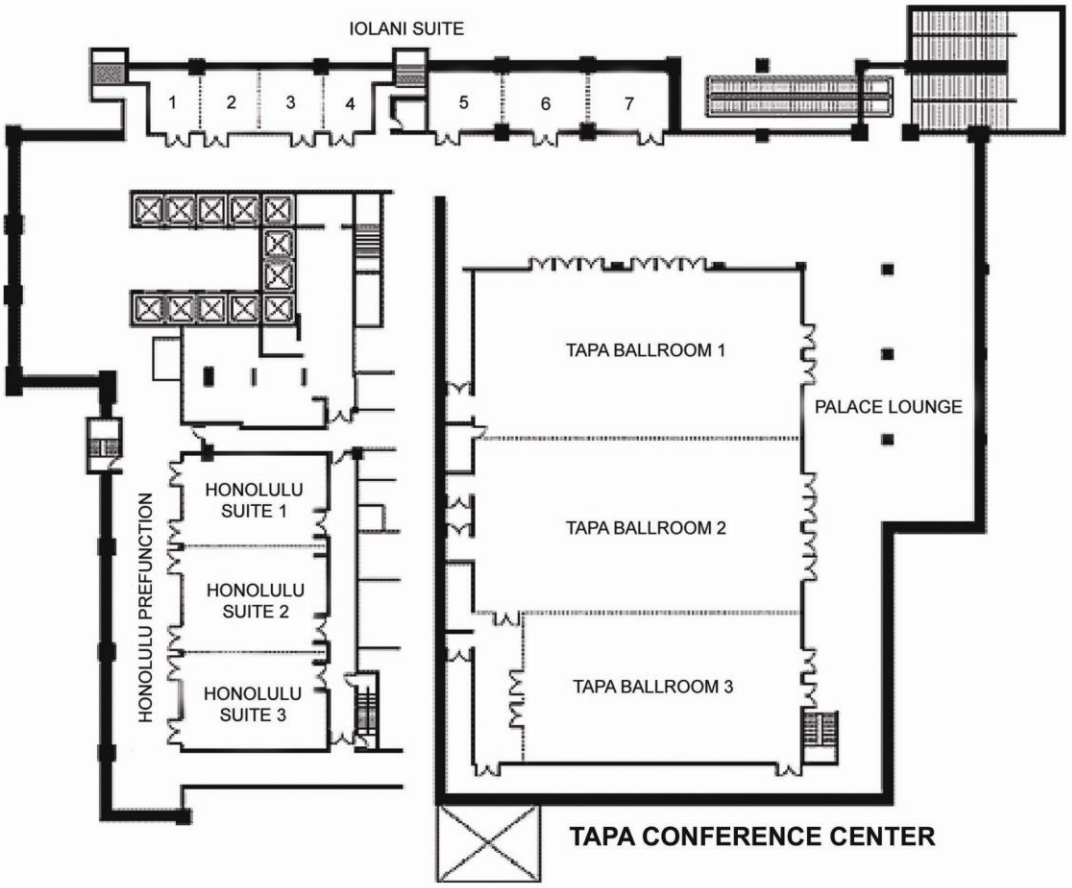
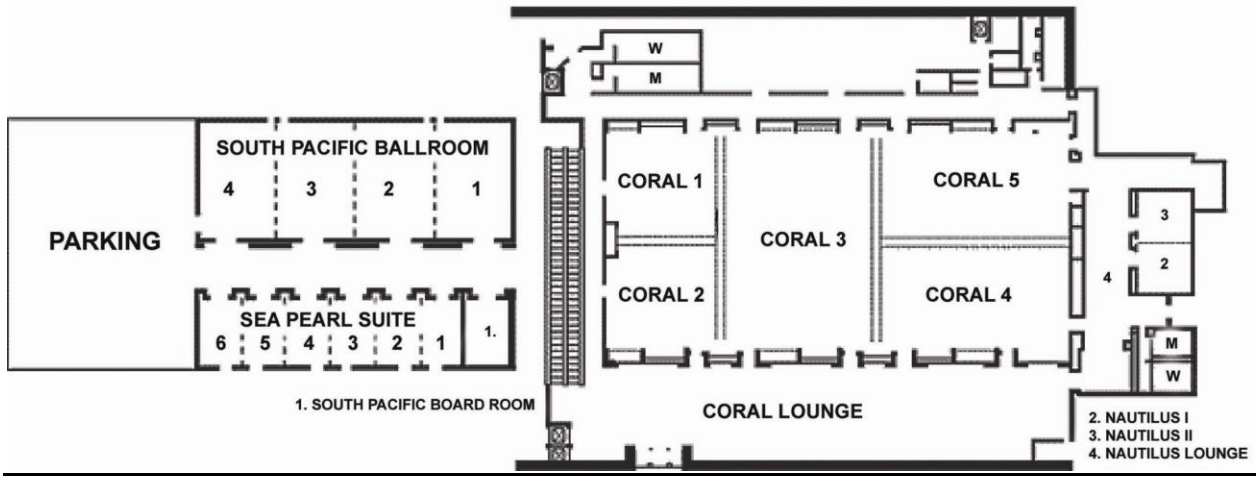
Onolicious Dog at Tapa Pool
Tapa Bar
TAPA POOL
Camp Penguin
Hatsuhana Restaurant
Ocean Crystal Chapel
DIAMOND HEAD TOWER
RAINBOW BAZAAR
Concierge Desk
Hanajuban Noodle Shop
ATM
VILLAGE GREEN
ALI'I TOWER PLAZA
CJ's New York Style Delicatessen
Activities Desk
Sergio's Italian Restaurant
(2nd Floor)
Front Desk
Starbucks
Concierge Desk
Kahanamoku Street
Round Table Pizza
Lappert's Ice Cream & Coffee
Lagoon Drive
Manager on Duty
Valet and Taxi
MAIN LOBBY
ALI'I TOWER
LAGOON TOWER
Concierge Desk
GREAT LAWN
Concierge Desk
Pronto Pickle
Tropics Bar & Grill
SUPER POOL
Port Waikiki Cruises
PARADISE POOL
Pool Stand
Pool Stand Atlantis Adventures
Concierge Desk
Beach Stand
Hau Tree Bar
Rainbow Lanai
Pool/Beach Stand
Paradise Lounge
Bali Steak & Seafood
RAINBOW TOWER
Onolicious Dog Beachside
DUKE KAHANAMOKU LAGOON
Port Hilton

# TAPA CONFERENCE CENTER




# MID PACIFIC CONFERENCE CENTER



**Agenda Matrix, Sunday, July 8**

| | |
|---|---|
| 1500 - 1800 | Early Registration |
| | |
| | |
| | |
| 1900 - 2100 | SOC, Session Chairs, Invited Guests Reception |

**Detailed Agenda, Sunday, July 8**

**1500 – 1800 Early Registration – Palace Lounge**

**1900 – 2100 Scientific Organizing Committee / Session Chairs / Invited Guests Reception (by invitation only) – Waialae Country Club – Transporation Provided**

**Agenda Matrix, Monday, July 9**

| | | | |
|---|---|---|---|
| 0700 - 0800 | Continental Breakfast | | |
| 0800 - 0815 | Welcomes/Announcements/Organizer's Remarks | | |
| 0815 - 0845 | Hawai'ian Blessing; Proclamations by the Governor of Hawaii and Mayor of Honolulu | | |
| 0845 - 0855 | Opening Address, President of IST (Gopal) | | |
| 0855- 0900 | Plenary #1 Set up | | |
| 0900 –1100 | Plenary 1: Biological Toxins as Bioterrorism Agents | | |
| 1100 – 1130 | Group Photo and Refreshment Break | Group Photo and Refreshment Break | Group Photo and Refreshment Break |
| 1130 – 1250 | Concurrent session #1: Toxin Proteomics & Genomics | Concurrent session #2: Envenomations | Concurrent session #3: Marine Toxins |
| 1250 - 1420 | Lunch on your own | | |
| 1420 - 1540 | Concurrent session #4: Evolution of Glands/Toxins | Concurrent session #5: Snakebite as a Tropical Disease | Concurrent session #6: Venom Activities |
| 1540 - 1600 | Refreshment Break | Refreshment Break | Refreshment Break |
| 1600 - 1720 | Concurrent session #7: Insecta, Metazoans, Scorpions | Concurrent session #8: Snakebites | Concurrent session #9: Snakebite:Ion Channels, Receptors, Peptides |
| 1720 | Day Ends | Day Ends | Day Ends |
| 1900 - on | Opening Reception | | |

**Detailed Agenda, Monday, July 9** **Location**

**0700 – 0800** **Continental Breakfast** **Palace Lounge**

**0800 – 0815** **Opening Session** **Tapa 1-2**
**Chairs: Carl-Wilhelm Vogel (USA); Steven A. Seifert (USA)**
**Welcomes; General announcements; Remarks by conference organizers**

**0815 – 0845** **Hawaiian Blessing: Dr. Kalani Brady** **Tapa 1-2**
**Proclamations**
**The Honorable Neil Abercrombie, Governor of Hawaii**
**The Honorable Peter Carlisle, Mayor of Honolulu**

**0845 – 0855** **Opening Address, President of IST** **Tapa 1-2**
**P.Gopalakrishnakone**

**0855 – 0900** **Plenary #1 set up** **Tapa 1-2**

**0900 –1100** **Plenary # 1: Biological Toxins as Bioterrorism Agents**
**Chair: P.Gopalakrishnakone (Singapore); Barbara Price (USA)**
**Abstracts:**
**7. Biological Weapons and Toxins: A Short History and Look at the Future.** Barbara B. Price
**5. Bioterrorism and Biological Toxins.** Cesare Montecucco
**8. Biotoxins and Bioterrorism: Ricin and Saxitoxin.** Peter G. Blain
**6. The Diverse Roles of Botulinum Toxins.** Jeffrey Brent
**1. Detection Technologies for Biological Toxins.** P. Gopalakrishnakone
**2. Medical Aspects of Bioterrorism.** Mahdi Balali-Mood

**1100 – 1130** **Group Photo and Refreshment Break** **Palace Lounge**

**1130 – 1250** **Concurrent Session #1: Toxin Proteomics & Genomics** **Tapa 1**
**Chairs: Juan Calvete (Spain); Reto Stöcklin (Switzerland)**

**231. Second Generation Antivenomics: Comparing Immunoaffinity and Immunodepletion Protocols.** Davinia Pla, José M. Gutiérrez, Juan J. Calvete
**307. Comparative Snake Venom-Gland Transcriptomics Based on Illumina Sequencing.** Darin Rokyta
**59. Understanding the Chemical Diversity of Spider Venoms Using a Combined Genomic, Transcriptomic and Proteomic Approach.** Sandy S. Pineda, Alun Jones, Graham M. Nicholson, Pierre Escoubas, John S. Mattick, and Glenn F. King
**57. Structural Characteristics and Evolution of A Novel Venom Phospholipase A2 Gene from *Protobothrops flavoviridis*.** Takahito Chijiwa, Naoki Ikeda, Haruna Masuda, Hiroaki Hara, Naoko Oda-Ueda, Shosaku Hattori, Motonori Ohno

**1130 – 1250** **Concurrent Session #2: Envenomations** **Tapa 2**
**Chairs: Richard C. Dart (USA); David Warrell (UK)**

**256. A Rapid Reconstitution Method for CroFab® Polyvalent Immune Fab (ovine).** David Gerring, Richard Branton, Terry Prime, Thomas R. King, Emmanuel M. Mahlis

**250. Critical Shortage of Coral Snake Antivenom is Impacting Patient Care.** Cynthia R. Lewis-Younger, Jeffrey N. Bernstein, Jay Schauben

**252. Coral Snake Antivenin's Deadly Deadline.** Robert Mannel, Olga A. Pudovka Gross, Gus A. Gross

**312. Epidemiology of Snakebites Reported to Poison Centers in Texas from 2002 through 2011.** Miguel C. Fernández

**234. Severity of Snakebites in Children in the United States: 2000-2009.** Scott A. Letbetter, Sharla A. Letbetter, David L. Morgan

**1130 – 1250** **Concurrent Session #3: Marine Toxins** **Tapa 3**

**Chairs: Dietrich Mebs (Germany); Dusan Suput (Slovenia)**

**105. Discovery, Characterization, and Functional Implications of Conotoxins from Cone Snails Species of the Americas.** Aldo Franco, Mari Heighinian, Monica Mejia, Jessica McCall, Shiva Nag, Kalyana Akondi, Christian Melaun, Norelle Daly, Charles W. Luetje, Paul F. Alewood, David J. Craik, Tanja Godenschwege, David J. Adams and Frank Marí

**106. Molecular Diversity of Box Jellyfish Toxins.** Diane L. Brinkman, Jason Mulvenna, Nicki Konstantakopoulos, Wayne C. Hodgson, Geoffrey K. Isbister, Jamie E. Seymour, James N. Burnell

**107. The Chemical Landscape of Cnidarians as Viewed Through the Lens of Pore-Forming Proteins.** Tamar Rachamim, Hen Kestenboim, Amir Zlotkin, Eliahu Zlotkin and Daniel Sher

**330. Discovery of a Scorpaeniform Toxin Gene in *Cephalopholis argus*.** Christie Wilcox

**1250 – 1420** **Lunch on your own**

**1420 – 1540** **Concurrent Session #4: Evolution of Glands/Toxins** **Tapa 1**

**Chairs: Bryan Fry (Australia), Juan Calvete (Spain)**

**64. Centipede Venoms: Old and Unusual.** Eivind A. B. Undheim, Alun Jones, John W. Holland, Rodrigo A.V. Morales, Brit Winnen, Bryan G. Fry, Glenn F. King

**53. Evolutionary Expansion of Venom Genes in the King Cobra Genome.** Freek J. Vonk, Christiaan V. Henkel, R. Manjunatha Kini, Harald M. IJ. Kerkkamp, Herman P. Spaink, Hans J. Jansen, S. Asad Hyder, Pim Arntzen, Guido E.E.J.M. van den Thillart, Marten Boetzer, Walter Pirovano, Ron P.H. Dirks, Michael K. Richardson

**58. Functional Redundancy in Venoms is an Evolutionary By-Product.** David Morgenstern, Ricardo C. Rodriguez de la Vega, Michael Ott, Glenn F. King, Bryan G. Fry

**56. The Evolutionary Origins of Monotreme Crural Glands.** Emily Wong, Camilla Whittington, Tony Papenfuss, Stewart Nicol, Wesley C. Warren, Katherine Belov

**62. Tentacles of Venom: Molecular Evolution of Coleoid Venoms.** Bryan G. Fry, Tim Ruder, Dessi N. Georgieva, David Morgenstern, Glenn King, Eivind A. B. Undheim

**1420 – 1540** **Concurrent Session #5: Snakebite as a Tropical Disease: Strategies for Improved Outcomes** **Tapa 2**
**Chairs: Denise Tambourgi (Brazil); Jorge Kalil (Brazil)**

**313. Estimating the global burden of snakebite can help to improve management.** Jean-Phillippe Chippaux

**317. The Global Snakebite Initiative: aims, objectives and an emerging plan of action.** David A. Warrell , David J. Williams, Nicholas I. Brown, Simon D Jensen, José-María Gutiérrez, Juan J. Calvete, Robert A. Harrison

**87. Antivenom Production by Instituto Butantan: 110 Years of Experience.** Jorge Kalil

**248. Venomous Mixtures, Gamma Irradiation and Antivipmyn Africa®.** Guillermo de la Rosa, Carlos Olvera, Andrés Alagón, Epifanio Cruz, Alejandro Alagón

**1420 – 1540** **Concurrent Session #6: Venom Activities** **Tapa 3**
**Chairs: Jay Fox (USA); Daniel Gillet (France)**

**124. Biogeography of Microcystins.** Cristiana Moreira, Vitor Vasconcelos, Agostinho Antunes

**128. Human iPS Neuronal Platform for Botulinum Neurotoxins.** Eric A Johnson, Sabine Pellett, Regina Whitemarsh, William H Tepp

**145. *In vitro* Vascular Activity of Crude *Bungarus candidus* and *Bungarus fasciatus* Crude Venoms.** Muhamad Rusdi Ahmad Rusmili, Iekhsan Othman, Mohd Rais Mustafa and Wayne Hodgson

**158. EqT II Causes Endothelial Cell Damage and Intracellular Ca2+ Riske in ECV-304.** Mitja Maružin, Miha Šušteršič, Jernej Sitar, Primož Humar, Miha Bartolič, Dušan Šuput

**1540 – 1600** **Refreshment Break** **Palace Lounge**

**1600 – 1720** **Concurrent Session #7: Insects, Metazoans, and Scorpions** **Tapa 1**
**Chairs: Ashis Mukherjee (India); Iekhsan Othman (Malaysia)**

**95. Biological and Immunochemical Characterization of *Premolis semirufa* Caterpillar-Bristles Toxic Components.** Isadora M. Villas-Boas, Rute M. Gonçalves-de-Andrade, Giselle Pidde-Queiroz, Suely L. M. R. Assaf, Fernanda C. V. Portaro, Osvaldo A. Sant'Anna, Carmen W. van den Berg, Denise V. Tambourgi

**61. A Phylogenetic Framework for the Study of Convergence and Divergence in Scorpion Venoms.** Ricardo C. Rodríguez de la Vega, Nicolas Vidal

**150. Tailoring the Selectivity of Anuroctoxin for Kv1.3 K+ Channels.** Ádám Bartók, Zoltán Varga, György Panyi

**65. The Phylogenetic Scale of Venom Variation in Haplogyne Spiders.** Greta J. Binford, Miles Dale, Andrew Wood, Jared Delahaye, Ian Voorhees, Jennifer Mullins, Pamela A. Zobel-Thropp

**91. Proteomic analyses of the Venom from the Giant Ant *Dinoponera quadriceps*: A Comparative Study and Characterization of the Major Components of the Venom Derived from 4 Different Areas of Brazil.** Camila T. Cologna, Jaqueline Cardoso, Michel Degueldre, Ana P. T. Uetanabaro, Eraldo M. C. Neto, Edwin de Pauw, Loic Quinton

**1600 – 1720** **Concurrent Session #8: Snakebites** **Tapa 2**
**Chairs: Allen Harvey (UK); Cynthia Lewis-Younger (USA)**

**329. Hump Nosed Viper Bite in Sri Lanka—A Lesson of its Clinical Features and Management Based on a Prospective Cross Sectional Study of 1583 Cases.** Kolitha Harischandra Sellahewa.

**314. Epidemiology and Severity of Snakebite in Guinea.** Mamadou C. Baldé, Jean-Philippe Chippaux, Mamadou Y. Boiro, Jean-François Trape, Roberto P. Stock, Achille Massougbodji

**232. Death Adder Envenoming Causes Neurotoxicity not Reversed by Antivenom – Australian Snakebite Project (ASP-16).** Christopher I. Johnston, Margaret A. O'Leary, Simon G.A. Brown, Bart J. Currie, Geoffrey K. Isbister for the ASP investigators

**149. The Role of the Lymphatic System in the Absorption of *Micrurus fulvius* Venom.** Dayanira Paniagua, Lucía Jiménez, Camilo Romero, Irene Vergara, Arlene Calderón, Melisa Benard, Michael Bernas, Carlos Sevcik, Marlys Witte, Leslie Boyer, Alejandro Alagón

**1600 – 1720** **Concurrent Session #9: Ion Channels, Receptors and Peptides** **Tapa 3**
**Chairs: Toru Tamiya (Japan); William Kem (USA)**

**102. Convergent Evolution of Sodium ion Selectivity in Metazoan Neuronal Signaling.** Maya Gur Barzilai, Adam M. Reitzel, Johanna E.M. Kraus, Dalia Gordon, Ulrich Technau, Michael Gurevitz, Yehu Moran

**315. Peptidome analysis of Viperinae and Crotalinae snake venoms demonstrates subfamily-specificity of the venom peptides in the family Viperidae.** Dessislava Georgieva, Aisha Munawar, Maria Trusch, Hartmut Schlüter,Nikolay Genov, Patrick Spencer, Raghuvir K. Arni, Christian Betzel

**262. Spider Venom Components Affecting the Function of Purinergic Receptors.** Eugene Grishin

**298. Identification and Phylogenetic Analysis of *Tityus pachyurus* and *Tityus obscurus* Novel Putative Na+-Channel Scorpion Toxins.** Jimmy A. Guerrero-Vargas, Caroline B. F. Mourão, Verónica Quintero-Hernández, Lourival D. Possani, Elisabeth F. Schwartz

**1900** **Opening Reception** **Lagoon Green**

**Agenda Matrix, Tuesday, July 10**

| | | | |
|---|---|---|---|
| 0700 - 0800 | Continental Breakfast | | |
| 0700 - 0800 | Poster Session #1 Setup | | |
| 0800 - 0810 | Welcomes/ Announcements | | |
| 0810 - 0930 | Plenary #2: Toxins as leads for drug development | | |
| 0930 - 0950 | Refreshment Break | Refreshment Break | |
| 0950 - 1110 | Concurrent session #10: Toxins and Ion Channel | Concurrent session #11: Systems; Training; Preparedness; Response | Concurrent session #12: Venom Components |
| 1110 - 1125 | Travel Break | Travel Break | Travel Break |
| 1125 - 1245 | Concurrent session #13: Anti-cancer drugs leads | Concurrent session #14: Scorpion venom/envenomation | Concurrent session #15: Mechanisms of Action |
| 1245 - 1400 | Lunch provided | Organizational meeting of the North American Society of Toxinology and Venom Week 5 Planning Session; w/ boxed lunch | |
| 1400 - 1500 | Pleanry #3: Translational Science | | |
| 1500 - 1520 | Refreshment Break | Refreshment Break | Refreshment Break |
| 1520- 1640 | Concurrent session #16: Toxins & Hemostasis | Concurrent session #17: Veterinary envenomations | Concurrent session #18: Spider toxins |
| 1640 - 1800 | Poster Session #1: Posters 1 - 177; Authors with Posters | | |
| 1800 | Day Ends | Day Ends | |
| 1800 - 1830 | Poster Session #1 Take-down | | |
| 1900 - 2200 | Toxicon Dinner (By Invitation) | | |

**Detailed Agenda, Tuesday, July 10** **Location**

**0700 – 0800** **Continental Breakfast** **Palace Lounge**

**0700 – 0800** **Poster Session #1 Set up (Abstracts #1 – 177)** **Tapa 3**

**0800 – 0810** **Welcomes and General Announcements** **Tapa 1-2**

**0810 – 0930** **Plenary # 2: Toxins as Leads for Drug Development** **Tapa 1-2**
**Chairs: Glenn King (Australia); Reto Stöcklin (Switzerland)**

**48. Use of Connectivity Maps and Platform Technologies for Drug Lead/Biosimilar Discovery in Venoms.** Jay W. Fox, Aramadhaka Lavakumar Reddy, Alyson Prorock, Bojan Dragulev, Yongde Bao[1]

**38. Development of the Sea Anemone Toxin ShK-186 for the Treatment of Autoimmune Diseases: PK and ADME Perspectives.** Christine Beeton, K. George Chandy, Shawn P. Iadonato, Ernesto Munoz-Elias, Eric J. Tarcha

**39. Discovery and Development of χ-Conopeptides for the Treatment of Pain.** Richard J. Lewis

**34. Miniaturization of μ-Conotoxins as Peptidomimetic Strategy to Develop Selective Sodium Channel Blockers.** Marijke Stevens, Steve Peigneur, Natalia Dyubankova, Eveline Lescrinier, Piet Herdewijn, Jan Tytgat

**35. Development of Guanidinium-Toxin-Based Sodium Channel Blockers as PET Imaging Agents and Therapeutics for Diagnosing and Treating Pain.** John Mulcahy, Justin Du Bois, David Yeomans, Sandip Biswal, Matthew Axtman, George Miljanich

**0930 – 0950** **Refreshment Break** **Palace Lounge**

**0950 – 1110** **Concurrent Session #10: Toxins & Ion Channels** **Tapa 1-2**
**Chairs: Lourival Possani (Mexico); Christene Beeton (USA)**

**37. A Sea Anemone Toxin to Treat Autoimmune Diseases: ShK and its Analogs.** Christine Beeton

**110. Voltage Sensor Trapping in Voltage-Gated K-Channels by the Marine Neurotoxin Gambierol.** Ivan Kopljar, Alain J. Labro, Jon D. Rainier, Jan Tytgat, Dirk J. Snyders

**303. Calcins as High-Affinity Probes of Calcium Release Channels/Ryanodine Receptors.** Héctor H. Valdivia, Georgina B. Gurrola, Fernando Z. Zamudio, Michelle E. Capes, Lourival D. Possani

**28. Sea Anemone Peptides Modulate TRPV1 Activity and Produce Analgesia Without Hyperthermic Effect.** Yaroslav A.Andreev , Irina V. Mosharova, Sergey A. Kozlov , Yulia V. Korolkova, Eugene V. Grishin

**0950 – 1110** **Concurrent Session #11: Systems: Training; Preparedness; Response** **Coral 1**
**Chairs: Julian White (Australia); Vitor Vasconcelos (Portugal)**

**343. The Short Course in Toxinology: Training the trainers.** Julian White

**276. Circus Venomous: An Interactive Tool for Toxinology Education.** Rais Vohra, Susanne Spano

**277. Prehospital Management of Envenomations in the State of Queensland, Australia.** John L. Rathbone, Jamie Quinn

**27. Development of a Virtual System to Support Clinical Toxinology Research.** Ana Silvia SSBS Ferreira; Benedito Barraviera, Silvia RCS Barraviera; Luciana PF Abbade; Rui Seabra Ferreira Jr, Carlos A Caramori

**279. Travel Toxinology; An Illustrative Case of Brown Spotted Pit Viper (*Protobothrops mucrosquamatus*) Bite With Review of Clinical Toxinology Issues in Travel Medicine.** Julian White, Bart Currie

**0950 – 1110** **Concurrent Session #12: Venom Components** **Coral 2**

**Chairs: Tom Turk (Slovenia); Bry Loyst (Canada)**

**160. Role of SVMPs, Matrikines and TLR4 in Snake Venom Induced Edema and Inflammation.** Jay W. Fox, Alexandra Rucavado, Teresa Escalante, Junho Kim, José M. Gutiérrez

**189. Neutralization Effect of Glycation on Myotoxic and Nephrotoxic Effects Induced by BthTX-I.** Veronica C. G. Soares, Camila L. Pires, Daniel Bristot, Henrique H. Gaeta, Daniela O. Toyama, Simone C. O.Buzzo, Selma D. Rodrigues, Marcos H. Toyama

**19. Purification and Determination of Antibacterial Constituent, L-Amino Acid Oxidase from *Calloselasma rhodostoma* and *Ophiophagus Hannah*.** Sugita Kunalan, Jaya Vejayan, Parasakthi Navaratnam, Wayne Hodgson

**29. Russelobin, a Non-toxic Thrombin-like Serine Protease from the Venom of Russell's Viper (*Daboia russelli russelli*): Possible Applications in Cardiovascular Drug Development.** Ashis K. Mukherjee, Stephen P. Mackessy

**1110 – 1125** **Travel Break**

**1125 – 1245** **Concurrent Session #13: Anti-Cancer Drug Leads from Toxins** **Tapa 1-2**

**Chairs: Carl-Wilhelm Vogel (USA); P. Gopalakrishnakone (Singapore)**

**23. Transformation of the Naturally Occurring Frog Skin Peptide, Alyteserin-2a into a Potent Anti-cancer Agent.** J. Michael Conlon, Milena Mechkarska, Kholoud Arafat, Samir Attoub

**18. Comparative Toxicity of Binase towards Tumor and Normal Cells.** Hector A. Cabrera-Fuentes, Pavel V. Zelenikhin, Aleksei I. Kolpakov, Klaus T. Preissner, Olga N. Ilinskaya

**152. Effect of Crotoxin on Secretory Activity of Peritoneal Macrophages Co-cultivated with Tumor Cells. Involvement of Formyl Peptide Receptors.** Yara Cury, Edilene S. Costa, Odair J. Faiad, Rui Curi, Sandra C. Sampaio

**139. Comparison of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Type 1 Receptor Blockade for the Prevention of Premalignant Changes in the Liver.** Mahmoud A. Mansour, Hani Al-Ismaeel, Ammar C. Al-Rikabi, Othman A. Al-Shabanah

**22. Engineering of an HB-EGF Inhibitor from the Diphtheria Toxin Receptor–Binding Domain for the Treatment of HB-EGF-Related Diseases.** Benoit Villiers, Sylvain Pichard, Alain Sanson, Stephanie Delluc, Bernard Maillere, Pierre-Louis Tharaux, Daniel Gillet

**1125 – 1245** **Concurrent Session #14: Scorpion Venom/Envenomations** **Coral 1**
**Chairs: Leslie V. Boyer (USA); Lourival Possani (Mexico)**

**175. Scorpion Toxins that Cause Human Intoxication.** Lourival D. Possani

**184. Development of Novel Scorpion Anti-Venoms in México.** Baltazar Becerril, Lidia Riaño and Lourival D. Possani

**183. Development of Immune Sera Against Algerian Scorpion Venoms: Which Antibodies for Envenoming Treatment in Regions At-Risk?** Amina Ladjel-Mendil, Sonia Adi-Bessalem, Djelila Hammoudi-Triki,Fatima Laraba-Djebari

**185. Safety of Equine F(ab')2 Antivenom for Scorpion Envenomation: Results of Prospective Clinical Trials.** Leslie V. Boyer, Michelle Ruha, Jan Degan, Jody Mallie, Alejandro Alagón

**1125– 1245** **Concurrent Session #15: Mechanisms of Action** **Coral 2**
**Chairs: Marcelo Diniz (Brazil); Nabih Baeshen (Saudi Arabia)**

**52. Divergence in the Biological Activity and Composition of Venom from Mackay (QLD) and Barossa/Adelaide (SA) Populations of Australian *Pseudonaja textilis* (Serpentes: Elapidae): An Important Role of Procoagulants in Rodent Prey Incapacitation.** Jure Skejić, Wayne C. Hodgson

**60. Glycan Structures and Intrageneric Variations of Acidic Phospholipases A2 from Tropidolaemus Venom.** Inn-Ho Tsai , Hui-Ching Chang, Jin-Mei Chen, An-Chun Cheng, Kay-Hooi Khoo

**63. Discovery of the Nicotinic Receptor Toxin Anabaseine in a *Polystyliferan Nemertine*.** William R. Kem, Juan Junoy

**67. Comparative Analysis of Transcriptomes of *Phoneutria pertyi* and *P. nigriventer* Venom Glands.** Marcelo R. V. Diniz, Camilla R. L. Machado, Ana Luiza B. Paiva

**141. Lipid Bilayer Condition Abnormalities Following *Macrovipera lebetina obtusa* and *Montivipera raddei* Snakes Envenomation.** Naira M. Ayvazian, Narine A. Ghazaryan, Lusine Ghulikyan

**1245 – 1400** **Lunch provided** **Palace Lounge and Coral Pre-function**

**1245 – 1400** **Organizational Meeting, North American Society of Toxinology and Venom Week 5 Planning Session w/ Boxed Lunch** **Coral 1**

**1400 – 1500** **Plenary #4: Translational Science** **Tapa 1-2**
**Chairs: David Craik (Australia); Keith Boesen (USA)**

**228. Venom Variability and Envenoming Severity Outcomes of the *Crotalus scutulatus scutulatus* (Mojave Rattlesnake) from Southern Arizona.** Daniel J. Massey, Juan J. Calvete, Elda E. Sanchez, Libia Sanz, Kelvin Richards, Ryan Curtis, Keith Boesen

**15. New Perspective for Therapy Against Seizures Using Molecules From *Rhinella schneideri* Toad Poison.** Mateus Amaral Baldo, José Luiz Liberato, Lívea Dornela Godoy, Wagner Ferreira dos Santos, Eliane Candiani Arantes

**203. Cellular and Humoral Immune Responses in Horses Immunized with Crotalus Venom.** Thaís R. Narcizo, Juliana J. Yamamoto, Mônica F. Silva, Ronaldo A. Ferreira, Sandra L. Moraes, Orlando G. Ribeiro, Olga M. Ibañez, José R. Marcelino, Mônica Spadafora-Ferreira

**1500 – 1520** **Refreshment Break** **Palace Lounge**

**1520 – 1640** **Concurrent Session #16: Toxins and Hemostasis** **Tapa 1-2**
**Chair: Manjunatha Kini (Singapore); Marc Edery (France)**

**74. Plant Latex Proteases: An Insight into their Procoagulant Activity.** Shivaprasad HV, Yariswamy. M, Rajesh R, Vishwanath BS.

**72. A Novel Family of Factor Xa Inhibitors from the Salivary Gland of Sandfly Vector of Leishmaniasis, *Lutzomyia longipalpis.*** Nicholas Collin, Teresa Assumpcao, Daniella Mizzurini, Robson Monteiro, Jesus Valenzuela, Ivo Francischetti

**73. Novel Anticoagulants from Snake Venom.** V. M. Girish, R. Manjunatha Kini

**81. BaPLA2-IV, a New Type Thrombin Inhibitor, Non Cytotoxic Phospholipase A2 From *Bothrops atrox* Venom.** Adelia C. O. Cintra, Cássio P. da Silva, Marco A. Sartim, Norival Alves Santos Filho, Luiz F. F.Tucci, João J. Franco, Suely V. Sampaio

**1520 – 1640** **Concurrent Session #17: Veterinary Envenomations** **Coral 1**
**Chair: Karen Seibold (USA); Craig Woods (USA)**

**297. A Retrospective Review of Coral Snake Envenomation in the Dog and Cat: 20 Cases, 1996 to 2011.** Mayrim L. Pérez, Karlie J. Fox, Michael Schaer

**294. A Randomized Multicenter Trial of Crotalidae Polyvalent Immune Fab Antivenom for the Treatment of Rattlesnake Envenomation in Dogs.** Michael E. Peterson, Michael Matz, Karen E. Seibold, Signe Plunkett, Scott Johnson, Kevin Fitzgerald

**296. Crotalidae Venom Levels in Dogs Before and After Administration of F(ab')2 Antivenom.** Craig W. Woods, Karen E. Seibold, Raegan I. Wells

**240. Development of a Double Sandwich Flourescent ELISA to Detect Rattlesnake Venom In Biological Samples from Horses with a Clinical Diagnosis of Rattlesnake Bite.** Lyndi L. Gilliam, Amy Giulioli Canida, Dianne McFarlane, Todd C. Holbrook, Mark Payton, Charlotte L. Ownby

**1520 – 1640** **Concurrent Session #18: Spider Toxins** **Coral 2**
**Chairs: Maria Elena de Lima (Brazil); Songping Liang (China)**

**263. Molecular Cloning and Characterization of a Sphingomyelinase D from *Loxosceles adelaida*, a Brazilian Brown Spider from Karstic Areas.** Giselle Pidde-Queiroz, Rute M. Gonçalves-de-Andrade, Cinthya K. Okamoto, Tiago J. Sobreira, Paulo S.L. de Oliveira, Mário T. Murakami, Carmen van den Berg, Denise V. Tambourgi.

**264. Milking and Partial Characterization of *Pamphobeteus spp* (Aranae; Theraphosidae) Venom, from the Colombian Andean Region.** Sebastian Estrada Gomez, Leidy Vargas Munoz, Alejandro Ramirez, Juan Quintana Castillo

**265. Poke but Don't Pinch: Risk Assessment and Defensive Behaviors of the Western Widow Spider (*Latrodectus hesperus*).** David R. Nelsen, Allen M. Cooper, Gerad A. Fox, Wayne Kelln, William K. Hayes

**267. A Survey of Venom from the Spitting Spider *Scytodes* includes Novel Toxins.** Pamela A. Zobel-Thropp; Sandra Correa; Jessica Garb; Greta Binford

**268. Biological activities of PnTx2-6, an exciting toxin from spider *Phoneutria nigriventer*.** Maria Elena de Lima, Carolina N. Silva, Juliana S. Cassoli, Fernanda S. Torres, Marcelo R. Diniz, Márcia H. Borges, Marta N. Cordeiro, Adriano M. C. Pimenta, Kênia N. Pedrosa, Steve Peigneur, Jan Tytgat, Paulo S.L. Beirão

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| **1640 – 1800** | **Poster Session #1: Abstracts #1 – 177**<br>**Session Chairs: Catherine Wood (USA); Dorrie Murray (USA)**<br>**Authors with Posters** | **Tapa 3** |
| **1800 – 1830** | **Poster Session #1 Take-down** | **Tapa 3** |
| **1900** | **Toxicon Editorial Board Dinner (by invitation only)** | |

**Agenda Matrix, Wednesday, July 11**

| | | | |
|---|---|---|---|
| 0700 - 0745 | Continental Breakfast | | |
| 0745 - 0750 | Welcomes/Announcements | | |
| 0750 - 0850 | Plenary #4: Elsevier Lecture: Leslie V. Boyer, MD | | |
| 0850 - 0955 | Setup for Plenary #5 | | |
| 0855 - 0955 | Plenary #5: The History of Toxinology | | |
| 0955 -1010 | Refreshment Break | | |
| 1010 - 1130 | Concurrent Session #19: Microbial Toxins | Concurrent session #20: Clinical Aspects of Envenomation | Concurrent session #21: Toxin Mechanisms of Action |
| 1130 - 1140 | Travel Break | Travel Break | Travel Break |
| 1140 - 1300 | Concurrent Session #22: Spider Toxins & Envenomations | Concurrent session #23: Venoms and Anti-Venoms | Concurrent session #24: Venom Components: Structure and Function |
| 1300 - on | Afternoon / Evening On Own | | |
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**Detailed Agenda, Wednesday, July 11** **Location**

**0700 – 0745** **Continental Breakfast** **Palace Lounge**

**0745 – 0750** **Welcomes and General Announcements** **Tapa 1-2**

**0750 – 0850** **Plenary # 4: Elsevier Lecture** **Tapa 1-2**
**Chairs: Alan Harvey (UK); Elizabeth Perill (USA)**
**Presenter: Leslie V. Boyer**

**0850 – 0855** **Setup for Plenary #5** **Tapa 1-2**

**0855 – 0955** **Plenary #5: The History of Toxinology** **Tapa 1-2**
**Chairs: Carl Wilhelm Vogel (USA); Steven A. Seifert (USA)**

**306. Toxicon: A Short History of 50 Years of the Official Journal of the International Society on Toxinology.** Alan L. Harvey
**85. TOXIN REVIEWS: The First 30 Years.** W. Thomas Shier
**83. Clodomiro Picado, Róger Bolaños, and the Beginnings of Toxinological Research in Central America.** José María Gutiérrez
**88. Saul Wiener: From Kristallnacht to Toxinology and Fragile X.** Kenneth D. Winkel

**0955– 1010** **Refreshment Break** **Palace Lounge**

**1010 – 1130** **Concurrent session #19: Microbial Toxins** **Tapa 1-2**
**Chair: Cesare Montecucco (Italy); Mahdi Balali-Mood (Iran)**

**344. Cessare Montecucco: Introduction on Bacterial Toxins. (5 min)**
**316. Assembly and Function of the Botulinum Neurotoxin Progenitor Complex.** Shenyan Gu, Sophie Rumpel, Jie Zhou, Jasmin Strotmeier, Hans Bigalke, Kay Perry, Charles B. Shoemaker, Andreas Rummel, Rongsheng Jin
**4. Biohazards of Botulinum Neurotoxins.** Ornella Rossetto
**125. Cadherin Binding Is Not a Limiting Step for *Bacillus thuringiensis subs. israelensis* Cry4Ba Toxicity to *Aedes aegypti* Larvae.** Claudia Rodríguez-Almazán, Esmeralda Z. Reyes, Isabel Gómez, Amy M. Evans, Supaporn Likitvivatanavong, Alejandra Bravo, Sarjeet S. Gill, Mario Soberón
**126. Magnetic Resonance Imaging and Spectroscopy Study of Microcystin LR Hepatotoxicity.** Jerneja Strupi Šuput, Igor Serša, Dušan Šuput

**1010 – 1130** **Concurrent session #20: Clinical Aspects of Envenomation** **Coral 1**
**Chair: Jude McNally (USA); Yara Cury (Brazil)**

**101. Manipulation of Zoanthids in Home Marine Aquarium: Unexpected Cause of Intoxication Involving a Whole Family.** Marieke A. Dijkman, Irma de Vries

**239. Combined Neurotoxicity and Hematotoxicity with Clinically Significant Bleeding after Mohave Rattlesnake (*Crotalus scutulatus*) Envenoming in Southern California.** Sean P. Bush, Eric T. Teacher, Linda Daniel-Underwood, Sarah R. Pearl, Joshua Westeren, Tammy H. Phan, Ellen Reibling

**295. F(ab')2 Antivenom in Dogs Envenomated by Pit Vipers.** Karen E. Seibold, Craig W. Woods

**251. Acute Hypersensitivity Reaction Following Administration of Crotalidae Polyvalent Immune Fab Antivenom: A Case Report.** Gus A. Gross, Olga A. Pudovka Gross

**1010 – 1130** **Concurrent Session #21: Toxin Mechanisms of Action** **Coral 2**

**Chairs: Grazyna Faure (France); Avner Bdolah (Israel)**

**21. Anti-endotoxin Effects and Pharmacology of the Immune Selective Anti-Inflammatory Derivatives (ImSAIDs).** Craig W. Woods

**26. nAChR Antagonist as Chemotherapeutic Agents of Certain Lung Cancer Types Expressing Cholinergic System. A Case of Snake Three-Fingered Toxins and Alkylpyridinium Polymers from Marine Sponge.** Ana Zovko, Metka Filipič, Katja Kološa, Tamara Lah Turnšek, Tom Turk

**30. Antimicrobial Peptides from Arachnid Venoms and their Biological Activity in the Presence of Commercial Antibiotics.** Francia García, Elba Villegas, Gerardo Pavel Espino-Solis, Alexis Rodríguez, Jorge Paniagua-Solis, Lourival D. Possani, Gabriel Sandoval, Gerardo Corzo

**31. Spider-venom Peptides that Target the Human NaV1.7 channel: Potential Analgesics for the Treatment of Chronic Pain.** Julie Klint, Raveendra Anangi, Mehdi Mobli, Oliver Knapp, David J. Adams and Glenn F. King.

**32. Development of High Throughput Calcium Channel Assays to Accelerate the Discovery of Novel Toxins Targeting Human Cav2.2 Channels.** Silmara R. Sousa, Lotten Ragnarsson, Irina Vetter, Volker Herzig, Glenn F. King and Richard J. Lewis.

**1130 – 1140** **Travel Break**

**1140 – 1300** **Concurrent Session #22: Spider Toxins & Envenomations** **Tapa 1-2**

**Chairs: Greta Binford (USA); Eugene Grishin (Russia)**

**326. Evolutionary crossroad: one peptide - two modes of action.** Lucia Kuhn-Nentwig, Irina M. Fedorova, Benjamin P. Lüscher, Lukas S. Kopp, Christian Trachsel, Johann Schaller, Xuan Lan Vu, Thomas Seebeck, KathrinStreitberger, Wolfgang Nentwig, Erwin Sigel, and Lev G. Magazanik

**259. Molecular Basis for the Interaction of Tarantula Toxin Jingzhaotoxin-III (β-TRTX-Cj1α) with the Voltage Sensor of Kv2.1 Channel.** Huai Tao, Jinjun Chen, Yucheng Xiao, Zhonghua Liu, Songping Liang

**261. Expanding Structural and Functional Diversity of Spider Venom Compounds.** Alexander A. Vassilevski, Eugene V. Grishin

**269. Understanding the Chemical Diversity and Evolution of Spider Venoms using Comparative Transcriptomics.** Sandy S. Pineda, Emily S. Wong, Bryan G. Fry, Greta J. Binford, Glenn F. King

**1140 – 1300** **Concurrent Session #23: Venoms and Anti-Venoms** **Coral 1**
**Chairs: Jonas Perales (Brazil); Jun Chen (China)**

**55. Intraspecific Variation of Biological Activities in Venoms from Wild and Captive *Bothrops jararaca*.** Eduardo Saad, Luciana Curtolo de Barros, Natalia Perussi Biscola, Daniel Carvalho, Pimenta, Silvia Regina Sartori Barraviera Barraviera, Benedito Barraviera, Rui Seabra Ferreira Jr.

**229. Geographic Variation of Venom Proteins and Neurotoxicity in the Southern Pacific Rattlesnake (*Crotalus oreganus helleri*).** Eric Gren, Wayne C. Hodgson, Rachelle Kornhauser, Carl Person, Wayne Kelln, William K. Hayes

**186. Effects of Captivity or Season on Venom Composition in Two Species of Rattlesnakes (*Crotalus atrox* and *C. v. viridis*).** Christopher J. Rex, Stephen P. Mackessy

**328. The Sri Lankan Antivenom Project.** Daniel E Keyler, Indika Gawarammana, José-María Gutiérrez, Kimberly McWhorter, Roy Malleappah

**1140 – 1300** **Concurrent Session #24: Venom Components: Structure and Function** **Coral 2**
**Chairs: Daniel Sher (Israel); Naira Ayvazyan (Armenia)**

**11. Effect of *Zingiber officinale* Plant Extract on the Differential Control of Growth, Apoptotic Activity and Gene Expression in Human Breast Cancer Cells.** Ayman I. Elkady, Osama A. Abuzinadah, Nabih A. Baeshen, Tarek R. Rahmy

**208. Fucose Moieties Are Essential for the Ability of Fucosylated Chondroitin Sulfate to Inhibit Muscle Damage Induced by *Bothrops jararacussu* Venom.** Marcos Monteiro-Machado, Marcelo A. Tomaz, Marcelo A. Strauch, Bruno L. Cons, Hilmar D. Ricardo, Vinícius V. Martins, Roberto J. Fonseca, Paulo A. S. Mourão, P. A. S., Paulo A. Melo

**209. Venom-Antivenin Binding and Neutralization of Venom Toxicity: Application of Size-Exclusion Chromatography to Assess Venom-Antivenin Binding.** Charles G. Sanny.

**213. Evaluation of Cabenegrin on the Enzymatic Activity and Structure of Basic sPLA2 of *Crotalus durissus terrificus* Venom.** Veronica C. G. Soares[1], Daniel Bristot[1], Camila L. Pires, Rafael M. Ximenes, Monteiro, H.S.A., Daniela de O. Toyama and Marcos H. Toyama

**218. Purification of a Metalloprotease from *Naja nigricollis* Venom and Production of Polyclonal Antibodies.** Andrew J. Nok, Binta G. Kurfi.

**1300** **Lunch, afternoon and evening free**

*Please take advantage of the many sights and activities that Waikiki, Honolulu, and the Island of Oahu have to offer, including Waikiki Beach with its many watersport activities, shopping in Waikiki or the Ala Moana Shopping Center, or taking a hike to the top of Diamond Head. The Hilton Hotel concierge will be able to help you with many more activities and tours.*

*In addition, both the Waikiki Aquarium and the Honolulu Zoo have generously offered to admit registered meeting attendants free of charge.*

**Agenda Matrix, Thursday, July 12**

| | | | |
|---|---|---|---|
| 0700 - 0750 | Continental Breakfast | | |
| 0700 - 0750 | Poster Session #2 Setup (Posters #178 + up) | | |
| 0750 - 0800 | Welcomes/Announcements | | |
| 0800 - 0920 | Plenary #6: Snakebites in Africa | | |
| 0920 - 0940 | Refreshment Break | Refreshment Break | |
| 0940 - 1100 | Concurrent Session #25: Scorpion Venoms | Concurrent Session #26: Controversies/Crotaline Envenomations | Concurrent session #27: Venom Components and Their Actions |
| 1100 - 1115 | Travel Break | Travel Break | Travel Break |
| 1115 - 1235 | Concurrent Session #28: Toxin-immune system | Concurrent session #29: Treatment of Envenomation | Concurrent session #30: Toxin Structure |
| 1235 - 1350 | Lunch on your own | International Society of Thrombosis and Haemostasis (ISTH) Meeting (open to all) | Lunch / Poison Center Directors w/ Gopal (Invitation only) |
| 1350 - 1510 | Plenary #7: Biomolecules/Uses in Health | | |
| 1510 - 1530 | Refreshment Break | Refreshment Break | Refreshment Break |
| 1530 - 1650 | Concurrent Session #31: Venom Metallopeoteinases | Concurrent Session #32: Envenomations/Developing World | Concurrent session #33: Venom Neurotoxicity |
| 1650 - 1810 | Poster Session #2: Abstracts #178 & higher: Authors with posters | | |
| 1810 - 1830 | Poster Session #2 – Take-down | | |
| 1900 | | | |
| | | | |

**Detailed Agenda, Thursday, July 12** **Location**

**0700 – 0750** **Continental Breakfast** **Palace Lounge**

**0700 – 0750** **Poster Session #2 set-up (Posters #178 – and higher)** **Tapa 3**

**0750 – 0800** **Welcomes and General Announcements** **Tapa 1-2**

**0800 – 0920** **Plenary # 6: Snakebites in Africa** **Tapa 1-2**
**Chairs: Jean-Philippe Chippaux (Benin); Abdul Habib (Nigeria)**

**238. Incidence and Management of Snakebite in Northern Central African Republic.** Séverine Gras, Gaëtan Plantefève, Jean-Philippe Chippaux

**311. Use of antivenoms for the treatment of envenomation by Elapidae in Guinea, Sub-Saharan Africa.** Mamadou C. Baldé, Jean-Philippe Chippaux, Mamadou Y. Boiro, Roberto P. Stock, Achille Massougbodji

**235. Antivenom Therapy Following Snakebite: Effectiveness and Strategies for Delivery in West Africa.** Abdulrazaq G. Habib

**236. Determinants of High Cost of Care Among Victims of Snake Bite in Kaltungo, Gombe State, Nigeria, 2009.** Mahmood M. Dalhat, Hamza Muhammad, Saidu B. Abubakar , Iliasu Garba, Ibrahim M.Yola, Abdulrazaq G. Habib

**0920 – 0940** **Refreshment Break** **Palace Lounge**

**0940 – 1100** **Concurrent Session #25: Basic Science of Scorpion Venoms** **Tapa 1**
**Chairs: Michael Gurevitz (Israel); Juri Siigur (Estonia)**

**172. Mapping the Receptor Sites of Scorpion Toxins at Voltage-gated Sodium Channels.** Michael Gurevitz

**178. Development of Nanobodies and Derivatives with High Neutralizing and Protective Capacity against Scorpion Envenoming.** Bouhaouala-Zahar Balkiss, Hmila Issam, Ben Abderrazek Rahma, Muyldermans Serge, El Ayeb Mohamed

**51. Evolution of a Neurotoxin from a Defensin.** Shunyi Zhu, Steve Peigneur, Bin Gao, Jan Tytgat

**176. Is the Endogenous Opioid System Involved in the Antalgic Effect of Scorpion Toxins in Mice?** Marie-France Martin-Eauclaire, Najwa Abbas, Pierre E. Bougis, Régis Guieu

**0940 – 1100** **Concurrent Session #26: Controversies in Crotalinae Envenomations** **Coral 1**
**Chairs: Dan Keyler (USA), Sean Bush (USA)**

**245. Pressure Bandaging with Immobilization in *Crotalinae* Envenomation Controversy.** Steven A. Seifert, Julian White, Bart J. Currie, Eric J. Lavonas

**243. Continuous Crotalidae Polyvalent Fab (Ovine) (FabAV) for Selected Snakebite Patients.** Sean P. Bush, Steven A. Seifert, Susan D. Smith, Tammy H. Phan, Sarah R. Pearl, Ellen E. Reibling

**69. Recurrent, Persistent, or Late, New-Onset Hematologic Abnormalities in Crotaline Snakebite.** Steven A. Seifert, Ronald I. Kirschner, Nancy Martin

**253. Medically Significant Late Bleeding Following Treated Crotaline Envenomation: A Structured Topic Review.** Lavonas EJ, Khatri V, Daugherty C

**0940 – 1100** **Concurrent Session #27: Venom Components and Their Actions** **Coral 2**
**Chairs: Richard Lewis (Australia); Brian Hew (USA)**

**25. Viability of Fibrin Sealant from Snake Venom as Scaffold to Rat Marrow-Derived Mesenchymal Stem Cells.** Vinicius Peron de Oliveira Gasparotto ; Fernanda da Cruz Landim e Alvarenga; Alexandre Leite Rodrigues de Oliveira; João Ferreira de Lima Neto; Midyan Daroz Guastali; Leandro Maia; Gustavo Ferreira Simões; Benedito Barraviera; Rui Seabra Ferreira Jr.

**71. Antiplatelet Activity and Mass Spectrometric Study of Venoms from Two Iranian Vipers, *Echis carinatus* and *Cerastes persicus fieldi*.** Toktam Mehdizadeh Kashani, Hossein Vatanpour, Hossein Zolfagharian, Hassan Hooshdar Tehrani , Farzad Kobarfard

**99. The Venom of *Conus geographus* Revisited.** Sébastien Dutertre, Ai-hua Jin, Paul F. Alewood and Richard J. Lewis

**299. Chemical and Biological Characterization of Ap1a: a New Toxin Isolated from the Venom of the Brazilian Spider, *Acanthoscurria paulensis* (*Theraphosidae*).** Caroline B. F. Mourão, Mari D. Heghinian, Eder A. Barbosa, Frank Marí, Carlos Bloch Jr, Rita Restano-Cassulini, Lourival D. Possani, Elisabeth F. Schwartz

**302. The Cystine Knot is a Conserved Structural Motif in Linear and Cyclic Plant Toxins.** David J Craik, Aaron G Poth, Michelle L Colgrave, Norelle L Daly

**1100 – 1115** **Travel Break**

**1115 – 1235** **Concurrent Session #28: Toxin-immune System Interactions** **Tapa 1-2**
**Chairs: Carl-Wilhelm Vogel (USA), Carmen van den Berg (UK)**

**266. C5a Receptor is Cleaved by Metalloproteases Induced by Sphingomyleinase D in *Loxosceles* Spider Venom.** Carmen W. van den Berg, Rute Maria Gonçalves-de-Andrade, Cinthya K. Okamoto, Denise V. Tambourgi

**89. Cobra Venom Factor, an Intriguing Venom Component: Over 100 Years of Research, and Counting.** Carl-Wilhelm Vogel

**210. Understanding the Preclinical Efficacy Profile of Antivenoms: From the Lethality Potency Assay to Antivenomics.** José María Gutiérrez, Bruno Lomonte, Guillermo León, Davinia Plá, Álvaro Segura, María Herrera, Mauren Villalta, Mariángela Vargas, Gabriela Solano, Libia Sanz, Julián Fernández, Yamileth Angulo, Juan J. Calvete

**216. Experimental, Immunochemical Reactivity and Neutralizing Capacity of *Rhinocerophis (Bothrops) alternatus* Antivenoms, from Distinct Geographical Sources.** Lanari, L.C. ; Olvera, A.; Costa de Oliveira, V; Laskowicz, R.D.; Regner, P.I. ; F. Olvera ; Stock, R.P.; Alagón, A.; de Roodt, A.R.

**217. IgY Antibodies Anti-*Crotalus durissus cumanensis* Venom: Purification and Neutralization Efficacy.** Montero P. Yuyibeth, Alvarez O. Aurora, Jimenez E. Eucarys, Zerpa Noraida, Malave Caridad

**1115 – 1235** **Concurrent Session #29: Treatment of Envenomation** **Coral 1**
**Chairs: Eric Lavonas (USA); Graham Nicholson (Australia)**

**54. Individual Venom Profiling of *Crotalus durissus terrificus* Specimens from a Geographically Limited Region: Crotamine Assessment and Captivity Evaluation on the Biological Activities.** Airton Lourenço Jr, Camila Fernanda Zorzella Creste, Luciana Curtolo de Barros, Lucilene Delazari dos Santos, Daniel C. Pimenta, Benedito Barraviera, Rui Seabra Ferreira Jr.

**211. Effect of Low Level Laser Therapy (LLLT) on *Bothrops jararacussu* Venom-Induced Myotoxicity in Muscle Cells.** Camila A. A. da Silva, Raquel A. Mesquita-Ferrari, José C. Cogo, Stella R. Zamuner

**147. Isolation and Pharmacological Characterisation of Neurotoxins from the Venom of Three Species of Australian Copperheads (*Austrelaps spp.*) and the Efficacy of Tiger Snake Antivenom to Prevent or Reverse Neurotoxicity.** Francesca Marcon, Mathieu Leblanc, Pierre Escoubas, Graham M. Nicholson

**212. Effect of Light Emitting Diode (LED) in the Inflammatory Response and Myonecrotic Effect Induced by *Bothrops asper* Snake Venom.** Katia M.B. Moura, Ana M. Barbosa, Carlos J. Lima, José M. Guttiérrez, Stella R. Zamuner

**241. Juvenile Rattlesnake Fang as a Retained Foreign Body: Clinical Diagnosis.** Joshua J. Ennis, Farshad Shirazi

**1115 – 1235** **Concurrent Session #30: Toxin Structure** **Coral 2**
**Chairs: Marie-France Martin-Eauclaire (France); John Michael Conlon (UAE)**

**17. Novel Marine Compounds in Studies of Nicotinic Acetylcholine Receptors.** Igor E. Kasheverov, Denis S. Kudryavtsev, Elena V. Kyukova, Tatyana **N.** Makarieva, Natalia K. Utkina, Valentin A. Stonik, Victor I. Tsetlin

**20. CFTR as a New Target for Crotoxin: Potential Application for Cystic Fibrosis.** Grazyna Faure, Naziha Bakouh, Frederick Saul, Haijin Xu, Gabrielle Planelles, Mario Ollero, Aleksander Edelman

**173. Characterisation of the Venom of an Australian Scorpion, *Urodacus yaschenkoi*: Proteome and Transcriptome Analysis.** Karen Luna Ramirez, Veronica Quintero Hernandez, Erika Meneses Romero, Ken Winkel, Cesar Ferreira Batista, Lourival D. Possani

**174. *In vitro* Folding of a Recombinant Beta-Scorpion Neurotoxin: The influence of N-Terminal Hydrophobic Regions.** Kenya Hernández-Salgado, Lourival D. Possani, Gerardo Corzo

**179. Automated Mass Fingerprinting of Venoms in the Nanogram Range.** Marie-France Martin-Eauclaire, Pierre E. Bougis

**1235 – 1350** **Lunch on your own**

**1235 – 1350** **International Society of Thrombosis and Haemostasis (ISTH) Meeting** **Coral 1**

**1235 – 1350** **Poison Center Directors w/ IST Leadership Meeting (Invitation only)** **Coral 2**

**1350 – 1510** **Plenary #7: Animal biomolecules: possibilities and approaches for allowing their uses in health and biotechnology** **Tapa 1-2**
**Chair: Yara Cury (Brazil); Ana Marisa Chudzinski-Tavassi (Brazil)**

**33. Mass Spectrometry as a Tool to Search Specific Ligands for G-Protein-Coupled Receptors.** Camila T. Cologna, Julien Echterbille, Edwin de Pauw, Loïc Quinton

**47. Rational Development of Novel Leads from Animal Secretion Based on Coagulation and Cell Targets.** Chudzinski-Tavassi, A.M.; Pasqualoto, K.F. M; Carrijo-Carvalho, L.C.

**144. Analgesic Effect of Crotalphine in a New Model of Rat Bone Cancer Pain.** Yara Cury, Vanessa P. Gutierrez, Patricia Brigatte, Vanessa O. Zambelli, Gisele Picolo, Juliana S. de Carvalho, Fabio Marques ; Pasqualoto, K.F. M

**24. Recombinant Hybrid Proteins from Cobra Venom Factor and Human C3: Promising Agents for Therapeutic Intervention in Complement-Mediated Diseases.** David C. Fritzinger, Brian E. Hew, Carl-Wilhelm Vogel

**86. From Medicine to Toxinology and Back to Medicine, and the Eternal Role of Snakes in Therapy.** Carl-Wilhelm Vogel (5 min)

**1510 – 1530** **Refreshment Break** **Palace Lounge**

**1530 – 1650** **Concurrent Session #31: Venom Metalloproteinases** **Tapa 1-2**
**Chairs: Jose Maria Gutierrez (Costa Rica); Nicholas Casewell (UK)**

**192. Action of Venom Metalloproteinases on Basement Membranes: Pathogenesis of Hemorrhage and Blistering in Snakebite Envenomings.** José María Gutiérrez, Teresa Escalante, Alexandra Rucavado, Jay W. Fox

**190. First Draft of the Genomic Organization of a PIII-SVMP Gene.** Libia Sanz, Robert A. Harrison, Juan J. Calvete

**187. Metalloproteinases from Rear-Fanged ("Colubrid") Snake Venoms: An Under-Utilized Resource for Evolutionary and Structure/Function Studies.** Stephen P. Mackessy

**49. The Origin and Evolution of Metalloproteinases in the Venom of Snakes.** Nicholas R. Casewell, Wolfgang Wüster, Simon C. Wagstaff, Camila Renjifo, Michael K. Richardson, Freek J. Vonk, Robert A. Harrison

**1530 – 1650** **Concurrent Session #32: Envenomations** **Coral 1**
**Chairs: Julian White (Australia); Marieke Dijkman (The Netherlands)**

**233. Hospital Based Retrospective Study of Snakebite Epidemiology in Western Development Region of Nepal.** Thapa CL, DevkotaK, Pandey DP

**247. Envenomation by *Daboia mauritanica* Snakes in Tiznit Province, Morocco: Report of Four Cases.** Chafiq Fouad, Chrouqui Nadia , El Jaoudi Rachid, Fekhaoui Mohamed, Soulaymani Abdelmajid, Rhalem Naima, Mokhtari Abdelghani, Soulaymani-Bencheikh Rachida

**246. Non-front-fanged Colubroids; a Current Analysis of Medical Significance.** Scott Weinstein, Julian White

**242. The Effect of Pre-hospital Care for Venomous Snakebite on Outcome in Nigeria.** Michael C. Godpower, Thacher D. Thomas, Shehu Mil

**1530 – 1650** **Concurrent Session #33: Venom Neurotoxicity** **Coral 2**
**Chairs: George Miljanich (USA); Peter G. Blain (UK)**

**94. Bee Venom and Pain.** Jun Chen
**143. Exploring 'Labyrinth' of Pain with Scorpion 'Sting'.** Liu Zhirui, Ji Yonghua
**188. The *In vitro* Neurotoxic Effects of the Newly Discovered Central Ranges Taipan (*Oxyuranus temporalis*).** Carmel M Barber, Peter Mirtschin, Nathan Dunstan, Terry Morley, Wayne C Hodgson
**36. Random Peptide Library Based on a Spider Neurotoxin, and Utilization of the Library in *in vitro* Evolution Directed to GPCR Ligands.** Tai Kubo, Seigo Ono, Tadashi Kimura, Suzuko Kobayashi, Tetsuro Kondo, Eriko Fukuda, Tatsuya Haga, Kimihiko Kameyama
**137. Neuropathies of Spinal Cord Development of Rat Pups Maternally Fed on Fried Potato Chips.** Gadallah A. Abdelalim, El-Sayyad I. Hassan, El-Shershaby M. Effat, Abdelatif M. Ibrahim.

**1650 – 1810** **Poster Session #2: Abstracts #178 – and higher** **Tapa 3**
**Session Chairs: Catherine Wood (USA); Dorrie Murray (USA)**
**Authors with Posters**

**1810 – 1830** **Poster Session #1 Take-down** **Tapa 3**

**1900** **Cocktail Reception** **Lagoon Green**

**1930** **Gala Dinner / Luau** **Lagoon Green**

**Agenda Matrix, Friday, July 13**

| | | | |
|---|---|---|---|
| 0700 - 0800 | Continental Breakfast | | |
| 0800 - 0810 | Welcomes/Announcements | | |
| 0810 - 0915 | Plenary #8: Redi Award (Recipient to be announced) | | |
| 0915 - 0930 | Refreshment Break | Refreshment Break | Refreshment Break |
| 0930 - 1050 | Concurrent session #34: Structure/Function of Venom | Concurrent session #35: Venomous Animal Biology | Concurrent session #36: Toxin Activity and Structure |
| 1050 - 1105 | Travel Break | Travel Break | Travel Break |
| 1105 - 1225 | Concurrent session #37: Toxins & Receptors | Concurrent session #38: Zoos and Collections | Concurrent session #39: Snake Venoms and Antivenoms |
| 1225 - 1340 | Lunch provided | Publishing in Toxicon w/ Alan Harvey w/ Boxed Lunch | |
| 1340 - 1350 | Awards: Best Posters; Best Young Investigator | | |
| 1350 - 1510 | Plenary #9: IST Business Mtg | | |
| 1510 - 1530 | Refreshment Break | Refreshment Break | Refreshment Break |
| 1530 - 1720 | Concurrent session #40: Marine Toxins | Concurrent session #41: Public Health Aspects of Envenomation | Concurrent session #42: Plant Toxins |
| 1720 - 1735 | Travel Break | Travel Break | Travel Break |
| 1735- 1800 | Closing Remarks | | |

**Detailed Agenda, Friday, July 13** **Location**

**0700 – 0800** **Continental Breakfast** **Palace Lounge**

**0800 – 0810** **Welcomes and General Announcements**

**0810 – 0915** **Plenary # 8: Redi Award** **Tapa 1-2**
**Chairs: P.Gopalakrishnakone (Singapore); Alan Harvey (UK); Julian White (Australia)**
**Recipient to be announced**

**0915 – 0930** **Refreshment Break** **Palace Lounge**

**0930 – 1050** **Concurrent Session #34: Structure/Function of Venom** **Tapa 1-2**
**Chair: Manjunatha Kini (Singapore), Bruno Lomonte (Costa Rica)**

**304. Snake venom metalloproteinases; Structure, function and relevance to the mammalian ADAM/ADAMTS family proteins.** Soichi Takeda

**146. An Insecticidal Spider Toxin that Acts as a Positive Allosteric Modulator of Insect Nicotinic Acetylcholine Receptors.** Monique J. Windley, Glenn F. King, Graham M. Nicholson

**196. Synthetic Peptides from Viperid Phospholipase A2 Myotoxins: Small Structures with Diverse Biomimetic Actions.** Bruno Lomonte

**148. Characterization of Inflamin from *Aipysurus eydouxii*: A Novel Class of Toxin that Induces Inflammation.** Bhaskar Barnwal, R. Manjunatha Kini

**0930 – 1050** **Concurrent Session #35: Venomous Animal Biology** **Coral 1**
**Chair: Stephen MacKessy (USA); Ben Okimoto (USA)**

**283. Relocator Proteins: Identification of the Chemical Component of Venoms Allowing Prey Recovery During Strike-induced Chemosensory Searching.** Anthony J. Saviola, Stephen P. Mackessy, David Chiszar, Chardell Busch

**292. How Do Komodo Dragons Kill Their Prey?: Lack of Role for Oral Flora in Predation.** Ellie JC Goldstein, Kerrin L. Tyrrell, Diane M. Citron, Cathleen R. Cox, Ian M. Recchio, Ben Okimoto, Judith Bryja, Bryan G. Fry

**280. Genetic Regulation of Venom Production during Embryonic Development of the Indochinese Spitting Cobra, *Naja siamensis*.** Jessica M. Logan, Peter J. Mirtschin, Anthony E. Woods

**281. The Desert Massasauga (*Sistrurus catenatus edwardsii*): Biology and Venom Biochemistry.** Stephen P. Mackessy

**0930 – 1050** **Concurrent Session #36: Toxin Activity and Structure** **Coral 2**
**Chairs: Inn-Ho Tsai (Taiwan); Ji Hyeong Baek (South Korea)**

**109. A Comparison of the Structural Characteristics of the Nematocysts of the "Fire Corals" *Millepora alcicornis* and *M. complanata*, and their Hemolytic and Vasoconstrictor Effects.** Alejandro García-Arredondo, Alejandra Rojas, César Ibarra-Alvarado, Roberto Iglesias-Prieto

**127. Urease of Helicobacter pylori: Roles in Inflammation and Platelet Activation.** Augusto F. Uberti, Deiber Olivera-Severo[1], Adriele Scopel-Guerra, Christina Barja-Fidalgo, Celia R. Carlini, Angela Piovesan

**191. Dexamethasone Antagonizes the Myotoxic and Inflammatory Effect of Bothrops Venoms.** Fernando C. Patrão-Neto, Marcelo A. Tomaz, Marcos M. Machado, José Roberto Da S. Rocha-Junior, Paulo A. Melo

**195. A Novel Vascular Endothelial Growth Factor-Like Protein from *Gloydius tsushimaensis* Venom.** Hitomi Nakamura, Tatsuo Murakami, Takahisa Imamura, Michihisa Toriba, Takahito Chijiwa, Motonori Ohno, Naoko Oda-Ueda.

**96. Chemical and Biological Characterization of a Novel Neuropeptide in the Venom of Solitary Digger Wasp.** Ken-ichi Nihei, Kohei Kazuma, Kenji Ando, Katsuhiro Konno

**1050 - 1105 Travel Break**

**1105 – 1225 Concurrent Session #37: Toxins and Receptors Tapa 1-2**
**Chair: Denis Servent (France); Victor T. Tsetlin (Russia)**

**142. From alpha-Conotoxins and alpha-Neurotoxins to Endogenous "Prototoxins" and Binding Sites in Nicotinic Acetylcholine Receptors.** Victor I. Tsetlin, Yuri N. Utkin, Igor E. Kasheverov, Ekaterina N. Lyukmanova

**136. The Allosteric Binding Site for ρ-TIA on the Extracellular Surface of the α1B-Adrenoceptor.** Lotten Ragnarsson, Ching-I Anderson Wang, Åsa Andersson, Dewi Fajarningsih, Thea Monks, Andreas Brust, K. Johan Rosengren, Richard J. Lewis

**129. Retrograde Trafficking at the Presynaptic Nerve Terminal Using Bacterial Toxins.** Sally Martin, Callista B. Harper, Frederic A. Meunier

**140. Identification, Pharmacological and Structural characterization and Engineering of Three-finger Toxins interacting with GPCRs.** Guillaume Blanchet, Gilles Mourier, Elodie Marcon, Bernard Gilquin, Nicolas Gilles, Denis Servent

**1105 – 1225 Concurrent Session #38: Zoos & Collections Coral 1**
**Chair: Jessi Krebs (USA); Chhabilal Thapa Magar (Nepal)**

**291. The Dilemma: Balancing Antivenom Cost vs. Investment in Conservation.** Jessi Krebs, Mary M. Cederstrand

**293. Coral Snakes, Antivenoms, Hospitals and Zoos: How Can One Little Snake Cause So Many Problems?** Stan Mays

**285. Venomous Workshop: Evolution of a Professional Training Course.** Douglas L. Hotle

**288. Unique Challenges Faced During the Creation of a New Herpetology Department with New Venomous Animal Species and Safety Policies within the City of Virginia Beach's Virginia Aquarium and Marine Science Center.** William G. Harshaw

**287. Logistics and Problems in Managing a Large Confiscation of Venomous Snakes.** Donal M. Boyer

**1105 – 1225 Concurrent Session #39: Snake Venoms and Antivenoms Coral 2**

**Chairs: Tom Shier (USA); Miguel Fernández (USA)**

**207. Developing of an Antielapidic Sera by Genetic immunization.** Henrique Roman Ramos, Inácio de Loiola Meireles Junqueira de Azevedo, Carlos Chávez Olórtegui, Paulo Lee Ho

**222. Molecular Mechanisms Involved in PGE2 Release Induced by the Snake Venom Metalloproteinase BaP1 in Synoviocytes.** Mariana Viana, Catarina Teixeira, Elbio Leiguez, José M. Gutiérrez, Alexandra Rucavado, Cristina M. Fernandes

**230. Determining the Interaction Region Between the Antimyotoxin DM64 and a Snake Venom Myotoxin.** Rocha, S.L.G., Neves-Ferreira, A.G.C., Trugilho, M.R.O., Valente, R.H., Domont, G.B., Perales, J.

**254. Failure to Develop Sensitization Despite Repeated Administration of Ovine Fab Snake Antivenom: A Single-Patient, Multi-Center Case Series.** Eric J. Lavonas, Blaine E. Benson, Steven A. Seifert

**260. Hainantoxin-III Inhibits Voltage-Gated Sodium Channel Nav 1.7 and Extenuates Inflammatory Pain in Animal Models.** Zhonghua Liu, Qi Zhu, Tianfu Cai, Ze Wu, Jing Li, Dan Li, Weiwen Ning, Yu Liu, Meichun Deng, Weijun Hu, Songping Liang

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|---|---|---|
| **1225 – 1340** | **Lunch Provided** | **Palace Lounge** |
| **1225 – 1340** | **Publishing in Toxicon w/ Alan Harvey w/ Boxed Lunch** | **Tapa 1-2** |
| **1334 – 1350** | **Awards Ceremony:**<br>**Best Poster Abstract;**<br>**Best Platform Abstract;**<br>**Best Young Investigator** | **Tapa 1-2** |
| **1350 – 1510** | **Plenary #9: IST Business Meeting** | **Tapa 1-2** |
| **1510 – 1530** | **Refreshment Break** | **Palace Lounge** |
| **1530 – 1720** | **Concurrent Session #40: Marine Toxins** | **Tapa 1-2** |

**Chair: Dietrich Mebs (Germany); Andrew Rossiter (USA)**

**108. Cardiovascular and Hemolytic Effects of Sp-CTx a Cytolysin Isolated from the Scorpionfish, *Scorpaena plumieri*.** Helena L. Gomes, Davi Jr. D. Freire, Filipe Andrich, Edna F. de Medeiros, Jader Cruz, Antonio N. S. Gondim, Dalton V. Vassalo, Suely G. Figueiredo

**50. Tetrodotoxin in North-American Newts.** Dietrich Mebs, Mari Yotsu-Yamashita

**103. Emergent Marine Toxins in Europe: New Challenges for Scientists and Regulatory Authorities.** Vitor Vasconcelos, Mafalda Batista, Rosa Cianca, Joana Azevedo, Marisa Silva

**104. New Actinoporin from the Northern Pacific Sea Anemone *Urticina crassicornis*.** Andrej Razpotnik, Peter Maček, Igor Križaj, Tom Turk

**300. Toxinological Point of View of Metalloproteinase-like Enzymes of Jellyfish Venoms.** Changkeun Kang, Yeung Bae Jin, Hyunkyoung Lee, Eun-sun Jung, Won Duk Yoon, Euikyung Kim

**100. The Nematocyst Venom of Hydra: What is it Composed of and How Did it Evolve?** Tamar Rachamim, Eliezra Glasser, Daniel Sher

**1530 – 1720** **Concurrent Session #41: Public Health Aspects of Envenomation** **Coral 1**
**Chairs: Mohammed Alhelail (Saudi Arabia); Rais Vohra (USA)**

**237. Snakebite Survivors Club: Ten-year, retrospective review of Crotaline envenomations in Central California.** Susanne Spano, Fernando Macias, Brandy Snowden, Rais Vohra

**244. Mulga snake (*Pseudechis australis*) Bites; A Review of Significant Cases Including an Exceptionally Severe Local Envenoming.** Julian White, Scott Weinstein, Sam Alfred

**282. Sexual Variation in Timing of Egress and Ingress in Tiger Rattlesnakes (*Crotalus tigris*).** Chip Cochran, Matt Goode

**286. Legal Conundrums Impeding Patient Safety Initiative to Prevent Exotic Envenomation in the United States.** Joshua Z. Silverberg, Michael Touger, Donal M. Boyer

**321. Scorpions of Arabia: Review and Update in Management.** Mohammed A Alhelail

**1530 – 1720** **Concurrent Sessions #42: Plant Toxins** **Coral 2**
**Chairs: Gyorgy Panyi (Hungary); Ashraf Morgan (Egypt)**

**162. Membrane-disturbing Properties of Urease and Derived Recombinant Peptides.** Anne H.S. Martinelli, Angela Piovesan, Karine Kappaun, Cristian Follmer, Jean-Louis Schwartz, Celia R. Carlini, Angela Piovesan

**161. Unusual Plant Poisoning from Anabasine in an Isolated Community Following Ingestion of Tree Tobacco Leaves (*Nicotiana glauca*).** Sharon E Semmler, Sam Alfred, Trevor Christensen, Georgina Tate, Julian White

**3. Capsaicin: A Novel Antidote against Botulinum Neurotoxin A.** Baskaran Thyagarajan, Shannon Schreiner, Padmamalini Baskaran

**333. P1/P2 proteins of the human ribosomal stalk are required for ribosome binding and depurination by ricin in human cells.** Xiao-Ping Li, Kerrie L. May, Francisco Martínez-Azorín, Juan P. G. Ballesta, Przemysław Grela, Marek Tchórzewski and Nilgun E. Tumer

**164. Evaluation of Anticancer Activity Promoted by Molecules Contained in the Extracts of *Thevetia peruviana*.** Tamiris Caroline Barbon, Cássio Prinholato da Silva, Suely Vilela Sampaio, Mateus Amaral Baldo

**1720 – 1735** **Travel Break**

**1735 - 1800** **Closing Remarks** **Tapa 1-2**
**Steven Seifert (USA)**
**Carl-Wilhelm Vogel (USA)**
**Alan Harvey (UK)**

**1800 -** **Meeting ends**

## Poster Session I

## Tuesday, July 10

## Abstracts #1 – 177 (#113 and #115 moved to Thursday)

**9. Genotoxic Potential of *Micrurus corallinus* Venom on the DNA of Human Lymphocytes.**
Silvana Marcussi, Marcus Vinicius C. Trento, Mateus W. Eleutério.

**10. Comet Assay and Micronucleus Tests to Assess Damage to the DNA of Human Lymphocytes Induced by the *Bothrops jararaca* Venom.**
Silvana Marcussi, Marcus V. C. Trento, Mateus W. Eleutério, Marcel J. Palmieri.

**12. Structural Interpretation for the Subnanomolar Affinity of Muscarinic Toxin 7 for Human Muscarinic Acetylcholine Receptor 1 by Modeling Protein-Protein Interaction.**
Jianrong Xu, Jun Xu, Hongzhuan Chen.

**13. Crotamine Pharmacology Revisited: Novel Insights Based on the Inhibition of Kv Channels.**
Steve Peigneur, Diego Orts, Alvaro Prieto da Silva, Nancy Oguiura, Malvina Boni-Mitake, Eduardo Brandt de Oliveira, André Junqueira Zaharenko, J C de Freitas, J Tytgat.

**14. Evaluation of the Cytotoxic Activity of Rhinella schneideri Toad Poison on Tumor Cells and on Healthy Mononuclear Cells.**
Elisa C. Fornari Baldo, Cássio P. da Silva, Suely V. Sampaio, Eliane C. Arantes.

**40. The Anti-cancer Activity of the Venom from Spider Macrothele raveni in vitro and in vivo.**
Li Gao, Yongqing Shen, Jing Zhang, Chunyun Li, Liang Li, Baoen Shan, Baohua Zhao, Jinglin Wang.

**41. Anti-Inflammatory Effect of Honey Bee Venom on Wistar Rats Induced Poly Cystic Ovarian Syndrome by Estradiol Valerate.**
Mohammad Nabiuni, Kazem Parivar, Bahman Zeynali, Azar Sheikholeslami, Latifeh Karimzadeh.

**43. Melittin Peptide Kills Trypanosoma cruzi Epimastigotes and Trypomastigotes Forms by Different Cell Death Phenotypes.**
Camila M. Adade, Isabelle Ribeiro, Joana Pais, Thais Souto-Padrón.

**44. Leishmanicidal Effects of a Phospholipase A2 Isolated from *Crotalus viridis viridis* Snake Venom.**
Camila M. Adade, Anne Cristine S. Fernandes, Ana Lúcia O. Carvalho, Russolina B. Zingali, Thais Souto-Padrón.

**45. Carbon-13 and Nitrogen-15 Turnover in Serum of Bubaline Donors of Biological Material for Medical Use.**
Daniela A. Fossato da Silva, Natália P. Biscola, Renato M. F. Souza, Denis A. Caetano, Juliana C. Denadai, Maria M.P. Sartori, Evandro T. da Silva, Carlos Ducatti, Cyntia L. Martins, André M. Jorge, Lucilene D. dos Santos, Rui S. Ferreira Junior, Benedito Barraviera.

**46. Biological Features of an Enantiomeric Antimicrobial Peptide from Scorpion Venom.**
Daniel Juarez Lopez, Gerardo Corzo, Alexis Rodriguez, Elba Villegas.

**66. β-defensin-like genes in Brazilian poisonous snakes.**
Poliana G. Corrêa, Taís Machado, Valdir J. Germano, Daniela P.T. Gennari, Álvaro R.B. Prieto-da-Silva, Nancy Oguiura.

**68. Substrate range and specificity of the SicTox phospholipase D toxins.**
Daniel M. Lajoie, Greta J. Binford, Vahe Bandarian, Matthew H. J. Cordes.

**70. Purification and Characterization of New Platelet Aggregation Inhibitor with Dissociative Effect on ADP-Induced Platelet Aggregation, from Protobothrops Venom in Japan.**
Etsuko Oyama, Naomichi Furudate, Kotaro Senuki, Hidenobu Takahashi.

**75. The P-I Metalloproteinase from *Cerastes cerastes* Snake Venom Inhibits Human Platelet Aggregation.**
Hinda Boukhalfa-Abib, Fatima Laraba-Djebari

**76. An Antiplatelet Peptide, Lahirin, from Indian Monocled Cobra Venom.**
C. Chandra Sekhar, Dibakar Chakrabarty.

**77. Anticoagulant Activity of Moon Jellyfish (*Aurelia aurita*) Tentacle Extract.**
Akriti Rastogi, Sumit Biswas, Angshuman Sarkar, Dibakar Chakrabarty.

**78. Evaluation of the Efficacy of Treatment Using Bothropic or Bothropic/Crotalic Antivenin in *Bothrops jararacussu* (VIPERIDAE) Experimental Envenomation.**
Marcio Y. Yano, Marcio H. Matsubara, Ida S. Sano-Martins.

**79. Hemostatic Disturbances Evoked by Young and Adult *Bothrops jararaca* Snake Venoms: Analysis of the Envenoming Process and the Recovery after Specific Antivenin Treatment.**
Luana V. Senise, Sâmella S. Oliveira, Marcio Y. Yano, Savio S. Sant´Anna, Marcelo L. Santoro, Ida S. Sano-Martins.

**80. Purification of a Prothrombin Activator from *Bothrops moojeni* Snake Venom.**
Marco A. Sartim, Renato C. Caetano, Norival A. Santos-Filho, Wallace de P. Adolpho, Adélia C. O. Cintra, Suely V. Sampaio.

**82. Anticoagulant Activity of Crotalic Venoms on Whole Blood Samples from Chickens and Rats.**
Thayane Ribeiro, Benedito C. Prezoto, Luciane L. Abbud, Nancy Oguiura.

**90. Proteomic Analysis of the Molecular Targets of a Peptide from Wasp Venom Through Developing 0of an Analytical Platform.**
Lucilene Delazari dos Santos, José Roberto Aparecido dos Santos Pinto, Anally Ribeiro da Silva Menegasso, Ana Maria Garcia Caviquioli, Daniel Menezes Saidemberg, Mario Sergio Palma.

**92. Centipede Envenomation: 104 Cases from Bangkok, Thailand.**
Rittirak Othong, Winai Wananukul, Rais Vohra.

**93. Mechanisms Implicated In Cell Proliferation And Cell Survival Induced By Recombinant Losac, A Cell Adhesion Molecule From *Lonomia oblique*.**
Miryam P. Alvarez-Flores, Cesar M. Remuzgo, Yara Cury, Rosemary V. Bosch, Beatriz B. Vaz-De-Lima, Durvanei A. Maria, Ana M. Chudzinski-Tavassi.

**97. Insulin-Binding Protein-Like Venom Protein of the Solitary Hunting Wasp, *Eumenes pomiformis* (Hymenoptera: Eumenidae).**
Ji Hyeong Baek, Si Hyeock Lee.

**98. Transcriptomic and Peptidomic Characterisation of the *Conus marmoreus* Venom: Insights on Conopeptide Diversity and Venomic Processing.**
Ai-hua Jin, Sébastien Dutertre, Quentin Kaas, Richard J. Lewis and Paul F. Alewood.

**111. State of the Art of Palytoxin and Analogs Analytical Methods for Seafood Monitoring.**
Vitor Vasconcelos, Joana Azevedo, Marisa Silva, Vitor Ramos.

**112. Cathepsin B/X is Secreted by *Echinometra lucunter* Sea Urchin Spines, a Structure Rich in Granular Cells and Toxins.**
Juliana M. Sciani, Marta M. Antoniazzi, Carlos Jared, Daniel C. Pimenta.

**114. Effect of Byproducts from *Artemia salina* Culture Medium on PSP Toxicity and Toxin Composition of *Alexandrium catenella*.**
Toshio Saito, Tadahiro Kogure, Tsuyosi Sagara, Kedarnath Mahapatra, Sachio Nishio.

**116. Systemic Toxicity of the "Fire Coral" *Millepora complanata*: Isolation of a Non-Protein Vasoconstrictor Fraction with Lethal Activity in Mice.**
Alejandro García-Arredondo, Alejandra Rojas, César Ibarra-Alvarado, Moustapha Bah.

**117. Identification and Characterization of α-Conotoxins in *Conus purpurascens*.**
Alena M. Rodriguez, Frank Marí.

**118. Primary Structures of Proteinaceous Toxins from Three Species of Scorpaeniform Fish (Lionfish, *Pterois lunulata*, Scorpionfish, *Inimicus japonicus* and Waspfish, *Hypodytes rubripinnis*).**
Aya Kiriake, Yasuko Suzuki, Yuji Nagashima, Kazuo Shiomi.

**119. Characterization of Local Inflammatory Response Induced by Scorpion Fish, *Scorpaena plumieri* Venom in a Mouse Model of Tissue Injury.**
Thiago N. Menezes, Juliana B. T. Carnielli, Pedro H. Lemos, Nazaré S. Bissoli, Mônica Lopes-Ferreira, Filipe Andrich, Suely G. Figueiredo.

**120. The Atypical Activity Profile of bru1b, an α-Conotoxin from the Venom of *Conus brunneus*.**
Mari D. Heghinian, Monica Mejia, Tanja A. Godenschwege, and Frank Marí.

**121. Venom Composition Changes during Prey Capture in *Conus textile*.**
Cecilia Prator and Joseph Schulz.

**122. Acute toxicity and brine shrimp cytotoxicity induced by the venom of the fire coral *M. alcicornis* collected in the Mexican Caribbean.**
Rosalina Hernández-Matehuala, Alma A. Vuelvas-Solórzano, Armando Zepeda-Rodríguez, Lurdes Palma, Alejandra Rojas.

**123. Effects of Cyanobacterial Bloom on Fish: Proteomics and Histological Investigation on the Medaka *Oryzias Latipes*.**
Marc Edery, Arul Marie, Benjamin Marie, Hélène Huet, Isabelle Trinchet, Lionel Dubost, Sahima Hamlaoui, Chakib Djediat.

**130. Water Bacterial Activities Involved in Immune Depression of Haemodialysis Patients.**
Meshref A. Al-Ruwaili, Samy A. Selim.

**131. Unexpected Hazard Due to Fuminaisin Toxin Contaminating Herbal Teas in Saudi Arabia.**
Fardos Bokhari, Magda M. Aly.

**132. Determination of Histamine and Histamine-forming Bacteria in Striped Marlin Fillets (*Tetrapturus audax*) Implicated in A Food-borne Poisoning.**
Yi-Chen Lee, Tzou-Chi Huang, Chung-Saint Lin, Chia-Min Lin, Yung-Hsiang Tsai.

**133. Root Toxicity of the Mycotoxin Botryodiplodin in Soybean Seedlings.**
W. Thomas Shier, Justin Nelson, Hamed K. Abbas, Richard E. Baird.

**134. Cytotoxic and Proteolytic Molecules of the Human Parasite Dientamoeba fragilis, Identified by RNA seq, Provide Support for its Pathogenic Capacity.**
Joel Barratt, Damien Stark, John Ellis.

**135. Evaluation of Cardiotoxic Effects of Microcystin–LR in Mouse Isolated Hearts.**
Siqueira-Lece , F.,Ricardo,H.D., Tomaz, M.A., Machado, M.M., J.M., Tavares, S.M., Strauch, M.A., Azevedo, S.M., Soares, R.M.,Melo, P.A.

**137. Neuropathies of Spinal Cord Development of Rat Pups Maternally Fed on Fried Potatoes Chips.**
Gadallah A. Abdelalim, El-Sayyad I. Hassan, El-Shershaby M. Effat, Abdelatif M. Ibrahim.

**138. Nickel hepatotoxicity in rats and trials for protection using antioxidants.**
Salah S. El-Ballal, Ashraf M. Morgan, Nemin B. Ebrahim.

**151. Immuno-Inflammatory Response After Scorpion Envenomation: Potential Role of Eïcosanoids and Histamine H1-Receptor.**
Sonia Adi-Bessalem, Amina Ladjal-Mendil , Djelila Hammoudi-Triki , Fatima Laraba-Djebari.

**153. Biochemical and Pharmacological Characterization of Three-Finger Neurotoxins from the Venom of Eastern Coral Snake (*Micrurus fulvius fulvius*).**
Chun Shin Foo, Selvanayagam Nirthanan, R. Manjunatha Kini, Peter T. H. Wong.

**154. First Pharmacological Study of the Venom of a Rare African Snake, *Naja multifasciata duttoni*.**
Alan L. Harvey, Edward G. Rowan, R. David G. Theakston, David A. Warrell.

**155. Expression of two endoplasmic reticulum stress markers, GRP78 and GADD153, is involved in the mechanism of action of the Amblyomin-X.**
Ana Marisa Chudzinski-Tavassi, Jean G. Souza, Simone M. Simons, Carolina M. Berra, Renata F. Sato, Roger Chammas R, Katia L. P. Morais.

**156. Neuromuscular activity of Bothrops fonsecai Snake Venom and its Neutralization by Commercial Bothropic Antivenom.**
Rita de Cássia de Oliveira Collaço, Gildo Bernardo Leite, José Carlos Cogo, Stephen Hyslop, Thalita Rocha, Priscila Randazzo-Moura, Léa Rodrigues-Simioni.

**157. Validation of an Analytical Method to Measure Neutralizing Potency of Anti *Loxosceles* Plasma.**
Chávez-Méndez A, Olvera C, Alagón A, Olguín L.

**159. Synaptophysin Expression and Neurotoxic Effects of Some Bothropic Venoms and Toxins.**
Thalita Rocha, Luis A. Ponce-Soto, Sérgio Marangoni, Maria Alice da Cruz-Höfling.

**165. Molecular Cloning, Expression and Structure-Function Analysis of Neopladine-2, an Antineoplastic Peptide from *Tityus discrepans* Scorpion Venom.**
Olvera F, D'Suze G, Olvera A, Diaz P, Rosales A, Sevcik C and Alagón A**.**

**166. Toxins of *Tityus Serrulatus* Scorpion Venom Induce Inflammatory Mediators *in vitro*.**
Karina F. Zoccal, Claudia da S. Bitencourt, Carlos A. Sorgi, Karla de C. F. Bordon, Suely V. Sampaio, Eliane C. Arantes, Lúcia H. Faccioli.

**167. Novel Potassium Channel Blocker Venom Peptides from Mesobuthus gibbosus (Scorpiones: Buthidae).**
Elia Diego-García, Steve Peigneur, Sarah Debaveye, Eveline Gheldof, Jan Tytgat and Figen Caliskan.

**168. Tityus serrulatus Venom Induces a Higher Lung Inflammation in Mice Selected for Maximal Inflammatory Response.**
Priscila G. Lara, Thaís R. Narcizo, Fernanda C. V. Portaro, Nancy Starobinas, Vera Aiello V, Luiz A. Benvenuti, Osvaldo A. Sant'Anna, Orlando G. Ribeiro; Mônica Spadafora-Ferreira**.**

**169. *Tityus serrulatus* Scorpion Laboratory Breeding and Venom Collection for Antivenom Production and Research.**
Claudio M. V. Souza, Jonathan R. L. Vieira, Jonathan R. Souza, Lana S. Sales, Luis E. R. Cunha.

**170. Identification of a Dynorphin-Degrading Metallopeptidase Releasing Leu-Enkephalin in Brazilian *Tityus spp.* Scorpion Venoms.**
Emerson J. Venancio, Fernanda C.V. Portaro, Alexandre K. Kuniyoshi, Daniela Cajado Carvalho, Giselle Pidde-Queiroz, Denise V. Tambourgi**.**

**171. Comments on the Venom Yield of *Tityus trivittatus*, Considering Two Methodologies of Extraction.**
Adolfo R. de Roodt, Rodrigo D. Laskowicz R.D., Silvina Saavedra, Miriam Vucharchuc, Laura C. Lanari, Gustavo Reati, Juan C. Beltramino J.C., Liliana Varni, Raúl López, Eduardo Bazan E., Costa de Oliveira V.

**177. IgY Antibodies Anti-*Tityus caripitensis* Venom: Purification and Neutralization Efficacy.**
Alvarez O. Aurora, Montero Yuyibeth , Jimenez Eucarys, Zerpa Noraida, Parrilla A. Pedro, Malave Caridad.

## Poster Session II

## Thursday, July 12

## Abstracts #113, 115, 180 - 341

**113. Effects of Successive Subculture and Various Culture Conditions on Growth and PSP Productivity of the Toxic Dinoflagellate *Alexandrium catenella*.**
Shanshan Jiang, Sho Miyata, Tomohiro Takatani, Osamu Arakawa.

**115. Two Proteins Homologous to Pufferfish Saxitoxin- and Tetrodotoxin-Binding Protein (PSTBP) Found in the Plasma of Non-Toxic Cultured Specimens of the Pufferfish (*Takifugu rubripes)*.**
Ryohei Tatsuno, Kenichi Yamaguchi, Tomohiro Takatani, Osamu Arakawa.

**180. Increasing of the Presence of *Tityus trivittatus* in Buenos Aires City.**
Guillermo Blanco, Rodrigo D. Laskowicz, Eduardo Scarlatto E., Natalia Casas, Vanessa Costa de Oliveira, Laura C. Lanari, Néstor R. Lago, Adolfo R. de Roodt.

**181. Evaluation of a Four-Hour Endpoint for Use in Scorpion Envenomation Studies in Morocco.**
Rachida Soulaymani-Bencheikh, Emmanuelle F. Mangin, Asmae Khattabi, Zachary T. Fellows, Leslie V. Boyer.

**182. Two Case Studies of Pregnancy Outcomes after Scorpion Envenomation and F(ab')2 Scorpion Antivenom Treatment.**
Joanne M. Mallie, Sue Hoopmann, Janice A. Degan, Leslie V. Boyer.

**193. A study of Venoms from Individual Snakes of Two Populations of *Rhinocerophis (Bothrops) alternatus* of Argentina.**
Laura C. Lanari, Rodrigo D. Laskowicz, Vanessa Costa de Oliveira, Daniela Rocco, Néstor R. Lago, Roberto P. Stock, Adolfo R. de Roodt.

**194. Effect of Heparin and L-Arginine on Skin Tissue Regeneration after *Cerastes cerastes* Envenomation.**
Habiba Oussedik-Oumehdi, Fatima Laraba-Djebari.

**197. Lupane Triterpenoids From *Dipteryx alata* Vogel As Snake Venoms Inhibitors.**
Miriéle C. Ferraz, Marta M. D. C. Vila, José C. Cogo, Marcio G. dos Santos, Luiz M. Franco, Pilar Puebla, Arturo San Feliciano, Yoko Oshima-Franco.

**198. Isolation, Enzymatic Characterization and Action as Spreading Factor of a Hyaluronidase from *Crotalus durissus terrificus* Snake Venom.**
Karla C. F. Bordon, Márcio G. Perino, José R. Giglio, Eliane C. Arantes.

**199. BaPLA2-IV, An Acidic Phospholipase A2, Isolated From *Bothrops atrox* Snake Venom: Biochemical and Functional Characterization.**
Thales M. Junqueira, Lanuze G. De Toni, Adelia C. O. Cintra, Cássio P. da Silva, Suely V. Sampaio.

**200. Antinociceptive Potential of Raw Venom of Egyptian Cobra and Black Tiger Snake: A Functional Magnetic Resonance Imaging Study.**
Susanne Wolz-Richter, Karl-Heinz Esser, Andreas Hess.

**201. Molecular Evolution of Snake Venom Phospholipase A2 (PLA2) Genes -Analysis of Group I PLA2 cDNAs from Venomus and Nonvenomous Snakes, and Lizards.**
Masahiko Yamashita, Tomonari Sawamoto, Toru Tamiya.

**202. Brazilian Coral Snake Phospholipases A2 Induce Neuronal Death in Primary Cultures of Hippocampal Neurons.**
Nathalia Delazeri de Carvalho, Raphael Caio Tamborelli Garcia, Ivo Lebrun, Durvanei Augusto Maria, Silvia Carneiro, Solange Castro Afeche, Maria Regina Lopes Sandoval**.**

**204. *Vipera Lebetina* Venom Nucleases and Nucleotidases.**
Ene Siigur, Katrin Trummal, Külli Tõnismägi, Anu Aaspõllu, Jüri Siigur.

**205. A Novel Fluorometric Assay for the Evaluation of Substrates for Phospholipase A2 from the Colombian Snakes *Bothrops asper* and *Crotalus durissus cumanensis*.**
Andres M. Tibabuzo, Jackson Ocampo, Barbara H. Zimmermann, Chad Leidy.

**206. Isolation and Characterization of a D49 Phospholipase A2 from *Rhinocerophis (Bothrops*) *Ammodytoides* venom.**
Herlinda Clement, Vanessa Costa de Oliveira, Fernando Z. Zamudio, Néstor R. Lago, Adriana Valdez-Cruz, Melisa Bernard Valle, Alejandro Alagón, Lourival D. Possani, Adolfo R. de Roodt.

**214. Evaluation of the Antiophidic Activity of Lapachol and Synthetic Analogues.**
Marcelo A. Strauch, Marcelo A. Tomaz, Marcos M. Machado, Jhonatha M. T. Cruz, Bruno L. Cons, Alcides J. M. da Silva, Paulo R. R. Costa, Paulo A. Melo.

**215. Ability of Polyanions to Antagonize the Cardiotoxic Effect of the *Bothrops jararacussu* Venom.**
Himar D.Ricardo, Vinicius V. Martins, Marcos Monteiro-Machado, Marcelo A. Strauch, Marcelo A. Tomaz, Matheus T Henriques, Bruno Lemos Cons, Jhonatha Mota-Texeira, Fernanda Siqueira-Lece, F.S.; Paulo A. Melo.

**219. Functional Characterization of a Recombinant Myotoxin Inhibitor from *Bothrops alternatus* Snake Plasma .**
Norival A. Santos-Filho, Danilo L. Menaldo, Marco A. Sartim, Adélia C. O. Cintra, Johara B. França, Ludier K. Santos-Silva, Flavio H. Silva, Eliane C. Arantes, Suely V. Sampaio.

**220. Evaluation of Extracts and Partitions from Aerial Parts of *Baccharis microdonta* on Enzymatic Activity, Pro-Inflammatory and Myotoxic Activities Induced by Secretory Phospholipase A2 from *Bothrops jararacussu*.**
Veronica C.G.Soares, Daniel Bristot, Camila L. Pires, Marcos H. Toyama, Paulete Romoff, Marcelo J. Pena, Oriana A. Favero and Daniela de O. Toyama.

**221. The Interaction of the Antitoxin DM43 with a Snake Venom Metalloproteinase Analyzed by Mass Spectrometry and Surface Plasmon Resonance.**
Guilherme D. Brand, Rune Salbo, Thomas J.D. Jørgensen, Carlos Bloch Jr, Elisabetta B. Erba, Carol V. Robinson, Isabelle Tanjoni, Ana M. Moura-da-Silva, Peter Roepstorff, Gilberto B. Domont, Jonas Perales, Richard H. Valente, Ana G.C. Neves-Ferreira.

**223. TLR2 and MyD88 Signaling are Required for Efficient Response of Macrophages to MT-III a Phospholipase A2 (PLA2) from *Bothrops asper* Snake Venom.**
Elbio Leiguez, Karina C. Giannotti, Vanessa Moreira, Márcio H. Matsubara, Bruno Lomonte, Catarina F.P. Teixeira**.**

**224. Snake Venomics of *Crotalus tigris*. Evolutionary Clues for Generating a Pan-Specific Antivenom Against Crotalid Type II Venoms.**
Juan J. Calvete, Alicia Pérez, Bruno Lomonte, Elda E. Sánchez, and Libia Sanz.

**225. Proteomic Analysis and Pharmacological Activities of the Venom of the Moroccan Cobra *Naja haje legionis.***
Ibtissam Malih, Muhamad Rusdi Ahmad Rusmili, Ting Yee Tee, Rachid Saile, Noreddine Ghalim, Iekhsan Othman.

**226. Processing of SVMPs: Detection of SVMP Zymogens and Pro-Domain in Bothrops jararaca Venom and Venom Glands.**
Portes-Junior, J.A., Magalhães, G.S., Sant'Anna, S.S., Junqueira, M.R., Yamanouye, N., Moura-da-Silva, A.M., Domont, G.B..

**227. Proteopeptidome Determination of *Bothrops jararaca* Venom: an Innovative Approach in Snake Venomics.**
Carolina A. Nicolau, André Teixeira-Ferreira, Paulo C. Carvalho, Magno Junqueira, Jonas Perales, Ana Gisele C. Neves-Ferreira, Richard H. Valente.

**249. Experience with Crotalidae Polyvalent Immune Fab (Ovine) for a non-North American Rattlesnake Envenomation.**
Sean P. Bush, Tammy H. Phan.

**255. Local Damage produced by *Vipera* and *Macrovipera* Venoms and Some Immunochemical Characteristics.**
Néstor R. Lago, Adolfo R. de Roodt, Irving Archundia, Daniela M. Rocco, Vanessa Costa de Oliveira, Pablo I. Regner, Jorge Zárate, Alejandro Alagón, Roberto P. Stock.

**257. Comparative Analysis of Transcriptomes of *Phoneutria pertyi* and *P. nigriventer* Venom Glands.**
Marcelo R. V. Diniz, Camilla R. L. Machado, Ana Luiza B. Paiva.

**258. Unusual Cases of the Spider *Cheiracanthium Punctorium* Biting in Volgograd Region, Russia.**
Vasiliy I. Emtsov, Yury N. Ostapenko, Sergey S. Larionov.

**270. Site-Directed Mutagenesis of rPnTx2-6 - a Recombinant *Phoneutria nigriventer* Spider Venom Toxin – Reveals Important Amino Acids for Its Pharmacological Activities.**
Marcelo R. V. Diniz, Maria Elena Lima, Fernanda S. Torres.

**271. Differential Expression of Aquaporin 4 in the Hippocampus of Neonate and Adult Rats after Envenoming by *Phoneutria nigriventer* (*Ctenidae, Araneomorphae*).**
Leila Miguel Stavale, Edilene S. Soares, Monique C. P. Mendonça, Maria Alice da Cruz Hofling.

**272. Cellular and Molecular Demonstration that Vascular Endothelial Growth Factor (VEGF) and its Receptor Flt-1 and Flk-1 are Involved in *Phoneutria nigriventer* Envenoming,**
Monique C. P. Mendonça , Edilene S. Soares, Leila M. Stávale, Catarina Râposo, Maria Alice da Cruz-Höfling.

**273. Heterologous Expression of PaluIT1, A Cysteine Knot Spider Toxin, in *E. coli*.**
Richa Mehta, Kenya Hernández-Salgado, Ernesto Ortiz, Gerardo Corzo, Elba Villegas.

**274. A National Serum Depot in the Netherlands; Encountered Antivenom Purchase Difficulties.**
Kees C.W. van der Zwan, Marieke A Dijkman, Ine de Vries, Truus W de Graaf**.**

**275. Safe Utilization of Ketamine as a First Line Induction Agent for Rapid Sequence Intubation (RSI) in the Aeromedical Setting.**
Janak K Acharya MD, Cameron LR Jones MD, Rais Vohra MD, Greg Hendey.

**278. Epidemiologic Situation of Envenomation by Venomous Animals in Argentina. 2007-2011 Period.**
Natalia Casas, Laura Geffner, Horacio Echenique, Vanessa Costa de Oliveira, Adolfo R. de Roodt.

**284. The Bio-Logic of Venom Complexity.**
David Morgenstern, Brett Hamilton, Daniel Sher, Alun Jones, Gideon Mattius, Eli Zlotkin, Deon Venter, and Glenn F. King.

**289. 2011 Putnam County Venomous Snake Confiscation: Antivenom Coverage Decisions.**
Michael Touger, Donal M. Boyer.

**290. Microbiological Evaluation of Different Strategies for Management of Snakes in Captivity.**
Michelle Vanessa Campagner MV, Sandra MG Bosco, Eduardo Bagagli, Maria de Lourdes RS Cunha, Bruna C Jeronimo, Eduardo Saad, Natalia P Biscola, Rui Seabra Ferreira-Junior, Benedito Barraviera.

**301. ELISA-based Detection of Ricin in Blood and Feces of the Rat following Non-Lethal Exposure.**
Ling Yann Foo, Tracey Sew, Hsiao Ying Chen, Weng Keong Loke.

**305. Characterization of the most dangerous snake venoms of Morocco.**
Naoual Oukkache, Norredine Ghalim.

**308. Comparison between two methods of scorpion venom milking from Morocco.**
Naoual Oukkache, Norredine Ghalim and Alejandro Alagon .

**309. Cytotoxic effects of Iranian Lebetina Snake Venom on Human Umbilical Vein Endothelial Cell.**
H. Vatanpour, M. Ghazi-Khansari, M. Kakanj, S. Jafarinejad, A. Zare- Mirakabadi.

**310. Analysis of some Biological Effects of *Hemiscorpius lepturus* Scorpion Venom from Khuzestan Province in Iran.**
Delavar Shahbazzadeh, Kamran Pooshang Bagheri, SeyedehTahereh Abdollahi, Mohammad Hosseini-Nejad Chafi, AtiehGhamnak, Fatemeh Torkashvand, Fahime Shahbazzadeh, Sima Rafati, Siamak Haddadi, Behrouz Vaziri**.**

**318. Cytotoxic and apoptotic effects of an L-amino acid oxidase from Calloselasma rhodostoma snake venom (CR-LAAO).**
Tássia R. Costa, Cássio Prinholato, Sandro Ghisla, Lusânia M. G. Antunes, Suely V. Sampaio.

**319. Prey-specific Toxins in Non-murine Models: Non-conventional Three-finger Toxins and Naja kaouthia Venom.**
Cassandra M. Modahl, Stephen P. Mackessy, Ashis K. Mukherjee**.**

**320. Snakes of the Arabia: Review and Update In the Management.**
Mohammed A Alhelail**.**

**322. Preventing the Development of Acute Kidney Injury from Hump-nosed Pit Viper (Hypnale hypnale) Bites in Mice with a Paraspecific Antivenom.**
Christeine Ariaratnam Gnanathasan, Choo Hock Tan, Nget Hong Tan, Si Mui Sim, Shin Yee Fung, Pailoor Jayalakshmi.

**323. Management of Envenomation Reported to the Veterinary Teaching Hospital, Zaria, Nigeria.**
Balarabe M. Jahun, Mujtaba S. Abubakar, Solomon W. Audu**.**

**324. Gambierol as an intra-membraneous anchor for immobilizing the voltage sensor movement in Kv channels.**
Ivan Kopljar, Alain J. Labro, Tessa de Block, Jon D. Rainier, Jan Tytgat, Dirk J. Snyders**.**

**325. Effectiveness of Rhazya Stricta Plant in Ameliorating Hepatic Alterations Induced by Leiurus Quinquestriatus Scorpion Envenoming.**
Osama A. Abuzinadah, Tarek R. Rahmy, Moustafa H. El Naggar, Mohammed I. Abo El Souad**.**

**327. The Composition of Spider Venoms.**
Wolfgang Nentwig, Reto Stöcklin, Lucia Kuhn-Nentwig**.**

**331. The protective Efficacy of Immunoglobulins Y (IgY) Prepared Against Cerastes cerastes Snake Venom in The Kingdom of Saudi Arabia.**
Ihab M. Moussa, Ashgan M. Hessan ,Abdulaziz M. Aleisa, Abdullah A. Al-Arfaj, Mounier M. Salem-Bekhit, Salim A. AlRejai **.**

**332. Comparative Transcriptomic View of the Body Organs from a Venomous Snake.**
Carolina M. V. Bastos, Aurelio Pedroso Jr, Norma Yamanouye,Paulo L. Ho, Inacio L. M. Junqueira-de-Azevedo.

**333. P1/P2 proteins of the human ribosomal stalk are required for ribosome binding and depurination by ricin in human cells.**
Xiao-Ping Li, Kerrie L. May, Francisco Martínez-Azorín, Juan P. G. Ballesta, Przemysław Grela, Marek Tchórzewski and Nilgun E. Tumer**.**

**334. Leucurolysin-B an ECD protein from snake venom as a tool for tumor molecular imaging.**
Lucilene M. Gabriel, Eladio F. Sanchez, Siléia G. Silva, Raquel G. Santos.

**335. Investigations into the mechanism of action of pinnatoxins E, F and G.**
Shane D. Hellyer, Andrew I. Selwood, Lesley Rhodes, D. Steven Kerr.

**336. Synthetic Pyridinium Polymer APS8 Non-competitively Nicotinic Acetylcholine Receptors.**
Hong Xing, Tom Turk, William R. Kem.

**337. The venom-gland transcriptome of the Eastern Coral Snake (Micrurus fulvius).**
Mark J. Margres, Darin R. Rokyta, Karalyn Aronow, Jacob Loyacano.

**338. Pharmacological activity of a new Asp49 phospholipase A2 isolated from Bothriopsis bilineata smargadina (forest viper) venom in vertebrate neuromuscular preparations.**
Rafael S. Floriano, Victor C. Carregari, Valdemir A. Abreu, Bruno Kenzo-Kagawa, Luis A. Ponce-Soto, Stephen Hyslop, Maria A. Cruz-Höfling, Sergio Marangoni and Léa Rodrigues-Simioni.

**339. Effects and Molecular Determinants of JZTX-V on the Kv4.3 Potassium Channel.**
Xiongzhi Zeng, Dehong Xu, Ji Luo, Yiya Zhang, Songping Liang.

**340. Initial Evaluation of the Cytotoxic Effects of Pseudechis porphyriacus Venom on Colon Cancer Cells.**
Elizabeth K. Maxey and Stephen P. Mackessy.

**341. Synergism between Snake Venom PLA2 and Metalloproteinase III.**
Ying Jia, Chunhui Yin, John Perez.

**342. Fer-de-Lance (*Bothrops asper*) venom activates and aggregates platelets and these effects are inhibited by antivenin, EDTA and hirudin.**
Mary E. Palmer, Michael A. Nardi.

# Supplemental Program Material

**Corrected version of Abstract #230, published in Toxicon:**

**230. Determining the Interaction Region Between the Antimyotoxin DM64 and a Snake Venom Myotoxin.**

Rocha, S.L.G.[1], Neves-Ferreira, A.G.C.[1], Trugilho, M.R.O.[1], Valente, R.H.[1], Domont, G.B.[2], Perales, J.[1]
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**Review:** Snake envenomations represent a public health problem in tropical countries. The opossum *Didelphis aurita* is resistant to the toxic effects of snake venoms due to the presence of serum neutralizing factors such as DM43 and DM64. The latter is a glycoprotein able to inhibit the in vivo myotoxicity and the in vitro cytotoxicity of myotoxins I (D49) and II (K49) from the venom of *Bothrops asper*, without inhibiting the phospholipase A2 activity of the first one. Our study aimed to map the region of interaction between DM64 and myotoxin II from *Bothrops asper* venom. The hydrolysis of DM64 by Lys-C generated several peptides that were chromatographed through a myotoxin/NHS-Sepharose affinity column. Three DM64 peptides bound to the column were identified by MS/MS: two located in the third domain and another one in the fifth domain of the inhibitor. Alternatively, DM64 was cross-linked to the myotoxin using $BS^3$, followed by trypsinization of the complex and nLC-LTQ-Orbitrap analysis. Most observed cross-links occurred between residues K241 (third domain) of DM64 and K15 of myotoxin II, and also between K452 (fifth domain) of DM64 and K60 of myotoxin II. In summary, the interaction of DM64 with myotoxin II seems to involve the third and fifth domains of the inhibitor, as suggested by two complementary methodological approaches. These results contribute to the molecular characterization of this important non-covalent complex and open the perspective that DM64 or its peptides may be used in the treatment of snake envenomations.
Support : Fiocruz, CNPq, Faperj, INCTTOX
Key Words: DM64, myotoxin, cross-linked

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**Additional reference materials for Abstract #245:**

**POSITION STATEMENT**
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POSITION STATEMENT
This position statement is being published jointly and simultaneously with Journal of Medical Toxicology

**Pressure immobilization after North American *Crotalinae* snake envenomation**
AMERICAN COLLEGE OF MEDICAL TOXICOLOGY, AMERICAN ACADEMY OF CLINICAL TOXICOLOGY, AMERICAN ASSOCIATION OF POISON CONTROL CENTERS, EUROPEAN ASSOCIATION OF POISON CONTROL CENTRES AND CLINICAL TOXICOLOGISTS, INTERNATIONAL SOCIETY ON TOXINOLOGY, ASIA PACIFIC ASSOCIATION OF MEDICAL TOXICOLOGY
**Keywords** Snakes; pressure immobilization; Crotalinae; envenoming

**Background**

The vast majority of venomous snake bites treated at health care facilities in the United States each year involve non-neurotoxic Crotalinae species. 1 Large case series reveal the major clinical effect associated with these envenomations to be local tissue injury. Extremity swelling and dermonecrosis are common, with compartment syndrome an infrequent but potentially limb-threatening effect of envenomation. 2,3,4,5 Life-threatening systemic toxicity and death are rare. Historically, many first-aid measures have been employed in the treatment of snake bites, but none has been shown to improve patient outcome. Pressure immobilization is a technique routinely employed in the pre-hospital management of neurotoxic snake species in Australia. First described by Sutherland and colleagues in the 1970s, pressure immobilization involves wrapping the entire extremity with a bandage and then immobilizing the extremity with a splint. 6 The bandage should generate a pressure between 40 – 70 mm Hg in the upper extremity and 55 – 70 mmHg in the lower extremity in order to effectively delay systemic absorption of venom. 7 Several animal studies have demonstrated delayed systemic absorption of venom with pressure immobilization. 6,7,8 However, studies have also revealed that pressure immobilization bandages are commonly applied incorrectly, even in a simulated setting following provider instructions and training. 9,10,11,12 Although the more common error is to apply the bandage too loosely, the bandage may function as a tourniquet when applied too tightly, causing limb ischemia, and may also increase systemic absorption of venom. 7

Animal models of North American Crotalinae envenomation demonstrate delayed systemic absorption of venom and delayed mortality following application of pressure immobilization bandages. 13,14,15 However, the local effects of sequestering cytotoxic venom in the extremity are less clear. In a swine model of pressure immobilization following *C atrox* lower extremity envenomation, intracompartmental pressure increased significantly compared to controls, from a non-surgical range to levels that would prompt fasciotomy. 13

**Position**

Given that the primary toxic effect of envenomation is local tissue injury, mortality is not an ideal outcome measure to extrapolate to human crotaline envenomation. Available evidence fails to establish the effi cacy of pressure immobilization in humans, but indicates the possibility of serious adverse events arising from its use. The use of pressure immobilization for the pre-hospital treatment of North American Crotalinae envenomation is not recommended.

**Acknowledgements**

The organizations acknowledge the efforts of Michael Levine, MD, and Michelle Ruha, MD in creating this position statement.

**Declaration of interest**

The societies endorsing this position statement have no conflicts to report. This work has been endorsed by American College of Medical Toxicology, American Academy of Clinical Toxicology, American Association of Poison Control Centers, European Association of Poison Control Centres and Clinical Toxicologists, International Society of Toxinology and Asia Pacific Association of Medical Toxicology

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**COMMENTARY**

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This commentary is being published jointly and simultaneously with Journal of Medical Toxicology.
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**Pressure bandaging for North American snake bite? No!**

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This issue of Clinical Toxicology includes a Position Statement regarding the use of pressure immobilization for the pre-hospital treatment of North American Crotalinae envenomation. This Commentary discusses the background behind the creation of the Position Statement and explores the issues involved in applying science to real world public health recommendations and practice.
**Keywords** Snakes; Toxinology; Pressure immobilization; Crotalinae

This issue of Clinical Toxicology includes a Position Statement regarding the use of pressure immobilization for the pre-hospital treatment of North American Crotalinae envenomation. 1 It has been jointly endorsed by the American College of Medical Toxicology (ACMT), the American Academy of Clinical Toxicology (AACT), the American Association of Poison Control Centers (AAPCC), the International Society on Toxinology, the European Association of Poison Centres and Clinical Toxicologists, and the Asia Pacific Association of Medical Toxicology, and concludes that pressure bandage with immobilization (PBI) cannot be recommended as pre-hospital care in areas such as North America, where non-neurotoxic snakebite is the norm. This Position Statement was formulated because of concern about recently published fi rst aid guidelines of the American Heart Association (AHA) and American Red Cross (ARC). 2 Those guidelines, designed to be applied by bystanders or the victim, included the following: "Applying [PBI] with a pressure between 40 and 70 mm Hg in the upper extremity and between 55 and 70 mm Hg in the lower extremity around the entire length of the bitten extremity is an effective and safe way to slow the dissemination of venom by slowing lymph flow (Class IIa, LOE C). For practical purposes pressure is sufficient if the bandage is comfortably tight and snug but allows a finger to be slipped under it. Initially it was theorized that slowing lymphatic flow by external pressure would only benefit victims bitten by snakes producing neurotoxic venom, but the effectiveness of pressure immobilization has also been demonstrated for bites by non-neurotoxic American snakes … ." Even though the AHA/ARC recommendation is weak (Class II: "conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. " Class IIa: "weight of evidence/opinion is in favor of usefulness/efficacy " ; Level of evidence C: " recommendation based on expert opinion, case studies, or standards of care. " ), 3 and meant to apply to snakebites worldwide, we are concerned that the recommendations will be applied to North American Crotalinae envenomations. We are also concerned that this guideline was graded above the level of current evidence and that the subtleties of the recommendation grading system are very likely to be under appreciated by most. The pre-hospital use of PBI in North American snakebite would be a major change in how such cases are managed. The history of snakebite first aid and emergency care is full of concepts that, despite initial theoretical appeal and/or anecdotal evidence, ultimately proved to be harmful. Once-common practices, such as tourniquets, cryotherapy, incision, suction, electrotherapy, and fasciotomy have been eliminated as their effectiveness was refuted, and more importantly, evidence of harm emerged. 4 – 9

With this perspective the introduction of a new practice must be based on the scientific demonstration of efficacy and safety. The application of science to real-world scenarios can be complex. The aim of PBI is to sequester venom in the limb, delaying its arrival into the central circulation and thereby delaying or even preventing the onset of the potential systemic consequences of envenomation. 10 Apart from directly measuring the clinical efficacy of PBI for various end-points, together with risks of harm of properly applied PBI, it is important to consider context-specific considerations. Key questions are: (1) the certainty regarding the kind of snake involved; (2) the expected time to arrival at a place where

definitive therapy can be provided; (3) whether lay individuals able to distinguish between scenarios with different management considerations; (4) the likelihood that PBI will be applied correctly or incorrectly, and that immobilization can be realistically maintained. In addition to these concerns the larger questions include when, how, and on what basis should a new recommendation in the management of snakebite be put forward? Moreover, when universal benefit may not result, should first aid training be guided by utilitarian endpoints in which many patients might benefit by an intervention that harms some, or even worse, harms many patients and benefits few? When evaluating the application of PBI to Crotalinae envenomations, the science is incomplete. Randomized, prospective, controlled, studies of PBI in human *Crotalinae* envenomations have not been performed. Our current state of knowledge comes primarily from animal models and a few studies in neurotoxic snakebite, where local tissue injury is not the major concern. This is an entirely different clinical problem to that posed by *Crotalinae* envenomations, where local tissue injury predominates. Furthermore extrapolating from animal models to humans can be problematic, especially when animal studies have used fatality from systemic effects – rather than tissue injury – as a primary end-point.

The data on tissue injury in animal studies is limited, but a porcine study demonstrated that tissue pressures in a range that would, in other contexts, result in the consideration of fasciotomy, and which might result in ischemic injury, can occur from PBI. 11 Recent studies in humans have demonstrated that both trained and lay individuals applied PBI that resulted in either ineffective or tissue pressures in the same range. 12 – 14 Finally, the porcine study of Crotalinae envenomation used in support of the AHA/ARC guidelines 2 actually drew the opposite conclusion, stating: “On the basis of our findings, we cannot recommend pressure immobilization widely for viper envenomation … . ” 11 Thus, the existing science points away from adoption of PBI in Crotalinae envenomation rather than towards it. Given that 98% of North American venomous snakebites are by Crotalinae, that fewer than 0.2% of those victims die, and that virtually all have soft tissue injury, the key question is whether deploying pressure immobilization as a first aid strategy in this context will lead to a large number of people with increased and/or permanent limb injury while saving virtually no lives. 15,16 Clearly, more work needs to be done. But our interpretation of the current state of knowledge is that the potential for harm of PBI in the vast majority of Crotalinae envenomations outweighs the potential benefits. In the context of limited evidence, it is understandable that learned and well-intentioned individuals may disagree. This makes the consensus of toxicologists and envenomation specialists worldwide in opposition to the use of PBI in the pre-hospital setting all the more striking. The six organizations that endorse the Position Statement represent the mainstream medical opinion among experts on four continents. There is currently strong consensus that this technique should not be promulgated or taught in areas where non-neurotoxic snakebite predominates. Thus, in North American Crotalinae snakebite, the evidence for PBI would be more properly graded as Class III: “conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases, may be harmful.”3 In response to criticisms from members of the clinical toxicology community, the AHA and the ARC have acknowledged that their guideline regarding snakebite does not define the snake groups, geographic locations, and individual circumstances in which PBI might be applicable, and also that the data regarding PBI in *Crotalinae* envenomation are limited and insufficient to deem PBI safe and effective. They are planning to clarify the guideline. For future guidelines, content experts from the Position Statement-sponsoring organizations will be invited to assist in the writing. 17 We applaud the AHA and ARC for their evidence-based approach and their ongoing process of review and clarification. We agree with the conclusions of the Position Statement: “The use of pressure immobilization for the pre-hospital treatment of North American Crotalinae envenomation is not recommended.”1

In the absence of definitive data on much of the prehospital management of *Crotalinae* snakebite, the following recommendations are based on the best available evidence, as well as expert consensus: 18,19
1. Get to a safe distance away from the snake.
2. Remove jewelry and loosen tight-fi tting clothing.
3. Loosely splint or otherwise immobilize the extremity in a functional position.
4. As a default option, maintain the bitten extremity in a neutral position with regard to the heart. Other potential actions should be guided by an experienced clinician.
5. Get to a hospital, preferably transported by an EMS provider. In general, supine positioning will prepare providers in managing possible effects such as hypotension and/or vomiting.
6. Avoid useless and/or potentially harmful interventions, such as tourniquets, incision, suction, cryotherapy, or electric shock.

**Declaration of interest**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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# Additional Abstracts (#298 – 341)

**298. Identification and Phylogenetic Analysis of *Tityus pachyurus* and *Tityus obscurus* Novel Putative Na+-Channel Scorpion Toxins.**

Jimmy A. Guerrero-Vargas[1], Caroline B. F. Mourão[1], Verónica Quintero-Hernández[2], Lourival D. Possani[2], Elisabeth F. Schwartz[1].
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**Background**: Colombia and Brazil are affected by severe cases of scorpionism. In Colombia the most dangerous accidents are caused by *Tityus pachyurus* that is widely distributed around this country. In the Brazilian Amazonian region scorpion stings are a common event caused by *Tityus obscurus*. The main objective of this work was to perform the molecular cloning of the putative $Na^+$-channel scorpion toxins (NaScTxs) from *T. pachyurus* and *T. obscurus* venom glands and to analyze their phylogenetic relationship with other known NaScTxs from *Tityus* species. **Methodology/Principal Findings**: cDNA libraries from venom glands of these two species were constructed and five nucleotide sequences from *T. pachyurus* were identified as putative modulators of $Na^+$-channels, and were named Tpa4, Tpa5, Tpa6, Tpa7 and Tpa8; the latter being the first anti-insect excitatory beta-class NaScTx in *Tityus* scorpion venom to be described. Fifteen sequences from *T. obscurus* were identified as putative NaScTxs, among which three had been previously described, and the others were named To4 to To15. The peptides Tpa4, Tpa5, Tpa6, To6, To7, To9, To10 and To14 are closely related to the alpha-class NaScTxs, whereas Tpa7, Tpa8, To4, To8, To12 and To15 sequences are more related to the beta-class NaScTxs. To5 is possibly an arthropod specific toxin. To11 and To13 share sequence similarities with both alpha and beta NaScTxs. By means of phylogenetic analysis using the Maximum Parsimony method and the known NaScTxs from *Tityus* species, these toxins were clustered into 14 distinct groups. **Conclusions/Significance**: This communication describes new putative NaScTxs from *T. pachyurus* and *T. obscurus* and their phylogenetic analysis. The results indicate clear geographic separation between scorpions of *Tityus* genus inhabiting the Amazonian and Mountain Andes regions and those distributed over the Southern of the Amazonian rainforest. Based on the consensus sequences for the different clusters, a new nomenclature for the NaScTxs is proposed.

**Keywords:** *Tityus pachyurus, Tityus obscurus*, NaScTx

**299. Chemical and Biological Characterization of Ap1a: a New Toxin Isolated from the Venom of the Brazilian Spider, *Acanthoscurria paulensis* (*Theraphosidae*).**

Caroline B. F. Mourão[1], Mari D. Heghinian[2], Eder A. Barbosa[3], Frank Marí[2], Carlos Bloch Jr[3], Rita Restano-Cassulini[4], Lourival D. Possani[4], Elisabeth F. Schwartz[1].
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**Background:** Spider venoms are complex mixtures of molecules which have raised interest in prospecting new drugs and pesticides due to their neurotoxic potential. Nevertheless, few studies are carried out with tarantula toxins, especially with species found in Brazil. The present study aimed to characterize chemically and biologically the first peptide toxin isolated from *Acanthoscurria paulensis* tarantula venom. **Results/Discussion:** The Ap1a toxin eluted with 41% acetonitrile in the crude venom

fractionation by RP-HPLC and was further purified. It showed 48 amino acid residues, with six cysteines, and an experimental monoisotopic molecular mass of 5457.79. Its putative sequence presented a signal peptide and pro-peptide containing 23 and 27 amino acid residues, respectively. The mature peptide presented 60 to 84% identity with toxins from the HWTX-II family. Although, unlike the structural pattern proposed for these toxins, Ap1a presented an arrangement of disulfide bonds typical of the ICK motif, which is also shared by the TxP1 toxin: $C_I$-$C_{IV}$, $C_{II}$-$C_V$, $C_{III}$-$C_{VI}$. This arrangement was identified by MS/MS sequencing of the ions obtained after digesting the peptide with pepsin and trypsin and also of their reduced forms. The Ap1a induced a dose-dependent and reversible paralytic effect in *Spodoptera frugiperda* caterpillars, with and $ED_{50}$ of 13.01±4.21 µg/g at 8h after injections. In a *Drosophila melanogaster* Giant Fiber circuit *in vivo* assay, Ap1a (0.23-4.60 pmol/fly) reduced both the amplitude and frequency of responses from GF-TTM and GF-DLM pathways, indicating a possible mode of action at the *Drosophila* neuromuscular junction, which is mediated by glutamatergic receptors. The Ap1a was also lethal to mice (30 µg/animal by intracranial route), causing hypermotility with circular and jump movements and generalized tonic seizures with *status epilepticus* and death between 25 and 35 min. These effects were similar to those reported with the i.c.v. administration of NMDA, a glutamatergic agonist. The Ap1a (1 µM) did not alter the response induced by acetylcholine on the rhabdomyosarcoma cells preparation, and presented no statistically significant effects on $hNa_v1.2$, $hNa_v1.4$, $hNa_v1.5$ and $hNa_v1.6$ channels. **Conclusions:** This study provided the chemical and partial biological characterization of the first peptide isolated from *A. paulensis* venom. It is toxic to both insects and mammals and seems to affect the glutamatergic neurotransmission, although more studies are needed in order to define its exact molecular target. Due to its unique sequence and cysteine pairing within the HWTX-II family, the Ap1a is a significant contribution to the structure-function study of this family of toxins.
**Keywords:** spider venom, Acanthoscurria, *Theraphosidae*, HWTX-II family, Drosophila Giant Fiber assay

**300. Toxinological Point of View of Metalloproteinase-like Enzymes of Jellyfish Venoms**

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Although antivenom therapy is a primary treatment of jellyfish envenomation especially for the patients stinged by *Chironex fleckeri* box jellyfish, many questions remain about their effectiveness in the clinical application. Previously, we have reported that most if not all of the Scyphozoa jellyfish venoms contain multiple components of various metalloproteinases, which largely contribute to the cytotoxic activity. Interestingly, all the examined Scyphozoan jellyfish venoms showed gelatinolytic, caseinolytic, and fibrinolytic activities, each of which contains a multitude of enzyme components with molecular weights between 17 and 130 kDa. Further, it has also been reported that there is a positive correlation between the inflammatory reaction of dermal tissues and their tissue metalloproteinase activity. Based on this, the use of metalloproteinase inhibitors appears to be a promising therapeutic alternative for the treatment of jellyfish envenomations. In the present study, we have investigated the ability of tetracycline (a well known matrix metalloproteinase inhibitor) to reduce or prevent the dermonecrotic lesion induced by *Nemopilema nomurai* jellyfish venom (NnV) using *in vitro* and *in vivo* models. HaCaT (human keratinocyte) and NIH3T3 (mouse fibroblast) incubated with increasing concentrations of venom showed a decrease in cell viability, which is associated with an increased expression of metalloproteinase-2 and -9. This result suggests that the use of metalloproteinase inhibitors, such as tetracycline, may prevent the jellyfish venom-mediated cell death. *In vivo* experiments showed that comparing with venom-alone treatment, tetracycline pre-mixed NnV demonstrated a significantly reduced progression of dermonecrotic lesion upon the inoculation onto rabbit skin. In addition, we have

also examined the protective effect of tetracycline compounds against jellyfish venom-induced lethality in mice. The preincubation of the venom with a tetracycline significantly reduced the toxicity as demonstrated by delaying the time to death of the venom-injected mice. The present findings show that tetracycline may be an effective therapeutic agent for the treatment of jellyfish envenomation.
**Keywords:** jellyfish, venom, toxicity, inhibition, tetracycline, matrix metalloproteinase

**301. ELISA-based Detection of Ricin in Blood and Feces of the Rat following Non-Lethal Exposure.**
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**Background:** Early confirmation of ricin poisoning with the aid of diagnostic devices permits early intervention and passive antibody therapy, which is critical in minimizing adverse effects associated with ricin intoxication. However, commercially available ricin immunoassay test kits are intended for use on environmental samples and none has been marketed for clinical applications. We have developed a sandwich ELISA and validated its ability to detect trace levels of ricin toxin in biological samples from the rat oral gavage ricin challenge model. **Method:** The assay utilizes two mouse monoclonal antibody as capture antibodies as well as a biotinylated rabbit polyclonal antibody as the detecting antibody. Each assay takes 100 minutes and the Limit of Detection (LOD) for ricin is defined as a Signal-to-Noise Ratio (S/N) of 2.00. To obtain biological samples, adult Wistar rats were administered, by oral gavage, a single challenge dose of crude ricin. Samples were collected once every four hours for the first day and then daily for the next 5 days. Venous tail blood was collected in vials containing EDTA while ricin was extracted from feces following solubilisation in phosphate buffer saline (50%w/v) and centrifugation. **Results:** All rats survived the entire 5 experimental days following oral ricin challenge. Ricin was detected in blood samples between 4 (75%, n=8) to 16 hours (25%, n=4) whereas in feces, ricin was detectable in all samples from 12 hours till 5 days (n=8) post challenge. In feces, high levels of ricin could be detected ($S/N_{max}$=60.00) while low levels of ricin toxin were detected in positive blood samples ($S/N_{max}$=2.90). The sensitivity of our ELISA kit was found to be 1.25ng/ml of ricin in blood. **Conclusion:** We have developed an ELISA kit that is sensitive and sufficiently robust to detect ricin toxin in both whole blood and feces following a non-lethal ricin challenge. This animal study suggested a diagnostic window starting as early as 4 hours to as late as 5 days post ingestion, indicating that both blood and feces should be the analytical samples of choice when poisoning by ricin ingestion is suspected. As the initial symptoms of oral ricin intoxication mimic those of food poisoning, this ELISA kit will be useful in picking up ricin poisoning from amongst common causes of food poisoning. The wide diagnostic window offered by this ELISA kit will allow medical professionals to correctly determine ricin poisoning during the course of illness and as a forensic tool.
**Keywords:** crude ricin, ricin ingestion, diagnostic kit, ELISA, whole blood, feces, limit of detection, diagnostic window

**302. The Cystine Knot is a Conserved Structural Motif in Linear and Cyclic Plant Toxins.**
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**Background**: The cystine knot motif comprises three intertwined disulfide bonds and appears to have evolved as a privileged framework in numerous toxins. Cyclotides are plant-derived proteins that have a unique cyclic cystine knot topology and are remarkably stable. Their natural function is defense against insect pests, but they have a diverse range of pharmaceutically important activities, including anti-HIV

activity, and have also attracted interest as templates in drug design. Here we report an unusual biosynthetic origin of a precursor protein of a cyclotide from the butterfly pea, *Clitoria ternatea*, a member of the Fabaceae plant family. Unlike all previously reported cyclotides, the domain corresponding to the mature cyclotide is embedded within an albumin precursor protein. **Methods**: We confirmed expression and processing of the cyclotide encoded by the Cter M precursor gene following extraction from *C. ternatea* leaf and sequencing by tandem mass spectrometry. NMR spectroscopy was used to determine the 3D structure of Cter M. Toxicity was assessed in insect larvae feeding trials and in hemolytic assays. **Results**: The Cter M sequence was verified by chemical synthesis and the peptide was found to adopt a classic knotted cyclotide fold as determined by NMR spectroscopy. Seven additional cyclotide sequences were also identified from *C. ternatea* leaf and flower. Cter M displayed insecticidal activity against the cotton budworm *Helicoverpa armigera* and bound to phospholipid membranes, suggesting its activity is modulated by membrane disruption. **Discussion**: All previous cyclotides were found to be encoded within dedicated precursors. Here we report a novel chimeric precursor for Cter M where the cyclotide domain replaces a linear cystine knot protein, PA1b, which is toxic to weevil pests. The discovery provides an example of "mixing and matching" two toxic defence proteins that have no sequence homology but have a conserved cystine knot core. **Conclusion**: The discovery of cyclotides in legume plants is significant because the Fabaceae is the third largest family of flowering plants and many Fabaceous plants are of huge significance for human nutrition. Knowledge of Fabaceae cyclotide genes should enable the production of modified cyclotides in crop plants for a variety of agricultural or pharmaceutical applications, including plant-produced designer peptide drugs.
Reference: Poth A G, Colgrave M L, Lyons R E, Daly N L, Craik D J: Discovery of an unusual biosynthetic origin for circular proteins in legumes. *PNAS* (2011) **108**, 10127-10132.
**Keywords:** cyclotides, plant toxins, cyclic peptides

**303. Calcins as High-Affinity Probes of Calcium Release Channels/Ryanodine Receptors**
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**Review:** The ryanodine receptor (RyR), recognized as the $Ca^{2+}$ release channel of the sarcoplasmic reticulum (SR) of cardiac and skeletal muscle, provides the majority of $Ca^{2+}$ needed for contraction. Precise regulation of $Ca^{2+}$ is essential to normal cardiac function. Abnormal $Ca^{2+}$ handling by RyRs can lead to arrhythmias, and has been implicated in the pathogenicity of Cathecholaminergic Polymorphic Ventricular Tachycardia (CPVT) and Sudden Death. Thus, an array of molecular tools is desirable to investigate the structure and function of RyRs in normal and disease states. Our laboratory previously identified Imperatoxin A (IpTxa) as such a probe due to its high-affinity, specific interaction with RyRs. IpTxa induces RyR hyperactivity, which appears to bear similarity to abnormal RyR activity associated with CPVT. This study characterizes the RyR-modulating properties of IpTxa to ascertain whether studies employing this toxin can be used to simulate pathological $Ca^{2+}$ signaling observed in CPVT, thereby enabling a better understanding of the etiology of the disease. Furthermore, hadrucalcin (HdCa) has been identified as a relative of IpTxa by virtue of a shared structural motif and by their RyR-activating biological activity. The experiments in this study were designed to test the general hypothesis that IpTxa and HdCa penetrate cellular membranes and bind RyRs to elicit acute, enhanced $Ca^{2+}$ release. Further, natural sequence variation between IpTxa, HdCa and other members of the calcin family offers an opportunity to test current hypotheses about structural characteristics that impart RyR-binding and cell-penetrating ability to these unique toxins. RyR activation by IpTxa results in enhancement of SR $Ca^{2+}$

release, which, in intact cells, is characterized by 1) increase of $Ca^{2+}$ transient amplitude, 2) increased diastolic signal, 3) increased $Ca^{2+}$ spark frequency and spatiotemporal parameters, and 4) bursting acitivty and spontaneous contractions. We demonstrate that HdCa, too, is a competent RyR activator and cell-penetrator despite critical differences in sequence and globular structure. HdCa increases [$^3$H]ryanodine binding to sarcoplasmic reticulum vesicles, induces subconducting states in RyR channels, and evokes rapid enhancement of SR $Ca^{2+}$ release in intact ventricular cardiomyocytes. Our study demonstrates that calcins are powerful, specific RyR agonists with tremendous potential not only for the study of $Ca^{2+}$ handling in various cell types, but also for intracellular delivery of various cargoes, including fluorescent probes and drugs for the treatment of arrhythmogenic disease.
**Keywords:** calcins, ryanodine receptors, imperatoxin

**304. Snake venom metalloproteinases; Structure, function and relevance to the mammalian ADAM/ADAMTS family proteins.**
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Metalloproteinases are among the most abundant toxins in many Viperidae venoms. Snake venom metalloproteinases (SVMPs) are the primary factors responsible for hemorrhage and may also interfere with the hemostatic system, thus facilitating loss of blood from the vasculature of the prey. SVMPs are phylogenetically most closely related to mammalian ADAM (a disintegrin and metalloproteinase) and ADAMTS (ADAM with thrombospondin type-1 motif) family of proteins and, together with them, constitute the M12B clan of metalloendopeptidases. Large SVMPs, referred to as the P-III class of SVMPs, have a modular architecture with multiple non-catalytic domains. The P-III SVMPs are characterized by higher hemorrhagic and more diverse biological activities than the P-I class of SVMPs, which only have a catalytic domain. Recent crystallographic studies of P-III SVMPs and their mammalian counterparts shed new light on structure–function properties of this class of enzymes. My talk will highlight these structures, particularly the non-catalytic ancillary domains of P-III SVMPs and ADAMs that may target the enzymes to specific substrates.
(Reference: S. Takeda *et al*. "Snake venom metalloproteinases: Structure, function and relevance to the mammalian ADAM/ADAMTS family proteins (Review)" *Biochim Biophys Acta* **1824**, 164-176 (2012))
**Keywords:** snake venom, metalloproteinase, disintegrin, SVMP, ADAM, ADAMTS

**305. Characterization of the most dangerous snake venoms of Morocco.**
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**Background:** Ophidian envenomation is a serious public health problem in Africa. More than 20,000 deaths per year are registered and 400,000 victims of envenomation develop severe and permanent functional sequelae. In Morocco, snake bites are frequent and of greater severity in children. They occur mostly in rural areas. The incidence of these bites remains poorly understood and largely underestimated due to the absence of a national registry, as well as the non-medical care of a significant proportion of envenomed patients, using only traditional treatment methods. Better characterization of the molecular mechanisms of Morocco snake venoms is needed to develop new approaches to patient treatment. **Methods**: We investigated the biological properties of the venom of those snakes most endemic to Morocco: *Cerastes cerastes* (Cc), *Vipera lebetina* (Vl), *Naja haje* (Nh), and we studied the immune cross reactivity between Cc and Vl venoms and *Bitis arientans* (Ba) venom, with the main objective to ultimately produce an effective antivenom. **Results**: The Cc venom is the most toxic, with an

$LD_{50}$ of 5.75 µg/mouse; Vl venom displays an $LD_{50}$ that average 5.97 µg/mouse. However, Ba venom is approximately 10 fold less toxic ($LD_{50}$ of 52.54 µg/mouse). Both Cc and Vl venoms contain three major classes of proteins with relative molecular weights (MW) of approximately 14, 30 and 67 KDa. Nh venom profile reveals protein bands of lower MW with ranging values from 21 KDa to less than 10 kDa (Figure.1). Interestingly, both Cc and Vl venoms possess hemorrhagic activities. This activity is dose dependent and proportional to the injected dose (figure.2). Cc and Vl are characterized by a high phospholipase A2 activities and their ability to degrade the α and γ chains of fibrinogen (figure.3). They display a very low proteolytic activity with the casein test. After injection in mice, Cc and Vl venoms induce myonecrosis in skeletal and cardiac muscles that is most likely the consequence of a direct action of myotoxins and an indirect action of hemorrhagic components in the venoms (Figure.4). In mice, this myonecrosis produces a decrease of creatine phosphokinase concentration in the muscle and its increase in the serum. Nh venom did not display any detectable hemorrhagic activity. We demonstrated the presence of edema, myotoxicity, very low proteolytic and phospholipase activities, and an absence of fibrinogenolytic activity with this venom. Table 1 show that Cc venom is a good immunogen and induces high protective antibodies against Vl and Ba venom antigens, higher than that of the antivenom produced against the Vl venom. Discussion: Phospholipase A2 and fibrinogen activities were an important characteristic observed with Cc and Vl venoms. Cc and Vl venoms induce myonecrosis in skeletal and heart muscles, likely from a direct myotoxin effect and indirect hemorragin activity. The myonecrosis produced a reduction of CPK concentration in muscle and its increase in serum. The data obtained from in vivo neutralization clearly indicate that both monovalent Cc and Vl antivenoms contain a high ratio of specific immunogenic antibodies to Cc, Vl and Ba venom components, with neutralization. Interestingly, we noticed a total absence of pro-coagulant activity in these venoms, in contrast to *Colubridae* family venoms. **Conclusions**: Our investigation demonstrated that viper venoms of Morrocco contain homologous proteins displaying hemorrhagic (39, 67 and 100 kDa), caseinolytic (72 to 74 kDa), phospholipasis (13 kDa), anticoagulant, myonecrotic (75 and 100 kDa) and edematous (29 to 39 kDa) activities. There is high immunogenicity of Cc venom, and a horse antivenom derived from it is able to protect against Cc, Vl and Ba whole venoms.

**Table.1**. Determination of effective doses ($ED_{50}$) in mouse

| ED50 in µl (95% c.i) | | |
|---|---|---|
| Venom | *Cc* antivenom | *VL* antivenom |
| *Cerastes cerastes (Cc)* | **18,7** | 78 |
| *Macrovipera libetina (VL)* | 62,4 | **48,3** |
| *Bitis arientis (Ba)* | 84,3 | 117,3 |

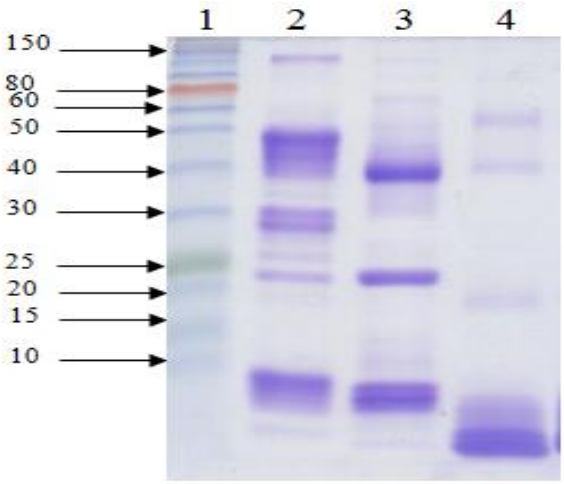


**Fig. 1.** Electrophoretic separation. Lane 1: molecular mass markers (KDa); Lane 2: *Cc* venom; Lane 3: *Vl* venom and Lane 4: *Nh* venom.

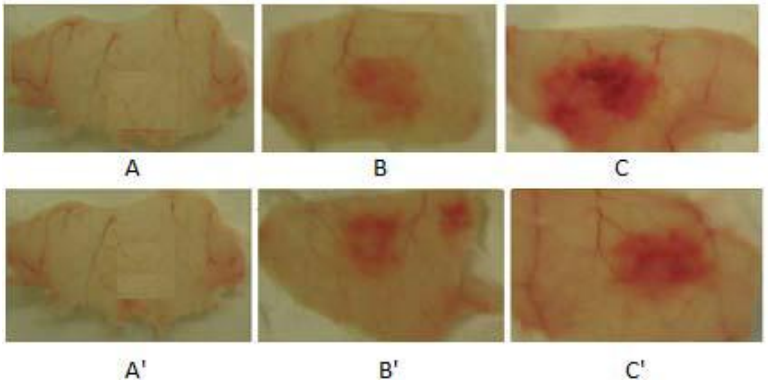


**Fig. 2.** Hemorrhagic activity of Cc (A, B, C, D) and Vl venoms (A', B', C', D') of the "Skin-Test". This activity is dose dependent. A: control, B: 5 µg, C: 10 µg, D: 20 µg of injected venom.

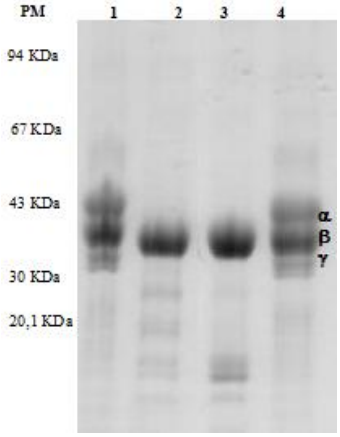


**Fig. 3.** Fibrinogen degradation profile. Lane 1: *Naja haje*; Lane 2: *Cerastes cerastes*; Lane 3: *Vipera*

*lebetina* venoms and lane 5: fibrinogen

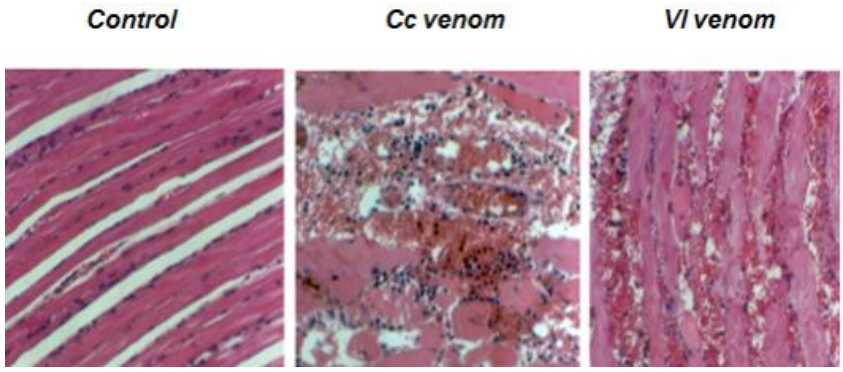


**Fig.4.** Effect of sublethal dose of Cc and Vl (7 µg/20g mice) venoms on the intestinal tissue.
**Keywords:** snake venom, toxicity, hemorrhage, biological activities, cross reaction

**306. Toxicon: A Short History of 50 Years of the Official Journal of the International Society on Toxinology.**
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**The Past:** The first edition of Toxicon was published by Pergamon Press in October 1962 as the official journal of the newly formed International Society on Toxinology. It contained four research articles and two short communications, 47 pages in all. In contrast, the first issue of the current year (volume 59) contained 25 research papers, requiring over 200 pages. The frequency of issues has also increased enormously over Toxicon's life: from four issues in 15 months with volume 1 to 16 issues per year since 2003. This reflects the growth in scientific activity an dclinical interest in topics related to venoms and toxins, but it also reflects the quality of the articles published by Toxicon: over the years, there have been several toxin-related journals started, but none have lasted long. **The Present:** Toxicon now includes full-length research papers, short communications, extensive reviews, topical mini-reviews and, most r4ecently, a new section on 'classic toxins'. There are also special issues around particular themes such as toxins in drug discovery. With the move to electronic handling of manuscripts and publications being made available on the web, the speed of processing of papers in Toxicon has increased dramatically and the awareness of Toxicon articles has heightened. Accepted articles appear on the web within three weeks, and there are almost half a million downloads of Toxicon articles from the web each year.
**Keywords:** toxinology history, Toxicon, publishing

**307. Comparative Snake Venom-Gland Transcriptomics Based on Illumina Sequencing.**
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**Background:** Snake venoms have significant impacts on human populations through the morbidity and mortality associated with snakebites and as sources of drugs, drug leads, and physiological research tools. Genes expressed by venom-gland tissue, including those encoding toxic proteins, have therefore been sequenced but typically only with the relatively sparse coverage that results from the low-throughput sequencing approaches available. **Results:** We sequenced the venom-gland transcriptomes

of the eastern diamondback rattlesnake (*Crotalus adamanteus*) and the timber rattlesnake (*C. horridus*) by means of Illumina technology (RNA-seq), generating approximately 100 million pairs of 100-nucleotide reads for each species. We developed and applied novel, computationally efficient approaches for transcriptome analysis, including *de novo* assembly, partial-transcript completion, and characterization of alternative splicing patterns without a reference genome. We found dramatic differences in the expressed toxins for our two congeneric species; *C. adamanteus* expressed patterns typical of type I rattlesnake venoms with high levels of snake-venom metalloproteinases, but *C. horridus* showed no significant metalloproteinase expression and instead had venom primarily composed of phospholipase A2's and serine proteinases, consistent with type II venom. In addition to the toxin sequences, we annotated approximately 3,000 nontoxin transcripts with full-length coding sequences from the venom glands of each species. We explored *dN/dS* ratios as indicators of toxic function. **Conclusion:** We have clearly demonstrated the ease of characterizing venom-gland gene expression on the basis of *de novo* assembly of Illumina sequences from cDNA libraries derived from snake venom glands. This approach is more cost effective than 454 pyrosequencing and traditional Sanger sequencing, and our extensive database of sequences will facilitate similar work in other species. The differences in toxin content between *C. adamanteus* and *C. horridus* have no clear ecological explanation, but the venom of *C. horridus* is known to range, according to geographic distribution, from extremely hemorrhagic to neurotoxic. The source population of our sequenced animal is presumably dominated by the neurotoxic venom type, and such venom expressed by such large snakes with commensurately large venom yields makes these animals potentially among the most dangerous snakes in the United States, warranting an in-depth mapping of the distributions of the neurotoxic populations.
**Keywords:** snake, venom, transcriptome

**308. Comparison between two methods of scorpion venom milking from Morocco.**
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**Background:** A number of ways of collecting venom from scorpions have been described, including manual extraction, electric stimulation and maceration. A technique may be chosen for its ability to maximize venom recovery, for consistency, purity, or other considerations. To obtain venom that is free of hemoplymph contaminants and can be used for production of specific neutralizing antibodies for antivenom manufacture, milking or electrical stimulation are possible considerations. **Methods:** This paper compared two methods used successfully in a large-scale program for the collection of scorpion venoms. Both methods were tested for the milking of adult scorpions: manual and electrical stimulations respectively. **Results:** Our biochemical investigations showed that venoms collected by manual stimulation have an additional band of 75 kDa which is absent in the electrophoretical venom profile collected by electric stimulation. The absorption profiles show that the venoms obtained by manual method have two absorption peaks regions at (220-380 nm) and at (520-600 nm), which are absent in the venoms obtained by electric stimulation. Toxicity of venom obtained by manual method was lower than that of venom obtained by electric stimulation. Therefore, variability in venom toxicity depends upon the method of venom extraction. Venom obtained by manual method, adopted by Pasteur Institute of Morocco, showed lower toxicity. Our result revealed that hemocyanin retrieved with manually collected venom is a contaminant protein of hemolymph origin. **Discussion:** We have demonstrated that there is a high hemocyanin contamination of venom obtained by the manual method adopted by the Pasteur Institute of Morocco. Venom obtained by electric stimulation has greater toxicity and a 3-fold greater $DL_{50}$ than venom collect manually. The corresponding antivenom produced using manually collected venom contains a high percentage of specific antibodies for hemolymph

contaminants and fewer specific antibodies neutralizing scorpion toxins. **Conclusion:** We concluded that electrical stimulation of venom is preferred in the production of scorpion antivenom, resulting in a higher volume of venom, higher potency, and increased purity, which results in an antivenom with a higher degree of protection against envenomation.

**309. Cytotoxic effects of Iranian Lebetina Snake Venom on Human Umbilical Vein Endothelial Cell.**

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**Introduction:** Angiogenesis consist of a complex process which is necessary for developing the new capillaries from pre-existing vessels, plays a critical role in a variety of normal physiological & pathological conditions events. Snake venoms are complex mixtures of biologically active proteins, peptides, metal ions and organic compounds, which have evolved to favor the survival of the snake in its particular environment. Also they are highly specific and have great affinity for different crucial and essential functional organization of cells and tissues. In this study in order to isolation of component involved in angiogenesis, we examined the cytotxicity effect and viability of lebetina snake venom on human umbilical vein endothelial cell lines. **Material & methods:** The effect of lebetina snake venom on proliferation of human umbilical vein endothelial cell line was determined by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) microculture tetrazolium viability assay. The cells were exposed to different concentrations (1, 5, 10, 20, 40, 80. and 120 µg/ml) of lebetina venom. Following treatment, the cells were exposed to Tetrazolium dye (5mg/ml) for 3 h. The formation of the purple coloured formazan complex was dissolved by adding DMSO (100 µl) and read at 562 nm using ELISA microtiter plate reader to determine the inhibitory concentration. **Result & Conclusion:** $IC_{50}$ About 50% increase in cell killing was seen when the dose of lebetina snake venom was 15 raised from 5 to 20 µg/ml. At a concentration of 40 µg/ml, 81.841% cytotoxicity was recorded. The $IC_{50}$ value of lebetina venom was 15.73 µg/ml after 72h of incubation. In this study, it was observed that lebetina venom induces a concentration dependent inhibition of HUVEC with an $IC_{50}$ value of 5 µg/ml after 72h of incubation. The purification and characterization of the lebetina venom along with researches are needed to give some additional approaching into the *in vivo* cytotoxic effect of the venoms with a view to obtaining functional antiangiogenic agent.

**Keywords**: antiangiogenic, snake, cytotoxicity

**310. Analysis of some Biological Effects of *Hemiscorpius lepturus* Scorpion Venom from Khuzestan Province in Iran.**

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**Background:** Scorpion envenomation is a public health problem in the south of Iran. Six medically important scorpion species exist in Iran. Among them *Hemiscorpius lepturus* is the most dangerous species, accounting for 95% of the mortality of all hospitalized scorpion sting cases. The venom from *H.*

*lepturus* is primarily a cytotoxic agent and has hemolytic dermonecrotic, nephrotoxic, and to some extent, hepatotoxic activities. In the present research we analyzed some biological activities of crude venom to understand its toxic properties. **Methods:** The venom was extracted by electric stimulation from the scorpions. The amount of 2 mg of crude venom was subjected to 2DE to evaluate the number of protein spots on the gel. Hemolytic activity performed on 2% of human blood cells that was obtained from healthy donor and citrate buffer was used as anticoagulant. Phospholipase A2 activity was performed by using *H. lepturus* venom on phosphatidylcholin as substrate. In order to study protease activity of the venom, gelatin SDS-PAGE was used. Local reaction and dermonecrotic activity was assayed by intradermal injection of 0.1 ml saline solution containing 25, 50, 100 and 150 µg of crude venom in rabbit dorsal skin after 72 h. **Results:** In the gel of 2DE, 90 protein spots were detected. The number of 46 spots below 17KDa, 4 spots between 21 and 31 KDa, 17 spots in 31-36KDa, 6 spots in 43KDa, 9 spots in 66-76KDa and 8 spots above 116KDa were observed. Hemolytic activity was determined as dose depended and complete lysis was detected with 150 µg of crude venom with 100% hemolysis after 1h incubation at 37°C. PLA2 activity of crude venom was determined by using colorimetric assay. The amount of 700 ng of the venom had 80% activity on phosphatidylcholin substrate. *H. lepturus* venom showed gelatinase activity in the protein band at 55 KDa. Histopathological study of dermonecrotic lesions showed necrosis of epidermal and dermal collagenous fibers surrounded by dense infiltration of inflammatory cells composed of many PMNs and few lymphoplasmacytic cells. **Discussion:** The venom of *Hemiscorpius lepturus* contains highly cytotoxic agents. The existence of PLAs and other enzymatic activities of the venom detected in this research can account for dermonecrosis and hemolysis activity observed clinically following envenomed by this species. **Conclusions:** Based on 2DE results, more extensive analytical studies are necessary to further characterize the main toxins responsible for the mortality in patients envenomed by *H. lepturus*.

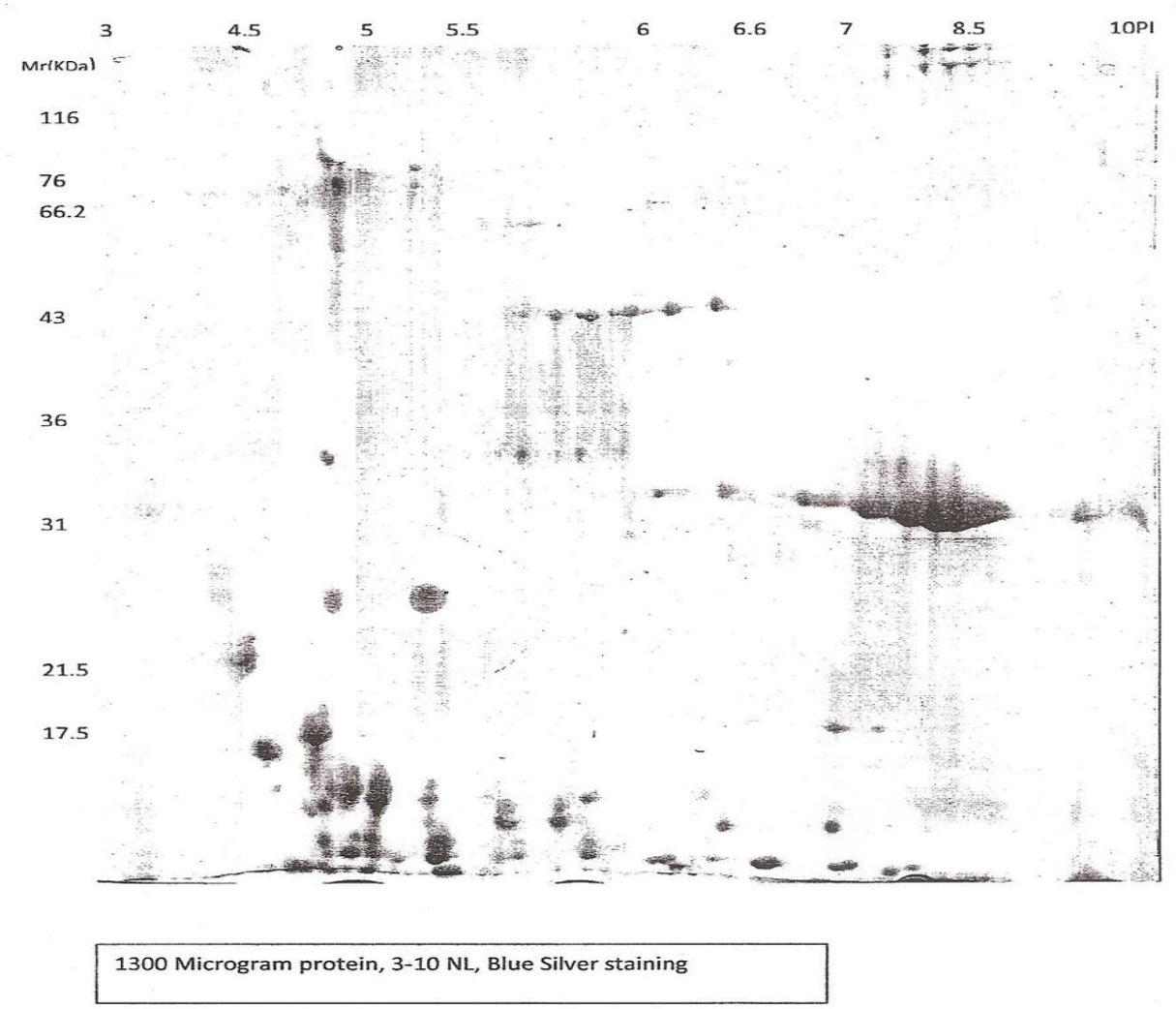


Fig 1. 2DE gel of the venom of Hemiscorpius lepturus venom. The amount of 2 mg of the crude venom was injected to the gel, and the gel was stained with Coomassie G-250 dye.

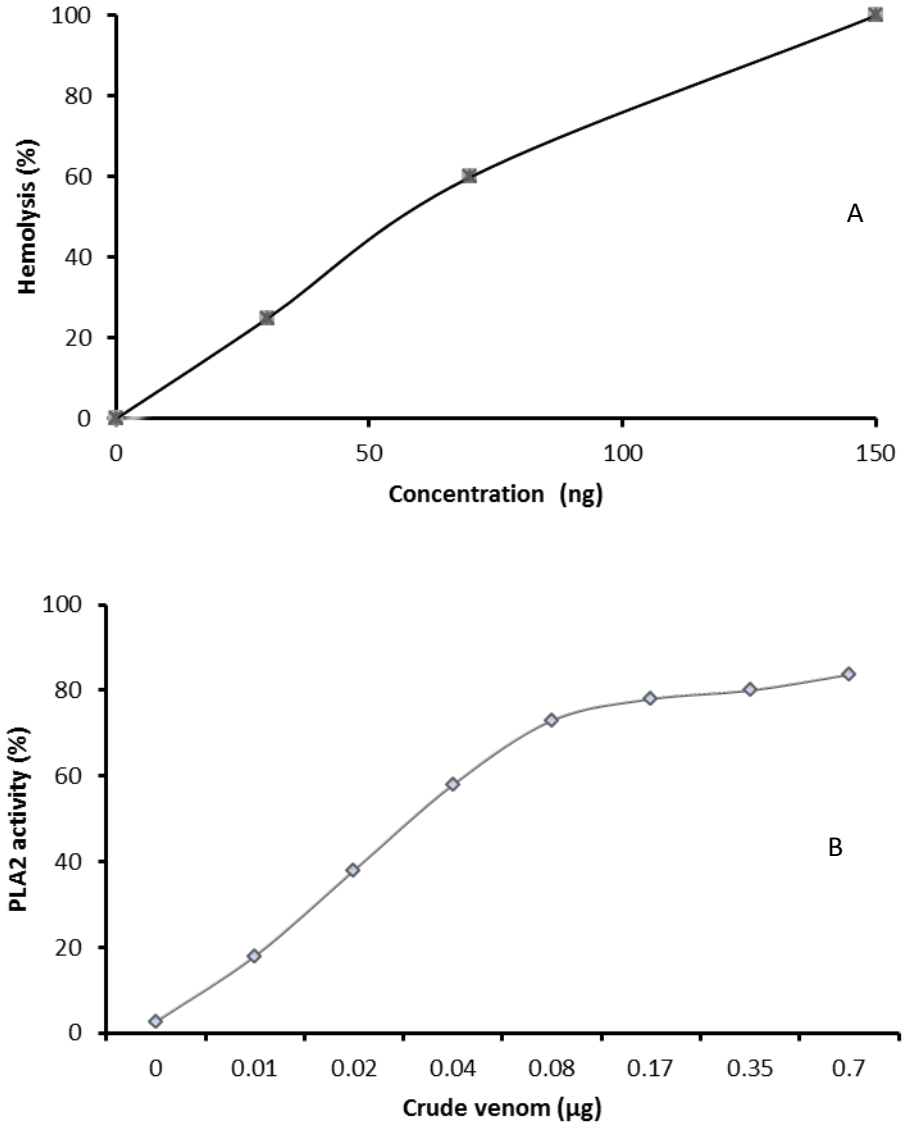


Fig. 2: Graphic presentation of the (A) hemolysis percentage of washed human red blood cells against HL venom concentration, (B) PLA2 activity against nano grams of HL crude venom.

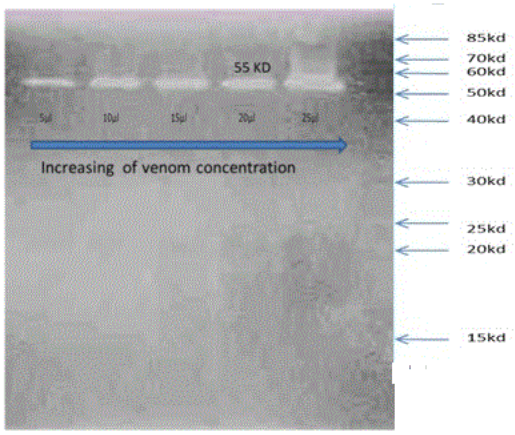


Fig. 3: Gelatinase activity of the HL venom on 15% SDS-PAGE containing respective substrate and analyzed by using zymography assay.

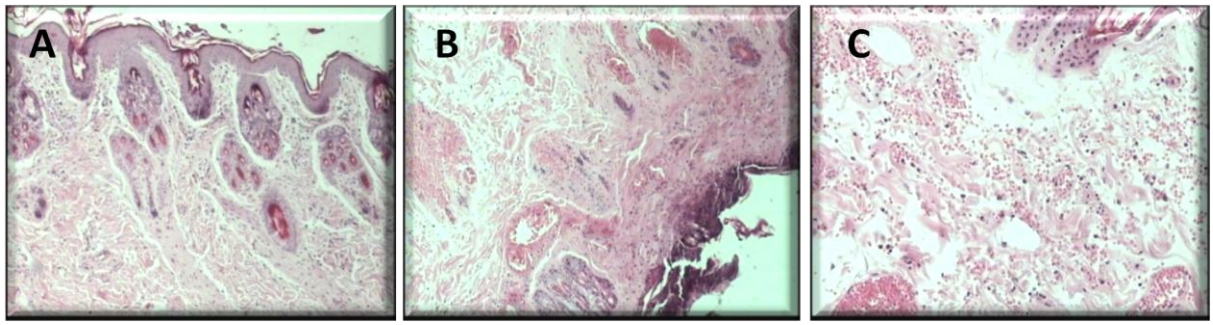


Fig. 4. Histopathology study of rabbit skin intradermally injected by H. Lepturus venom with H&E, Gx400. (A) Negative control injected with normal saline. (B) Histopathological features of rabbit skin 72 h after venom exposure: Massive inflammatory response with edema, strike polymorphous influx in dermohypodermal vessels with dermohypodermal band, thrombosis formation and necrosis, a degeneration and necrosis of muscle fibers. (C) Diffuse of neutrophils infiltrate through the different skin layers and muscle.

**Keywords**: venom, haemolytic, dermonecrotic

**311. Use of antivenoms for the treatment of envenomation by Elapidae in Guinea, Sub-Saharan Africa.**

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**Backgroud**: The incidence of elapid envenomations in Guinea is high. Elapidae are responsible for around 15% of snakebites and 20% of envenomations. The associated case fatality rate (CFR) is estimated to fall between 15 and 27%, irrespective of treatment. **Methods**: We studied 78 neurotoxic envenomations that we divided in 3 groups: a set of patients that received only traditional or

symptomatic treatments as antivenom was unavailable, and two other groups that received Antivipmyn® Africa in two distinct protocols consisting of either 2 or 4 vials of antivenom renewed as necessary, respectively. **Results**: CFR in the first group was 9 of 33 patients (27.3%), 4 of 26 in the second group (15.4%), and 3 of 17 (17.6%) in the third. Although antivenom treatment was likely to reduce CFR, it didn't seem to have an obvious clinical benefit for the patients, even at the higher doses. While this may be related to the small sample size, it indicates a low treatment efficacy. Five species are potentially involved in these neurotoxic envenomations: *Dendroaspis polylepis*, *D. viridis*, *Naja melanoleuca*, *N. nigricollis* and, in Upper Guinea, *N. katiensis*. The venom of some of these species (particularly *D. polylepis*) could be either poorly neutralized by the antivenom and/or the therapeutic window may be very narrow. Mean delay to treatment was long (10 hours) but it was not significantly different between the patients who recovered and the patients who died, or between patients treated with antivenom and those in the first group. The clinical stage of envenomation upon arrival at the health center was also not significantly different between groups; all patients had confirmed neurological signs. **Discussion**: Interpretation of these results is complicated by the lack of systematic studies in comparable conditions that quantitatively address the efficacy of antivenom treatment in neurotoxic envenomations in Africa that could be used for reference in statistical comparisons. The apparent lack of clinical benefit may have several causes. A low neutralizing capacity by the antivenom cannot be excluded, although preclinical testing indicates a specific neutralizing potency >250 $LD_{50}$/vial against the relevant species. The administration of too low doses of antivenom seems unlikely as there is no correlation between doses and outcome, irrespective of treatment protocols. **Conclusion**: The hypothesis of a limited therapeutic window, that is, an insufficient formation of antigen-antibody complexes once toxins are bound to their targets and/or distributed beyond the reach of intravenously administered antivenom must be explored.
**Keywords:** envenomation; elapid; antivenom; Africa

**312. Epidemiology of Snakebites Reported to Poison Centers in Texas from 2002 through 2011.**
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**Background**: Texas is the second most populous state in the United States and ranks highly for reported snakebites, including native, non-native, venomous and non-venomous species. There are at least 109 species and subspecies of snakes endemic to Texas, including 14 venomous Crotalinae species and one venomous Elapidae species, the Texas coral snake. Some species of the family Colubridae found in Texas may bite but rarely cause significant envenomation effects and are not generally considered venomous. Worldwide reported epidemiology data on venomous and nonvenomous snakebites are limited by incomplete reporting. With no legal mandate to report snakebites in the US, it is considered likely, as in many other nations, that many more unreported bites occur, especially those that are not treated in a health care facility. **Methods**: The Texas Poison Center Network database from the years 2002-2011 was retrospectively analyzed for reports of bites of humans by snakes. Results: Reported snakebites revealed interesting and significant demographic and clinical features. Over the last 10 years, rates of snakebites in Texas, including those considered venomous, are increasing in number and proportion to the total reported in the US to the American Association of Poison Control Center's National Poison Data System. While over an average of over 6,600 snakebites have been reported annually in recent years, Texas' share has grown from under 7% to nearly 10% of all reported. **Discussion**: Individuals in their first decade of life accounted for the smallest and slowest growing proportion of cases than any other decade in this data set, while reports of snakebites to individuals in all decades showed increases of up to 50% overall. Although most snakebites involved adults with mild

to moderate outcomes, the overall outcome severity reports of snakebites to younger patients were classified as more severe than in adults. Of cases when sex was reported, males were more likely to have reported snakebites than females, but the ratio of males to females has decreased significantly from 2.5 to less than 2 over the past decade. Geographic distribution of bite reports by species identified correlate with historical distribution for venomous species. Bites are most common from April-September and have been trending to an earlier peak in frequency over the past decade. **Conclusions**: Reports of snakebites in Texas are increasing and the demographics and other related factors related to those bitten are changing.
**Keywords:** snakebite, Texas, epidemiology

**313. Estimating the global burden of snakebite can help to improve management.**
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**Background:** In tropical countries, the incidence of envenomation is very high due to environmental, social and economic factors that promote encounters between humans and poisonous animals. Despite the importance of this issue, the management of envenomation is insufficient, resulting in high mortality and disability. **Methods:** Many surveys have shown that the epidemiological data collection was defective and the incidence and mortality were dramatically undervalued. As a result, health authorities are unaware of the problem and underestimate its importance. In addition, health authorities are reluctant to develop strategies for the management of bites or stings by poisonous animals, give training to health personnel and provide equipment and therapeutic resources, such as antivenom. **Results:** In Africa, for example, supply of antivenoms were reduced by nearly 90% during the last 20 years, leading many manufacturers to stop production of antivenoms and many others to reduce the quality of their products to optimize production costs. In many countries, first of antivenom stocks are insufficient and, secondly, they are poorly distributed throughout the country for lack of information on the distribution of envenomations. **Discussion:** Prospective epidemiological surveys are long and expensive. Several methods, including statistical models, have been proposed to replace them with quick and cheap retrospective studies to enable health authorities to better estimate the incidence and severity of envenomations. **Conclusion:** It is proposed to improve the reporting of snake bites and scorpion stings as well as to promote both hospital and household studies to enable health authorities assessing the significance of the problem and rapidly finding effective solutions. Besides decisive contribution to the organization of management of envenomation, actual epidemiological data will be important to support advocacy for funding antivenoms which remain too expensive for the majority of the populations concerned.
**Keywords:** Africa, surveys, epidemiology, envenomations

**314. Epidemiology and Severity of Snakebite in Guinea.**
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**Background**: Snakebite is a frequent event and an important public health problem in SubSaharan Africa with poor management. **Methods**: Two epidemiological studies on snakebites were performed in Upper Guinea in the Kankan region (2005-2006) and Lower Guinea in the region of Kindia (2009-2011) to

estimate the needs for envenomation management. Over the same periods, captures of snakes were carried out by the villagers based on encounters. Clinical data were collected through surveys and community hospitals. **Results**: In Upper Guinea, 848 snakes were captured. The vipers accounted for 21.9% of the sample, with 11.2% of *Bitis arietans*, 6.5% *Causus maculatus* and 3.6% *Echis ocellatus*. Elapids represented 8.9% of the collected specimens, with 3.8% of *Naja katiensis*, 2.8% *N. nigricollis*, 2% *N. melanoleuca* and 0.3% *Dendroaspis* sp. During the two years of investigations, 226 snakebites were recorded, out of which 69 (30.5%) were indeterminate or dry bites. Viper envenomations (inflammatory, necrosis and/or hemorrhagic) involved 124 patients (54.9%) and neurotoxicity regarded 33 (14.6%). Fourteen patients died (6.2%), 9 (4%) following a neurotoxic syndrome and 5 (2.2%) after viper envenomation. Treatment was symptomatic or traditional in all patients, due to lack of antivenom. In Lower Guinea, 916 snakes were collected including 174 vipers (19%) with a majority of *C. maculatus* (12.8%) and *B. arietans* (6.1%) but no *E. ocellatus*; and 64 elapids (9.6%), with 3.8% *N. nigricollis*, 3% *N. melanoleuca*, 1.9% *D. viridis* and 0.8% *D. polylepis*. A total of 521 snakebites were registered including 175 (33.6%) indeterminate or dry bites, 302 (58%) viper envenomations and 44 (8.4%) neurotoxic envenomations. Eight patients died (1.5%), all from elapid bite. All patients in Lower Guinea received at least one dose of antivenom (Antivipmyn® Africa, Bioclon). It appears that snake sampling by this method has a poor predictive value on the risk of snakebites and specific incidence of envenomations, especially in Lower Guinea. In addition, although the benefit of treatment with polyvalent antivenom is confirmed in the case of viper envenomation, the lethality of neurotoxic envenomation remains high despite the use of antivenin.
**Keywords:** epidemiology, snakebite, Guinea, management

**315. Peptidome analysis of *Viperinae* and *Crotalinae* snake venoms demonstrates subfamily-specificity of the venom peptides in the family *Viperidae*.**
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**Background:** Snake venoms are valuable sources of pharmacologically active compounds. **Methods:** In a comparative research approach we analyzed in detail the venom peptidome of selected *Viperinae* and *Crotalinae* snake venoms. The entire peptidomes, peptides with molecular masses <10.000 Da were characterized applying latest versions of liquid chromatography/mass spectrometry (LC/MS), electrospray mass spectrometry (ESI/MS) and matrix-assisted desorption/ionization time-of-flight mass spectrometry (MALDI-TOFMS) techniques. **Results:** A variety of new venom peptides were identified. So far not identified peptides in the range *m/z* 6841 - 7401 belonging to the Kunitz/BPTI family of protein inhibitors and homologous bradikinin-potentiating peptides (BPPs) of *m/z* 444 - 1445 were identified in the *Vipera a. meridionalis* venom peptidic fraction. BPPs of *m/z* 643 - 1619 were identified in the low molecular mass peptide fraction of the *Bothrops jararacussu* venom. A cluster of peptides with masses above 6000 Da was found in the venom of the Viperinae snake but not observed in the Crotalinae snake venoms. **Discussion:** The differences in the venom peptidome compositions of the selected snakes probably reflect specificity of the venom peptide biosynthesis at a sub-family level. The results demonstrate that BPPs are the major peptide components of the Crotalinae venom peptidome lacking Kunitz-type inhibitors while the Viperinae venom, in addition to BPPs, can contain peptides of the

bovine pancreatic trypsin inhibitor family. This suggests differences in the evolution of the two Viperidae subfamilies. Analysis of literature data confirmed the above conclusion with only one exception of a very low content of Kunitz type inhibitor in Crotaline snake venom. We found indications for a post-translational phosphorylation of serine residues in *Bothrops jararacussu* venom BPP which might influence the hypotensive effect of the angiotensin-converting enzyme inhibition. Homology between venom BPPs from Viperidae snakes and venom natriuretic peptide precursors from *Elapidae* snakes suggests structural similarity between the respective peptides from the peptidome of both snake families. Venom peptide homologies in snakes quite distant phylogenetically and geographically suggest an evolutionary pressure for the preservation of BPPs and natriuretic peptides as important components of the snake venom arsenal. The peptidome analysis of *Bothrops jararacussu* and *Notechis ater niger* will be presented as well. **Conclusions:** The obtained results demonstrate that the venoms of both snake families are rich sources of low molecular weight peptides influencing important physiological systems such as hemostasis and blood pressure regulation. Details will be presented and the data can be used for pharmacological and medical applications and will support drug discovery investigations.
**Keywords:** peptidome; snake venoms; drug discovery;

**316. Assembly and Function of the Botulinum Neurotoxin Progenitor Complex.**
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**Background:** Botulinum neurotoxins (BoNTs) are among the most poisonous substances known to man, but paradoxically, BoNT-containing medicines and cosmetics have been used with great success in the clinic. Accidental BoNT poisoning mainly occurs through oral ingestion of food contaminated with *Clostridium botulinum*. BoNTs are naturally produced in the form of progenitor toxin complexes (PTCs), which are high molecular weight multi-protein complexes composed of BoNT and several non-toxic neurotoxin-associated proteins (NAPs). NAPs protect the inherently fragile BoNTs against the hostile environment of the gastrointestinal tract and help BoNTs pass through the intestinal epithelial barrier before they are released into the general circulation. These events are essential for ingested BoNTs to gain access to motoneurons, where they inhibit neurotransmitter release and cause muscle paralysis. We sought to understand the molecular mechanism by which the PTC functions as sophisticated toxin protection and delivery machinery. **Methods:** We successfully prepared the recombinant forms of a catalytically inactive BoNT serotype A (BoNT/Ai) and the corresponding NTNHA (non-toxic non-hemagglutinin), which is the largest NAP. BoNT/Ai and NTNHA were reconstituted *in vitro* into a minimally functional PTC (M-PTC). The structure of the M-PTC was determined by X-ray crystallography. **Results and Discussion:** This is the first high resolution structure of a BoNT PTC. It has revealed a wealth of information and shown many unanticipated features. First, BoNT/Ai adopts a distinct quaternary arrangement in the M-PTC in comparison to that of the free toxin. Second, NTNHA adopts a surprisingly similar architecture to that of BoNT/A. Despite this, NTNHA is devoid of the characteristic structural features of BoNT/A that are crucial to its biological functions. Third, BoNT/Ai and NTNHA form an interlocked compact complex, reminiscent of a handshake. Biochemical and functional studies show that NTNHA provides large and multivalent binding interfaces to protect BoNT/A from gastrointestinal degradation. Moreover, the M-PTC structure also helps pinpoint several pH-sensing residues that are

key players in balancing the seemingly contradictory needs of BoNT/A and NTNHA: strong binding for protection in the gut and timely release upon gaining entry to the general circulation. **Conclusions:** Our findings define the molecular mechanisms by which NTNHA shields BoNT in the hostile gastrointestinal environment and releases it upon entry into the circulation. These results will assist in the design of small molecules for inhibiting oral BoNT intoxication. Furthermore, we suggest that PTC-based vehicles could be engineered to shield proteinaceous drugs from GI destruction and thus allow their oral administration.
**Keywords:** botulinum neurotoxin, progenitor complex, crystal structure, inhibitor

**317. The Global Snakebite Initiative: aims, objectives and an emerging plan of action.**
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The Global Snakebite Initiative (GSI) is an Australian-registered charity organisation established to provide a collaborative framework through which toxinologists and other enthusiasts could work together to address the global tragedy of snake-bite envenoming. The main aim of GSI is to reduce the risk of snake-bite in endemic regions through community education and to improve the management of snake-bite victims. Results must be measured by assessing incidence, morbidity, mortality and disability-adjusted life years (DALYS). GSI's programme will seek to (a) improve the understanding, prevention and treatment of snake-bite, (b) provide advocacy and strategic advice to promote this cause and (c) drive coordinated scientific and medical research through partnerships in both the developed and developing worlds. Snake-bite envenoming is a particularly cruel misery inflicted on many of the most impoverished, mostly rural, populations throughout the tropical world. In attempting to develop solutions to snake-bite problems in these communities, effective collaboration with local researchers, policy-makers and governments will be of paramount importance. However, snake-bite remains the most neglected of all the recognised "Neglected Tropical Diseases" (NTDs). It still lacks local champions in many of the countries that are most severely affected and it is rarely if ever featured among priorities for national or WHO in-country funding. GSI has been successful in attracting corporate sponsorship to establish a sustainable business plan that will enable it to raise much needed capital to fund its projects. Important elements of GSI's emerging plan of action include:

1-Development of an international collaboration between a consortium of Indian-based researchers (clinicians, herpetologists and laboratory toxinologists) and the GSI to evaluate the effectiveness of commercial Indian antivenoms against venoms of the major species of medical importance in different parts of the country;
2-Designing an initiative driven by GSI partners in the UK, Spain, Costa Rica and Australia that will use the power of modern immune-proteomic techniques to identify optimal mixtures of venoms to raise a new Pan-African polyvalent antivenom;

3-Using donations to The GSI Public Fund to purchase established antivenoms for distribution to community hospitals and clinics through local charities in Kenya and Swaziland, and, eventually, organisations in other African countries;
4-Funding small projects by local researchers in the developing world, which address snake-bite issues and develop local capacity;
5-Working with antivenom manufacturers, governments and other organisations to improve the distribution and availability of antivenoms in developing countries such as Papua New Guinea, Nigeria and Sri Lanka.
**Keywords:** WHO; Global Snakebite Initiative; snakebite; developing world

**318. Cytotoxic and apoptotic effects of an L-amino acid oxidase from Calloselasma rhodostoma snake venom (CR-LAAO).**
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**Backgound:** L-amino acid oxidases (LAAOs) constitute a major component of snake venoms and have been extensively studied due to several pathophysiological effects in which they are involved, such as induction of apoptosis, cytotoxicity, effects on platelet aggregation, edema, bactericidal and leishmanicidal activities, among others. In the present study, we evaluated the cytotoxic and apoptotic effects of an L-amino acid oxidase from *Calloselasma rhodostoma* snake venom, named CR-LAAO. **Methods:** The tumor cell lines HL-60 and HepG2 were obtained from the American Type Culture Collection (ATCC), and the human peripheral blood mononuclear cells (PBMC) were extracted using Histopaque-1077. Cell viability was assessed by MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide]. MTT solution was added to the culture medium 3 h after the end of the treatment and the reaction was stopped by the addition of 100 μL of DMSO to the cell culture. CR-LAAO concentrations of 0.1; 0.25; 0.5; 1; 5; 10; 25; 50 and 100 μg/mL were used for cell treatment. Non-treated culture cells were used as negative control and cisplatin as positive control. Phosphatidyl serine exposure was determined by the annexin V binding using flow cytometry. After exposure to different concentrations of CR-LAAO for 24 h, cells were washed twice with PBS, resuspended in the working solution of propidium iodide (5 μg/mL) and annexin V (0.25 μg/mL), incubated for 15 min in an ice bath and analyzed with a FACSCanto flow cytometer. **Results:** CR-LAAO was highly cytotoxic to HepG2 and HL-60 tumor cells, providing approximately 80% cell death in the highest concentration tested (100 μg/mL), but showed low toxicity toward PBMC. It was also observed that this enzyme induces apoptosis in PBMC. In HepG2 the lowest concentrations (0.1-2.5 μg/mL) caused apoptosis, and the largest (5-100 μg/mL) caused apoptosis and necrosis. The toxicity promoted by CR-LAAO in HL-60 cells also induces apoptosis and necrosis. **Discussion and Conclusion:** CR-LAAO is a toxin that has been widely explored regarding its physicochemical properties and effects on blood coagulation, however, little is known about its antitumor effects. Based on the results obtained, we can say that the CR-LAAO is a multifunctional enzyme with great biotechnological potential as an antitumor agent.
Financial support: FAPESP
**Keywords:** snake venom, L-amino acid oxidase, cytotoxicity, apoptosis.

**326. Evolutionary crossroad: one peptide - two modes of action.**
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**Background:** Several spider families of a higher evolved branch of hunting spiders around Lycosoidea and Zodariidae exhibit at least two different peptide types for immobilizing prey: cysteine rich mini-proteins and cytolytic peptides with exert two different modes of action.
In the venom of the ctenid spider *Cupiennius salei* dozens of membranolytic peptides and ICK-motif containing neurotoxic acting mini-proteins are present. The neurotoxic acting peptide CsTx-1 (ω-ctenitoxin-Cs1a) has an exceptional position in the venom. It is the most often expressed neurotoxin and within all investigated peptides the most insecticidal one, inhibiting L-type Ca-channels. Two functional domains can be identified within the peptide: the ICK-motif is localized in the N-terminal and middle part of the peptide followed by a highly cationic C-terminus. The partial α-helical C-terminus exhibits different membranolytic activities on pro- and eukaryotic cells.
This reflects a new evolutionary strategy for spider venoms: highly specific ion channel inhibitors are seconded by cytolytic peptides to enlarge the paralytic/toxic effect of the venom. In the case of CsTx-1 this strategy can even be found within one peptide with two functions.

**319. Prey-specific Toxins in Non-murine Models: Non-conventional Three-finger Toxins and *Naja kaouthia* Venom.**
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**Background:** Many elapid venoms are predominantly composed of various three-finger toxins (3FTXs), some of which can be lethal and others apparently non-toxic. Several previous studies have demonstrated a correlation between venom composition and snake dietary preferences. Because the only currently identified prey-specific toxins are 3FTXs which are lethal to lizards and/or birds, we hypothesized that 3FTXs from *Naja kaouthia* previously found to be non-toxic in murine models (non-conventional/weak neurotoxins and muscarinic 3FTXs) might be toxic towards non-murine prey. The diet of *N. kaouthia* consists of prey besides mammals, including amphibians, lizards and fish. The majority of toxicity assays are performed using murine models, but this could obscure the biological roles provided by these toxins if non-mammal species are the targets. **Methods:** Toxicity assays ($LD_{50}$) were conducted with lizards (*Hemidactylus frenatus*) and fish (*Carassius auratus*) using adult *N. kaouthia* crude venom. Venoms were also subjected to low pressure BioGel P100 size exclusion, FPLC MonoS, and reversed-phase HPLC to purify toxins from *N. kaouthia* venom that occur in high abundance or are non-toxic. These toxins included alpha-cobratoxin, cobrotoxin-c, two cytotoxins, a known weak 3FTX, a muscarinic 3FTX, and two abundant $PLA_2$s. All purified proteins were identified using MALDI-TOF mass spectrometry and molecular mass matching. $LD_{50}$ assays were then performed on lizards with each purified toxin. **Results:** *Naja kaouthia* crude venom toxicity towards fish was almost identical to murine values, with an $LD_{50}$ of 0.75 µg/g. However, *N. kaouthia* venom was found to be considerably more toxic to lizards, with an $LD_{50}$ of approximately 0.3 µg/g. Of the purified venom proteins, only alpha-cobratoxin was found to be significantly toxic to lizards ($LD_{50}$ < 0.1 µg/g). The other purified proteins did not display significantly lethal $LD_{50}$ values for lizards ($LD_{50}$ > 5 µg/g). **Discussion:** Even though *N. kaouthia* crude venom was twice as toxic to lizards than toward mice, prey-specific 3FTXs were not identified, and *N.*

*kaouthia* non-lethal venom components were not observed to be more toxic in lizards. It appears that alpha-cobratoxin, the main mammalian lethal venom component, is also the main lethal component to lizards. **Conclusions:** Several colubrid non-conventional 3FTXs that are lethal and prey-specific are also completely non-lethal to mammals, but in the case of *N. kaouthia,* the same 3FTX, alpha-cobratoxin, is responsible for venom toxicity in both mammal and lizard prey. At present, the sequence/structural features for this selectivity are not known.
**Keywords:** alpha-cobratoxin, non-conventional 3FTX, toxicity

**320. Snakes of Arabia: Review and Update in Management.**
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**Background**: Exposure to variety of venomous animals, including snakes represents an environmental health risk in Saudi Arabia. Snake envenomation in Saudi Arabia and surrounding countries have been always of great interest. The aim of this review is to discuss the species of snakes identified in the Arabian peninsula with their geographic distribution, demographic and clinical presentation of snake envinomation, the development of local management protocols and history of antivenom development in Saudi Arabia. **Methods**: A structured literature search (1950 to 2012) was conducted using PubMed, EMBASE, Google, bibliography reviews of articles and major toxicology textbooks, and contact with content experts. Both human and animal studies and articles in all languages were included and translated. **Discussion**: This historical review of snakes in the Arabian peninsula and envinomation will be a good reference for all physicians working directly in managing envenomated patients and develop an easy to use management protocol.
**Keywords:** snake, Saudi Arabia, review

**321. Scorpions of Arabia: Review and Update in Management.**
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**Background**: Scorpion stings in Saudi Arabia and surrounding countries have been always of great interest. Publication about the fauna of Saudi Arabia can be tracked to as early as 1966. The aim of this review is to discuss the species of scorpions identified in the Arabian peninsula with their geographic distribution, demographic and clinical presentation of scorpion envenomation, the development of local management protocols and history of antivenom development in Saudi Arabia. **Methods**: A structured literature search (1950 to 2012) was conducted using PubMed, EMBASE, Google, bibliography reviews of articles and major toxicology textbooks, and contact with content experts. Both human and animal studies and articles in all languages were included and translated. **Discussion**: This historical review of scorpions and envenomation in the Arabian peninsula helped to update the Arabian peninsula scorpions' map and developed an easy to use management protocol.
**Keywords:** scorpion, Saudi Arabia, review

**322. Preventing the Development of Acute Kidney Injury from Hump-nosed Pit Viper (*Hypnale hypnale*) Bites in Mice with a Paraspecific Antivenom.**
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**Background;** Hump-nosed pit viper (*Hypnale hypnale*) is a medically important snake in Sri Lanka and Southwestern coast of India, which bite causes systemic complications such as hemostatic disturbance and acute kidney injury (AKI). To date, there is no effective antivenom available as clinical treatment for *H. hypnale* envenomation. A parasepcific antivenom (Hemato polyvalent antivenom, HPA) however has been shown effective to neutralize the lethal, hemorrhagic and necrotic effects of *H. hypnale* venom using rodent models. **Methods**; As AKI is one of the most severe complications that often causes death, this study aimed to examine the ability of HPA to confer protection against the development of AKI in mice challenged with *H. hypnale* venom. **Results & Discussions;** *H. hypnale* venom at median lethal dose ($LD_{50}$) caused serum biochemical derangement suggestive of acute kidney injury, most prominently uremia (and observably increased creatinine level) that affected all challenged mice. Significant hematuria and proteinuria correlated with the development of deteriorating renal function and signs observed in mice which were dead by 24 h. Much severe azotemia (with creatinine increased higher than urea) was observed in all mice challenged with 1.5x $LD_{50}$, indicating that the renal function was further compromised, with a shorter duration to death (within 8 h). In addition, prolonged blood clotting time and hemorrhage in lungs implied bleeding tendency in most of the mice challenged with the venom. When envenomation was repeated (at both 1x and 1.5x $LD_{50}$), intravenous infusion of Hemato polyvalent antivenom effectively prevented death and AKI complication in all mice. **Conclusion;** This finding supports the previous cross-neutralization study of Hemato polyvalent antivenom against *H. hypnale* envenomation in mice, and suggests that HPA may be a potential treatment for *H. hypnale* envenomation in future.
**Keywords** acute kidney injury , Hump-nosed viper, antivenom

**323. Management of Envenomation Reported to the Veterinary Teaching Hospital, Zaria, Nigeria.**
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Snakes and Scorpions are common in Nigeria but bites from them are not frequent. Bites from snakes most of the time occur in the rural areas and when they do occur, they are rarely reported to the hospitals this may be due to the unavailability of anti-snake venom and where available, is always expensive. People therefore, consult herbalist and snake charmers for treatment. Six dogs were presented to the Veterinary teaching Hospital, Ahmadu Bello University Zaria in 2011 with complaints of envenomation. Three dogs were bitten by cobra, two had spits into the eyes by cobras and a puppy was stung by a scorpion. Only one out of the three bitten dogs and the puppy stung by a scorpion died. Management generally involves the use of anti venin, antibiotics, crystalloids and pain relievers. However, only one dog received antivenin. For the spit, the eyes were flushed with saline, while ocular antibiotics and steroid were administered. Management of snake bites without anti-snake venom is hereby discussed.
**Keywords:** anti-snake venom, dogs, envenomation

**324. Gambierol as an intra-membraneous anchor for immobilizing the voltage sensor movement in Kv channels.**

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**Background:** The binding site for the polyether toxin gambierol in Kv3.1 channels is located at lipid facing residues on the S5 and S6 segments outside the permeation pathway. Therefore, this novel binding site in Kv channels would be the topological equivalent to the neurotoxin "site 5" in Nav channels. However, the mechanism by which gambierol inhibits Kv channels remains unknown.
**Methods:** Voltage clamp recordings of ionic and gating currents were obtained from $Ltk^-$ cells. Concatemers with wild-type and insensitive mutant subunits were used to constrain subunit stoichiometry. **Results:** Analysis of gating currents after application of 300 nM gambierol revealed a 120 mV depolarized shift of the charge versus voltage (QV) curve, resulting in immobilization of channel gating at physiological potentials. Furthermore, no activating ionic current could be observed on the time scale of gating current movement ($I_{gON}$ decay). This suggests that gambierol-bound channels could move up to the activated state upon strong depolarization, but that they could not pass the concerted opening step. State-dependent experiments indicated that the rested conformation is the high-affinity state whereas open channels could not be inhibited in the nM range. Prolonged and strong membrane depolarization (from +60 to +140 mV) in presence of gambierol resulted in significant recovery of ionic current (29% after a 5-s depolarization to +140 mV), consistent with a lower affinity for the open state. A tetrameric concatemer with only 1 high-affinity binding site still displayed high toxin sensitivity, but displayed faster gambierol unbinding at strong depolarization (>120mV).
**Discussion:** Based on the state-dependent affinity, the rested conformation would be the high-affinity state where gambierol acts as an anchor, hereby immobilizing the voltage-sensing domain (VSD). Hence, binding at a single binding site is sufficient to preclude channel opening (which requires all 4 VSDs to reach the activated state). Depolarizations above +80 mV result in VSD movement to the activated state with gambierol still bound, but without channel opening. The activated state represents a low-affinity binding site for gambierol due to an increase in the apparent dissociation rate constant. Channel opening can only occur after dissociation of gambierol from all 4 binding sites (requiring sufficiently long time in the low-affinity activated state). **Conclusions:** Gambierol acts as a profound gating modifier at a lipid exposed binding site. The mechanism is distinct from the gating modification of hanatoxin-related toxins in that gambierol bound subunits preclude channel opening even at potentials where they reach the activated state.

**Keywords:** ciguatoxins, gambierol, Kv channels

**325. Effectiveness of *Rhazya Stricta* Plant in Ameliorating Hepatic Alterations Induced by *Leiurus Quinquestriatus* Scorpion Envenoming.**

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**Background:** In Saudi Arabia, there are many types of medicinal plants among which *Rhazya stricta*, is widely used in local folk medicine practices. The ecosystem of Saudi Arabia also includes a dangerous and widely distributed scorpion, , which creates many health problems and threat the life of the human being. The present study was planned to examine the safety of using the aqueous extract of *R. stricta* in reducing the toxic effects induced by the venom of *L. quinquestriatus* scorpion in hepatic tissues of mice.
**Methods:** The study included four experimental groups, Group (A): control group treated daily by

stomach tube with distilled water for 45 days. Group (B): treated daily with the plant extract (2.36 ug/g b.wt.) for 15 or 30 or 45 days. Group (C): intramuscularly injected with ½ $LD_{50}$ dose of the venom (0.225 ug/g b.wt.) and sacrificed after 3 or 6 or 12 or 24hr from envenoming. Group (D): treated with plant extract as in group (B), then envenomed as in group (C) and sacrificed after 24hr from envenoming. **Results:** Plant treatment revealed normal histological and ultrastructure patterns after treatment for 15 or 30 days, while induced some alterations in the hepatic tissues of mice treated for 45 days. Envenoming revealed several alterations in a time dependant manner. The hepatocytes of envenomed mice revealed cellular swelling with consequent narrowing of the hepatic sinusoids, hydropic degeneration and nuclear pyknosis. Cellular necrosis or damage as well as increased number of hypertrophied von-Kupffer cells and inflammatory cells were also common. At the ultrastructure level, the hepatocytes revealed loss of many glycogen granules, dilatation or fragmentation of the endoplasmic reticulum, ribosomal detachment, cytoplasmic vesiculation, vacuolization, mitochondrial condensation or damage, nuclear irregularity, low electron dense chromatin, fusion of the nuclear membranes. Necrotic hepatic and sinusoidal cells, besides loss of the cell membrane integrity in some cells were common. The sinusoidal wall showed destroyed plasma lemma and dilated Disse spaces. The severity of most of these changes was decreased in Group (D) especially after 30 days of *R. stricta* pretreatment. **Discussion:** The ameliorating effects of *R. stricta* are believed to be due to the antioxidant and anti-inflammatory effects of some of its components. **Conclusions:** These results may indicate the possibility of using the aqueous extract of *R. stricta* in a particular dose and for durations not exceeds 30 consecutive days to reduce the alteration induced by the venom of *L. quinquestriatus*.
**Keywords:** *Rhazya Stricta*, *Leiurus Quinquestriatus*, liver, histopathology, ultrastructure

**326. Evolutionary crossroad: one peptide - two modes of action.**
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**Background:** Several spider families of a higher evolved branch of hunting spiders around Lycosoidea and Zodariidae exhibit at least two different peptide types for immobilizing prey: cysteine rich mini-proteins and cytolytic peptides with exert two different modes of action. **Discussion:** In the venom of the ctenid spider *Cupiennius salei* dozens of membranolytic peptides and ICK-motif containing neurotoxic acting mini-proteins are present. The neurotoxic acting peptide CsTx-1 (ω-ctenitoxin-Cs1a) has an exceptional position in the venom. It is the most often expressed neurotoxin and within all investigated peptides the most insecticidal one, inhibiting L-type Ca-channels. Two functional domains can be identified within the peptide: the ICK-motif is localized in the N-terminal and middle part of the peptide followed by a highly cationic C-terminus. The partial α-helical C-terminus exhibits different membranolytic activities on pro- and eukaryotic cells. **Conclusions:** This reflects a new evolutionary strategy for spider venoms: highly specific ion channel inhibitors are seconded by cytolytic peptides to enlarge the paralytic/toxic effect of the venom. In the case of CsTx-1 this strategy can even be found within one peptide with two functions.

**327. The Composition of Spider Venoms.**
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**Background:** Our recently set up a database with all known components of spider venoms investigated so far contains > 1600 compounds from 174 spider species belonging to 32 families. **Result:** Spider venoms contain a remarkable diversity of compounds which can be classified into six major categories:

low molecular mass compounds, acylpolyamines, linear cationic peptides, cysteine-rich mini-proteins, large neurotoxic proteins and enzymes. The venoms from many mygalomorph species, containing several mini-proteins, a variety of low molecular mass compounds and enzymes, represent a very well-functioning and reliable mixture and may be seen as the basic form of spider venoms. Nevertheless, numerous modifications, changes and replacements occurred. At least three spider groups developed very different venom compositions: Araneidae and Nephilidae rely mainly on amino acids containing acylpolyamines, Theridiidae developed large neurotoxic proteins and Sicariidae venoms predominantly contain phospholipase D. In addition, the venoms of several wolf spider-related families contain cytolytic peptides. **Discussion:** This development within major spider families or family groups indicates fascinating evolutionary directions to obtain "better" venoms.
**Keywords:** spider venom, compounds, database, evolution

**328. Sri Lanka Antivenom Project.**
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**Background:** Sri Lanka, a tropical island nation, is a developing country that endures significant economic and medical burden as a result of snake envenomation. The native people suffer 40,000 venomous snakebites annually, and the country has one of the highest snakebite mortality rates in the world. Ironically, the very snakes responsible for these statistics are a valuable national resource, both ecologically and medically, despite the medical and economic consequences of snake envenomation. Currently, no antivenom is produced using venoms from native Sri Lankan snakes as immunogens, and there is a true need for an optimally efficacious, Sri Lanka poly-specific antivenom. **Methods:** Animal Venom Research International (AVRI), a non-profit charity, has coordinated and bridged the knowledge and resources from the United States and Costa Rica with those of Sri Lankan official governmental agencies, legal counsels, environmental, medical and veterinary academic institutions, and religious and cultural leaders to achieve development of an efficacious poly-specific snake antivenom. The initial phase of the Sri Lanka Antivenom Project has involved the acquisition of land and fund raising, in addition to the acquisition of legal permits, documents, and establishment of official agreements between different institutions. Development of protocols to ensure the humane housing, maintenance, and venom collection from Sri Lanka's medically important species of snakes needed to be established. Additionally, the timely communication between all agencies, institutions and personnel involved was essential to move forward. **Results**: A serpentarium and water-well (built and funded by AVRI) have been completed. The building is thermally controlled for optimal snake health, and has a fulltime staff. Five medically important species, *Daboia russelli, Naja naja, Hypnale hypnale, Echis carinatus, and Bungarus caeruleus* have been collected from different geographic areas in order to provide representation of venom component variability within a species. Snakes have been humanely maintained, and have received regularly monitored veterinary care. Venom collection from each species is ongoing at this time, and is lyophilized post collection for shipment to Insituto Clodomiro Picado, Costa Rica where equine immunization protocols will be instituted, aimed at generating a pilot batch of poly-specific antivenom. On days of venom collection a medical toxicologist is in attendance at the serpentarium. **Conclusion**: A successful collaboration with the Sri Lanka government, official agencies, academic institutions, and implementation of the Sri Lanka Antivenom Project for developing a

poly-specific antivenom, derived from Sri Lankan snake venom/immunogens, has been effectively coordinated and implemented via the efforts of AVRI.
**Keywords:** snakebite, epidemiology, antivenom, poly-specific

**329. Hump Nosed Viper Bite in Sri Lanka—A Lesson of its Clinical Features and Management Based on a Prospective Cross Sectional Study of 1583 Cases.**
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**Background**: Hump nosed viper bite is the commonest venomous snakebite in Sri Lanka Most of the deaths result from coagulopathy and ensuing acute renal failure, prevention of which could reduce mortality. Clinical effects are poorly understood and specific antivenom serum is not available **Methods**: Descriptive observational study of 1543 patients admitted with hump nosed viper bites, to 5 hospitals in Sri Lanka, were studied for their clinical effects and therapeutic interventions. Only patients who brought the dead or live biting snakes identified as hump nosed viper by the physician were included. Details of local and systemic clinical effects were documented. Investigations included serial 20 minute whole blood clotting tests (20WBCT), FBC, serum creatinine, serum electrolytes, PT and APTT. Patients who developed coagulopathy were treated either with fresh frozen plasma (FFP) at a dose of 15ml/kg body weight or isotonic saline. FFP was repeated 4 hourly until the coagulopathy was normalized**.**
**Results:** There were 1146 males and 397 females with an age range 13-79 years and mean age 37.3 years .1535 (99.5%) had local swelling**.** All had local pain while 424(26.8%) had regional lymphadenopathy, 230 (14.9%) had a hemorrhagic blister at the bite site, 89 developed systemic effects, 61 (3.8%) developed only coagulopathy of whom and 43 received FFP, 18 received isotonic saline. Time taken for correction of coagulopathy was 4.74 hours in FFP group and 6.22 hours in saline group. Seventeen patients developed acute renal failure. The other systemic effects were shock, diarrhea, abdominal pain, vomiting, external ophthalmoplegia and coma. Three patients died. All patients with acute renal failure and one with shock had coagulopathy. None of the others with systemic effects had coagulopathy. Four patients received polyvalent antivenom serum imported from India, and three of them developed acute renal failure and one died due to shock. Only Paracetomol was used for pain
**Conclusions:** Local effects were managed without antibiotics. Paracetomol was adequate for pain relief. Systemic effects were rare. It varied from coagulopathy and nephropathy to neuropathy, raising the possibility of species variations in the venom composition. 20WBCT is useful to detect coagulopathy. Early detection of coagulopathy, adequate hydration and treatment with FFP at inception of coagulopathy could reduce mortality and morbidity. In the absence of species specific anti venom serum, FFP may be a safe therapeutic option for hump nosed viper bite with coagulopathy. Randomized control trial to test prevention of acute renal failure with FFP is suggested.
**Keywords:** Hump nosed viper bite, clinical effects, management , fresh frozen plasma

**330. Discovery of a Scorpaeniform Toxin Gene in *Cephalopholis argus*.**
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Fears of ciguatera poisoning have directly limited the fishery for the most abundant nearshore predatory fish in Hawaii, the introduced grouper *Cephalopholis argus*, commonly known as roi. Although roi and other groupers are classified as Perciformes, molecular evidence has suggested that they belong among the venomous Scorpaniformes. If this is true, groupers may, like other Scorpaeniformes, produce proteinaceous toxins. To determine if *Cephalopholis argus* possess the genes for a Scorpaeniforme toxin

(Scorpaenitoxin), primers were designed against the published cDNA for stonustoxin (the Scorpaenitoxin from the estuarine stonefish, *Synanciea horrida*). A 535 bp portion of the Scorpaenitoxin gene were amplified using polymerase chain reaction in several species of lionfish and scorpionfish as well as *Cephalopholis argus*. A BLASTn query of these sequences did not find any matches other than Scorpaenitoxins in the NCBI database. These data confirm the presence of a Scorpaenitoxin gene in roi. There are similarities between the affects of scorpaenitoxins and ciguatoxin in bioassays used fo ciguatera detection, including hemolysis and sodium channel activation. If further research determines that roi express this gene, it could be leading to false positives in ciguatoxin detection bioassays. Clarifying the affect of Scorpaenitoxins on ciguatera tests will increase the accuracy of ciguatera detection in roi, potentially expanding the fishery for this reef predator in the Hawaiian islands.
**Keywords:** Scorpaeniformes, fish Venoms, roi

**331. The protective Efficacy of Immunoglobulins Y (IgY) Prepared Against Cerastes cerastes Snake Venom in The Kingdom of Saudi Arabia.**

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**Background**: Chickens hens are highly cost-effective producers of antibodies as compared to mammals, which are traditionally used for the same purpose. Therefore, main goal of this study is to prepare and evaluate the protective efficacy of immunoglobulin Y (IgY) prepared against local Saudi *Cerastes* cerastes snake venom. **Methods:** The study was conducted during the period from 1st October 2009 to 1st October 2011 at the Center of Excellence in Biotechnology Research, King Saud University. Four groups of eight chickens were immunized intramuscularly with Cerastes *cerastes* snake venoms mixed with Freund's complete adjuvant. Three weeks later, the injections were repeated with the venoms in incomplete Freund's adjuvant. Three boosters were given with the venoms at 3 weeks intervals. The immunoglobulins Y was extracted by ammonium sulphate-caprylic acid method, the antibody titer were tested by enzyme linked immunosorbant assay and the protective efficacies of the extracted immunoglobulins were performed. **Results:** IgY preparation extracted by ammonium sulphate-caprylic acid method showed lack of low molecular weight bands (non-immunoglobulin proteins) and the bands representing IgY - antibodies, which have molecular weights ranged from 180- 200 KD, appeared sharp and clear. Moreover, evaluation of the protective value of the IgY - antibodies prepared revealed that, one ml of extracted IgY -antibodies containing 15 mg/ml anti *Cerastes cerastes* venom specific IgY could produce 100% protection against 50 $LD_{50}$ and 75% protection against 60 $LD_{50}$. **Conclusion:** Laying hens could be used as an alternative source of polyclonal antibodies against *Cerastes cerastes* snake venoms due to several advantages as compared with mammals traditionally used for such purpose.

Table (1): Comparison between the anti *Cerastes cerastes* venom antibody ELISA titers in serum samples and in IgY-antibody preparations from hens immunized with *Cerastes cerastes* venom at different time intervals post immunization:

| Mean $log_{10}$ antibody titer of the IgY extracted with | | Mean $log_{10}$ antibody titer of the serum samples | Immunization | Period (Weeks) |
|---|---|---|---|---|
| Ammonium - caprylic acid | Ammonium sulphate | | | |
| 0.00±0.00 | 0.00± 0.00 | 0.00± 0.00 | Pre-immunization | Zero |
| 2.1*** ±0.17 | 1.78 *** ±0.02 | 2.18 ±0.16 | 2 weeks following primary immunization | 2 |
| 2.8*** ±0.17 | 2.2*** ±0.17 | 3.08*** ±0.062 | 2 weeks following 1st booster dose | 4 |
| 2.7*** ±0.17 | 3.4*** ±0.17 | 3.38*** ±0.16 | 2 weeks following 2nd booster dose | 6 |
| 4.0*** ±0.17 | 3.7*** ±0.17 | 3.68*** ±0.16 | 2 weeks following 3rd booster dose | 8 |
| 4.1*** ±0.00 | 3.8*** ±0.00 | 3.68*** ±0.16 | 2 weeks following 4th booster dose | 10 |
| 3.9*** ±0.17 | 3.6*** ±0.17 | 3.14*** ±0.13 | 2 weeks following 5th booster dose | 12 |
| 3.6*** ±0.17 | 3.4*** ±0.17 | 2.84*** ±0.13 | - | 14 |

** : Moderately significant (p<0.01).

***: Highly significant (p<0.001).

*: Non significant.

$SD_n$; stander deviation, n=3.

Table (2): Neutralization test for measurement of the protective value of the IgY-antibodies prepared against *Cerastes cerastes* venom.

| Protection% | No. of inoculated mice | Amount of IgY used* | Amount of venom in µg/0.5ml saline | Venom potencies |
|---|---|---|---|---|
| 4/4 (100%) | 4 | 15mg/ml | 83 µl | 10 $LD_{50}$ |
| 4/4 (100%) | 4 | 15mg/ml | 166 µl | 20 $LD_{50}$ |
| 4/4 (100%) | 4 | 15mg/ml | 249 µl | 30 $LD_{50}$ |
| 4/4 (100%) | 4 | 15mg/ml | 332 µl | 40 $LD_{50}$ |
| 3/4 (75%) | 4 | 15mg/ml | 415 µl | 50 $LD_{50}$ |
| 2/4 (50%) | 4 | 15mg/ml | 498 µl | 60 $LD_{50}$ |
| 0/4 (0%) | 4 | 15mg/ml | 581 µl | 70 $LD_{50}$ |

*The venom and the specific IgY antibodies were mixed and incubated before injection of mice.

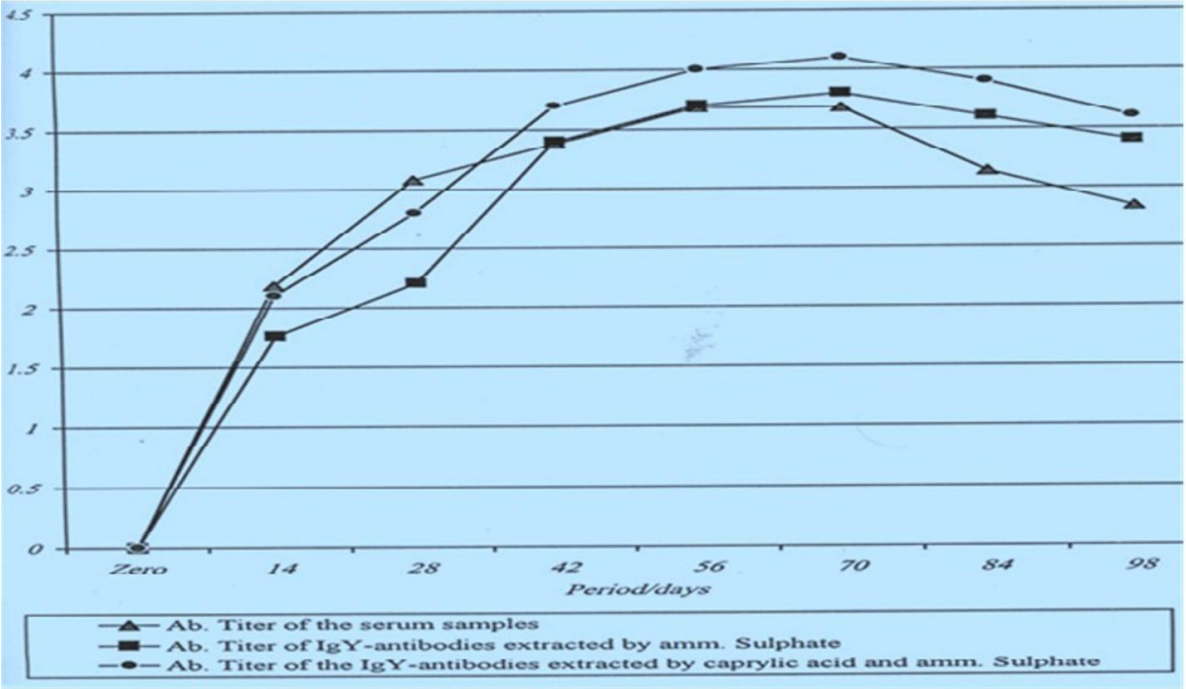


**Figure 1: Comparison between the anti *Cerastes cerastes* venom antibody ELISA titers in serum samples and in IgY-antibody preparations from hens immunized with *Cerastes cerastes* venom at different time intervals post immunization:**

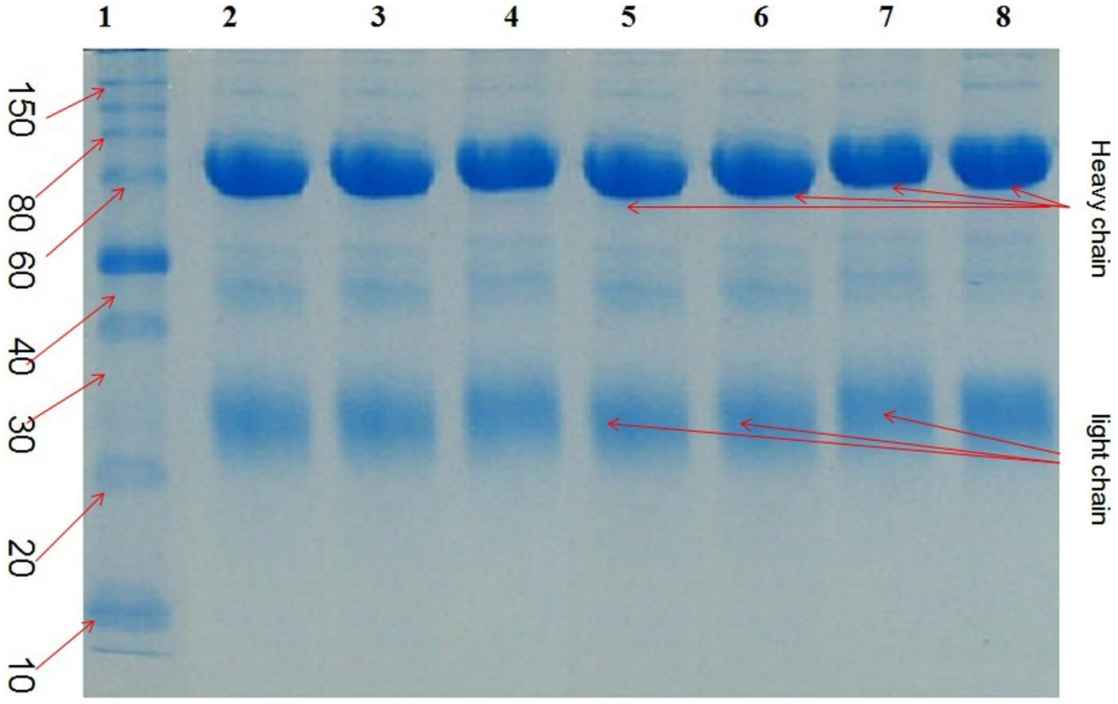


**Figure ( 2 ): SDS-PAGE profile of immunoglobulin-IgY prepared against *Cerastes cerastes* extracted by ammonium sulphate – caprylic acid method**

**Keywords**: snake venom, *Cerastes cerastes*, immunoglobulins Y, protective efficacy, caprylic acid.

**332. Comparative Transcriptomic View of the Body Organs from a Venomous Snake.**

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**Background**: The snake venom gland (VG) is a very specialized organ capable of producing high amounts of proteins that are stocked in the lumen at high concentrations. The venom synthesis is triggered by the release of venom, starting a circle of transcription, translation, secretion and accumulation that last up to 40 days. However, there are no systematic high throughput studies aiming at characterizing the regulation of this process or the differences in toxin gene expression in different physiological conditions. **Methods:** mRNA sequencing by 454-pirosequencing and differential expression analysis through RNAseq. **Results and Discussion: W**e produced 1,2 million long reads from different organs (VG, pancreas, brain, lung, heart, liver and kidney) from *Bothrops jararaca*, Viperidae. This allowed the assembly of a high coverage transcript panorama of the species, represented by about 35.000 unique combined sequences (unigenes). The unigenes were further annotated by similarity and Gene Ontology and the reads mapped back to identify genes that are VG-specific or differentially expressed. We also compared VG in the 4$^{th}$ day of venom producing circle from animals treated or not with agonists and antagonists of adrenoreceptors that seem to regulate the venom system. **Conclusion:** We were able to detect the main differences in the gene expression pattern from the venom glands and other organs, the presence of low expressed toxin transcripts and several novel snake-specific gene products, which may aid in the understanding of the venom gland functioning and regulation.

**Keywords**: transcriptome; organs, snake

**333. P1/P2 proteins of the human ribosomal stalk are required for ribosome binding and depurination by ricin in human cells.**

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**Background:** Ricin A chain (RTA) depurinates the sarcin/ricin loop (SRL) of 28S ribosomal RNA and inhibits protein synthesis in mammalian cells. We previously showed in yeast that the ribosomal stalk facilitates the interaction of RTA with the ribosome and subsequent depurination. Despite significant homology between the stalk structures from yeast and humans there are notable differences. The human ribosomal stalk contains two identical heterodimers of P1/P2 bound to P0, while the yeast stalk consists of two different heterodimers, P1α/P2β and P2α/P1β, bound to P0. RTA exhibits higher activity towards mammalian ribosomes than ribosomes from other organisms, suggesting the mode of interaction with ribosomes may vary. **Methods:** We examined whether the human ribosomal stalk proteins facilitate the interaction of RTA with human ribosomes using surface plasmon resonance (SPR) with a Biacore and subsequent depurination of the SRL using real time PCR. **Results:** Using siRNA-mediated knockdown of P1/P2 expression in human cells, we demonstrate that the depurination activity of RTA is lower when P1 and P2 protein levels are reduced. Ribosomes from P1/P2-depleted cells have a reduced ability to bind RTA by SPR, which correlates with reduced depurination activity both *in vitro* and

inside cells. RTA interacts directly with purified human P1/P2 dimer, further demonstrating the importance of the human P1/P2 proteins in enabling RTA to bind and depurinate human ribosomes. **Discussion:** Ribosome inactivating proteins (RIPs) differ in their ability to inactivate ribosomes from different organisms. RTA displays higher activity on rat liver ribosomes than on plant or yeast ribosomes and no activity on bacterial ribosomes. A possible explanation for these differences is that the interaction of RIPs with ribosomes may be influenced by their interaction with ribosomal proteins. Our results suggest that species dependent differences in the stalk structure may account for the differences in the activity of RTA for ribosomes from different organisms. **Conclusions:** These results present the first evidence that the ribosomal stalk is required for ribosome binding and depurination by ricin in human cells and suggest that inhibition of ricin binding to stalk proteins may be an attractive target for therapeutic intervention.
Keywords: ricin, Shiga toxins, ribosomes

**334. Leucurolysin-B an ECD protein from snake venom as a tool for tumor molecular imaging.**
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**Background**: Angiogenesis, the formation and differentiation of blood vessels, plays a key role in tumor growth and metastasis spread and has become the new frontier for tumor control. Integrins are cell adhesion molecules able to recognize and bind to proteins in the extracellular matrix (ECM) involved in multiple steps of angiogenesis and metastasis. This recognition is done mainly through the RGD domain present in both cell surface and ECM. The overexpression of αv-integrins (αvβ3 and αvβ5) on solid tumor and activated endothelial cells has aroused interest in the development of radiolabelled RGD and RGD-like peptides for imaging and therapy of cancer. The RGD domain is also found in some snake venoms named disintegrins. Disintegrins inhibit cell-matrix and cell-cell interaction mediated by integrin and has been shown that these proteins are able to inhibit metastasis. The disintegrin-like (ECD), as well as RGD-disintegrin are also able to bind to cell surface integrins and inhibit their adherence to the natural ligands. Leucurolysin-B (Leuc-B) is a metalloproteinase class P-III isolated from *Bothrops leucurus* and possesses a disintegrin-like domain (ECD). The goals of this study were to characterize the antitumoral effect of Leuc-B against different solid tumors and to evaluate the binding of Leuc-B with tumor targets in vitro and in vivo, as well as, evaluate its applicability for tumors diagnosis. **Methods**: Firstly, the cytotoxic effects of Leuc-B against glioblastoma (U87, T98, RT2) and melanoma (UACC) cells were determined and characterized. Secondly, Leuc-B was labelled with radioiodine ($^{125}$I and $^{131}$I) using lactoperoxidase method and radiochemical analysis was performed by chromatography. $^{125}$I-Leuc-B was used for biodistribution and pharmacokinetics studies on Swiss mice bearing Ehrlich solid tumor, while $^{131}$I-Leuc-B was used for single photon emission computed tomography (SPECT) imaging. **Results and Discussion:** Leuc-B had potent cytotoxicity effect on the tumor cell lines evaluated (IC50 at mM range). It was observed that $^{125}$I-Leuc-B presented specific binding sites (>70%) on tumor cells and had very fast clearance from the blood stream ($T_{1/2}$= 0.01 h). $^{131}$I-Leuc-B demonstrated to interact with solid tumor in vivo allowing good quality images of tumor. **Conclusion:** Results suggest that Leuc-B may constitute a good template for development of a tool for molecular imaging detection of solid tumors.
**Keywords**: Leucurolysin B, disintegrin, tumor molecular imaging

**335. Investigations into the mechanism of action of pinnatoxins E, F and G.**
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**Background:** Pinnatoxins E, F and G are the most recently discovered isomers of the pinnatoxin family, a member of the cyclic imine group of toxins. Other cyclic imines (eg., gymnodimine and the spirolides) are highly toxic *in vivo* via antagonism of both CNS and neuromuscular nicotinic acetylcholine receptors (nAChRs) and CNS muscarinic acetylcholine receptors (mAChRs). However, the mechanism of action of the pinnatoxins is less well known. Recent work by our lab and others has shown that pinnatoxins E and F cause neuromuscular block *in vitro* and pinnatoxin A can bind to and antagonise nAChRs. The aim of the current study was to further investigate the mechanism of action of pinnatoxins E, F and G.
**Methods:** Pinnatoxins E, F and G were tested for neuromuscular blocking actions using an *in vitro* rat phrenic nerve-hemidiaphragm preparation. Time course of toxicity, response to depolarising agents and nicotinic agonists, and toxin washout were assessed. A rat ileum preparation was also used to determine potential anti-muscarinic activities of these toxins. **Results:** Pinnatoxins E, F and G all caused a rapid neuromuscular block in the hemidiaphragm preparation, with $IC_{50}$ values in the 10-50nM range and a rank order of potency of PnTx F (11.2nM) > PnTx G (14.3nM) > PnTx E (53.8nM). All 3 isomers blocked the response of the tissue to phrenic nerve stimulation without affecting the response to the depolarising agent KCl. Partial washout of isomers F and G was observed only at lower concentrations, while pinnatoxin E was readily washed out, even at concentrations as high as 1 µM. In the rat ileum assay, 1µM pinnatoxin G had no effect on the contractile response of the tissue to ACh. Conversely, pinnatoxin F at 1µM caused a small but significant right shift in the ACh dose-response curve.
**Discussion:** The results show highly potent actions of pinnatoxins E, F and G at the neuromuscular junction. The inability of pinnatoxins to alter the response of skeletal muscle to depolarising agents suggests antagonism of nicotinic receptors rather than a direct myotoxic action. Pinnatoxin F also has a small, possibly anti-muscarinic effect in the rat ileum, deserving of further attention.
**Keywords**: pinnatoxins, neuromuscular, antagonism

**336. Synthetic Pyridinium Polymer APS8 Non-competitively Nicotinic Acetylcholine Receptors.**
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**Background:** A variety of polypyridinium compounds have been isolated from sponges, starting with the polymeric halitoxins. A number of biological effects including cytotoxicity, acetylcholinesterase inhibition and antifouling actions have been reported for the halitoxins and for the Mediterranean sponge (*Reniera sarai*) polymer mixture APS. Recently it was shown that very small concentrations of APS and its synthetic analog APS8 inhibit the proliferation of certain lung cancers. Since a variety of lung cancers express nicotinic acetylcholine receptors, particularly the alpha7 subtype, and it has been demonstrated that inhibition of this receptor with snake and *Conus* alpha-toxins can inhibit the rate of proliferation of lung cancer cells, we have investigated the interaction of APS8 with mammalian alpha7 receptors.
**Methods:** The functional effects were tested on Xenopus oocytes expressing human alpha7 or alpha4beta2 nAChRs using two-electrode voltage clamp recordings. The ability of APS8 to affect the binding of 1nM radiolabeled alpha-bungarotoxin to alpha7 receptors and 1 nM radiolabeled cytisine to alpha4beta2 receptors was measured using washed rat brain membranes and non-radioactive nicotine to measure non-specific binding. **Results:** *A*PS8 totally inhibited alpha7 nAChR response to 1 mM acetylcholine (ACh) at subnanomolar concentrations. The onset and degree of block was concentration dependent; the effect was slowly reversible at the lowest concentrations tested. At much higher concentrations APS8 depolarized and was toxic to the oocyte. This action also occurred with

alpha4beta2 nAChR expressing oocytes but at much higher concentrations. APS did not affect the binding of the radioligands to the rat brain receptors at concentrations that were 10,000-fold higher than necessary for functional antagonism. **Conclusions:** APS8 potently inhibits the response of two mammalian nicotinic acetylcholine receptors to ACh through a non-competititve mechanism. Since this inhibition occurs at APS8 concentrations that are much lower than are needed for acetylcholinesterase inhibition or cytotoxic membrane disruption, it is possible that the anti-proliferative action of this synthetic polymer is due to nAChR inhibition. (Supported by Slovenian-American Joint Research Project).
**Keywords**: sponge toxin, nicotinic receptor, cancer

**337. The venom-gland transcriptome of the Eastern Coral Snake (Micrurus fulvius).**
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**Background:** Snake venom is the inverse biochemical fingerprint of the physiological processes maintaining prey homeostasis and defines the ecology and evolution of venomous species because of its involvement in predation, digestion, and defense. Snake venom is also of pharmacological importance, not only due to frequent human envenomation and mortality but recent proteomic research has shown that venom proteins and enzymes could aid in the treatment of heart attack, stroke, and several diseases. Yet the genes expressed during venom production have been poorly characterized, and modern high-throughput sequencing methods have yet to pervade snake venom transcriptomics. **Methods:** We describe the *de Novo* assembly and analysis of the venom-gland transcriptome for the Eastern Coral Snake (*Micrurus fulvius*) based on 79,573,048 quality-filtered pairs of Illumina reads. Full-length toxin and non-toxin transcripts were identified via blastx searches. **Results and Discussion:** Among the 13 unique toxin classes identified, three-finger toxins and phospholipase A2's were the most abundant and diverse classes, characteristic of elapid venom. Protein-folding sequences and ribosomal transcripts were the most abundant non-toxin sequences, concordant with the role of the venom-gland in producing large amounts of various proteins. **Conclusions:** This is the most complete characterization of the genes expressed in an elapid venom gland to date. Expression patterns of the various toxin families should provide insights for antivenom production and pathological treatment of Coral Snake envenomation.
**Keywords**: venom gland, transcriptome, *Micrurus fulvius*

**338. Pharmacological activity of a new Asp49 phospholipase A2 isolated from Bothriopsis bilineata smargadina (forest viper) venom in vertebrate neuromuscular preparations.**
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[1]*Department of Pharmacology, Faculty of Medical Sciences, State University of Campinas (UNICAMP), Campinas, SP, Brazil;* [2]*Department of Biochemistry,Institute of Biology, State University of Campinas (UNICAMP), Campinas, SP, Brazil;* [3]*Adventist University of SãoPaulo (UNASP), São Paulo, SP, Brazil;* [4]*Department of Histology andEmbryology, Institute of Biology, State University of Campinas (UNICAMP), Campinas, SP, Brazil.*
*simioni@unicamp.br*
**Background**: *Bothrops* snake venoms contain a variety of Asp49 and Lys49 phospholipases $A_2$. Several of these $PLA_2$ (mainly Lys49 $PLA_2$) appear to produce neuromuscular blockade via presynaptic mechanisms, generally at concentrations (1-50 µg/ml) lower than those required to produce blockade with the corresponding venom. We have previously shown that the venom of the forest viper (*Bothriopsis bilineata smargadina*) produces neuromuscular blockade in vertebrate nerve-muscle preparations. In this work, we examined the neuromuscular activity of BbilTX, an Asp49 $PLA_2$ isolated from *B. b.*

*smargadina* venom. **Methods**: The neuromuscular activity of BbilTX was examined in chick biventer cervicis (BC) and mouse phrenic nerve-diaphragm (PND) preparations mounted for conventional myographic and electrophysiological recordings followed by morphological analysis. **Results**: In BC preparations, BbilTX (1, 5 and 10 µg/ml) caused time- and concentration-dependent blockade that was not reversed by washing; the time for 50% blockade was 87±7, 41±7 and 19±2 min (mean±SEM, n=4-6) for 1, 5 and 10 µg/ml, respectively. Muscle contractures to exogenous ACh and KCl were unaffected. BbilTX (10 µg/ml) also did not interfere with the twitch-tension of directly-stimulated curarized (10 µg d-tubocurarine/ml) BC preparations. However, BbilTX (10 µg/ml) produced mild morphological alterations (edematous and/or hyperchromic fibers) in BC; there was also a progressive release of CK (from 116±17 IU/ml at 0 min to 710±91 IU/ml after 45 min; n=6). BbilTX (5 µg/ml)-induced blockade was markedly inhibited at 24-22 °C whereas pretreatment with *p*-bromophenacyl bromide (*p*-BPB) abolished the blockade. In PND preparations BbilTX (1-30 µg/ml, n=4-6) caused partial time- and concentration-dependent blockade (52.2±2% at the highest concentration). BbilTX (30 µg/ml) also markedly reduced the quantal content of PND preparations [from 94±14 (control) to 24±3 after 60 min; n=5; $p<0.05$] but caused only minor membrane depolarization (membrane resting potential -80±1 mV (control) vs -66±2 mV after 120 min; n=5; $p<0.05$) and no change in the depolarization caused by exogenous carbachol. **Discussion**: These results show that BbilTX causes neuromuscular blockade in isolated preparations *in vitro* essentially by a presynaptic mechanism without a significant direct action on skeletal muscle. The enzymatic activity of BbilTX apparently contributes to this neuromuscular blockade since incubation at a low temperature and treatment with *p*-BPB markedly attenuated the blockade.
**Financial support:** This work was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, Brazil).
**Keywords**: Asp49 PLA2, *Bothriopsis bilineata smargadina*, neuromuscular blockade, presynaptic action, snake venom

**339. Effects and Molecular Determinants of JZTX-V on the Kv4.3 Potassium Channel.**
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**Background:** Kv4.3 channel is present in many mammalian tissues, predominantly in the heart and central nervous system. In the hearts of most mammals, it is responsible for repolarization of the action potential of ventricular myocytes and is important in the regulation of the heart rate. Because of its central role in this important physiological process, Kv4.3 channel is a promising target for anti-arrhythmic drug development. **Results:** JZTX-V was an inhibitor cystine knot toxin isolated from the venom of the Chinese tarantula *Chilobrachys Jingzhao*, which could selectively inhibit Kv4.3 currents expressed in HEK293 cells and the $IC_{50}$ value was about 10.0 nmol/L. Electrophysiological assays further showed that 25 nmol/L JZTX-V could shift significantly the voltage dependence of both activation and steady-state inactivation to depolarization, and slow markedly the time constant of both activation and inactivation but not the recovery from inactivation. Thus, we concluded that JZTX-V was a gating modifier toxin. To further investigate the molecular determinants of the interaction between JZTX-V and Kv4.3 channel, we performed an alanine-scanning mutagenesis in the S3b-S4 region of Kv4.3 channel, and researched the interaction between the mutant channels and JZTX-V. Experimental results showed that both V282 and F286 of Kv4.3 channel might be the binding sites of JZTX-V. When the both residues were substituted simultaneously with alanines, the mutant channel could not be activated under a series of potentials. Importantly, if JZTX-V was applied simultaneously, the mutant channel could be activated and the peak current would become more and more with an increase in toxin concentration from 10 to 100 nmol/L. However, when the toxin concentration exceeded 100 nmol/L, JZTX-V could not

inhibit or promote the current of the mutant channel. **Conclusion:** Present findings should be helpful to develop JZTX-V into a molecular probe and drug candidate targeting to Kv4.3 channel in the myocardium.
**Keywords**: JZTX-V; Kv4.3 channel; mutant channels; molecular determinants, patch clamp

**340. Initial Evaluation of the Cytotoxic Effects of Pseudechis porphyriacus Venom on Colon Cancer Cells.**

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Background: Cancer is characterized by uncontrolled growth and metastatic spread of abnormal cells that, if not controlled, commonly results in death. In 2011, there were approximately 1.6 million new cancer cases with approximately 572,000 cancer related deaths in the United States alone. Colorectal cancer is the fourth most commonly diagnosed cancer in the United States, with approximately 140,000 new cases diagnosed and approximately 49,000 deaths (second only to lung cancer) in 2011. Treatment options are limited and depend on the stage of the cancer at diagnosis; therefore there is a need to examine novel sources, such as snake venoms, for potentially useful cancer therapeutics. In this study the cytotoxicity of *Pseudechis porphyriacus* venom and ion exchange fractions toward Colo205 cancer cells was explored. Previous work showed that the venom contains metalloproteinases (MMPs), phospholipases $A_2$ ($PLA_2$), three-fingered toxins (3FTxs) and cysteine-rich secretory proteins (CRiSPs); in spite of these components, the venom is only moderately toxic ($LD_{50}$ ~ 2.5 mg/kg). Colo205 cells are colorectal adenocarcinoma cells; 95% of colorectal cancers are adenocarcinomas. Results: Crude *Pseudechis* venom showed concentration-dependent toxicity toward Colo205 cells. Fractionation of crude venom via cation exchange FPLC resulted in 13 prominent peaks; four fractions (peaks 1, 11, 12, 13) were cytotoxic, producing 50, 30, 62 and 74% cell death, respectively. Examination of the 13 fractions via gel electrophoresis showed prominent bands at 6 and 14 kD as the most common components. Analysis using MALDI-TOF mass spectrometry confirmed that masses of 13-14 kDa, consistent with $PLA_2$s, were present in all 4 peaks; masses of 6.4-6.9, typical of many elapid 3FTxs, were also observed in peaks 1, 11 and 12. Discussion: *Pseudechis* crude venom showed dose-dependent decreases in cell proliferation, and the four fractions with potent cytotoxic effects were likely due to the actions of $PLA_2$s and 3FTxs. This preliminary analysis of *Pseudechis porphyriacus* venom and fractions suggests that cytotoxic effects toward Colo205 cells may be specific, and future characterization will evaluate purified venom protein toxicity toward Colo205 and non-cancer cells. Conclusion: The need to develop alternative treatments for colorectal cancer is essential, as current options are limited and often have severe side effects, due in part to the sensitivity of the colorectal area to traditional cancer therapies. If apparent anti-cancer effects observed with this venom are specific, these results may produce leads for novel drug therapies to treat colorectal cancer.
**Keywords**: pseudechis, colorectal, cancer

**341. Synergism between Snake Venom PLA2 and Metalloproteinase III.**

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**Background:** Snake venoms contain many enzymes and non-enzyme proteins (toxins) that act individually or synergistically to induce various enhanced toxins in order to efficiently capture prey. Snake venom Phospholipase $A_2$ ($PLA_2$) and metalloproteinase (SVMP) are two of the major toxic

components in snake venom, and both have various pharmacological effects. Thus, it is important to elucidate the functional relationship of these two major components in order to better understand their pharmacologic and toxinologic roles in venoms. **Results:** In this study, by using yeast two-hybrid (Y2H) screening, we found that two snake venom basic $PLA_2$s (01D06 and 05E04) separately interact with a metalloproteinase III (SVMPIII). cDNAs encoding $PLA_2$s and the metalloproteinase III (SVMPIII) isolated from the same snake (*Agkistrodon piscivorus leucostoma*) venom glands. Further dissecting the SVMPIII based on domains found that $PLA_2$ 05E04 only interacts with disinterin-like domain of SVMPIII, while $PLA_2$ 01D06 only interacts with cystein domain. Disintegrin-like domain and cystein domain of SVMP III were successfully expressed and purified from *E.coli*. **Conclusions:** The heterologous expression of both $PLA_2$s is currently under investigation. The synergism of different $PLA_2$s and different domains of SVMP III will be investigated *in vitro*.
**Keywords**: syngergism, phospholipase A2 , metalloproteinase III

**342. Fer-de-Lance (*Bothrops asper*) venom activates and aggregates platelets and these effects are inhibited by antivenin, EDTA and hirudin.**
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**BACKGROUND:** Globally, snakebites cause 100, 000 deaths per year. Despite efforts by the WHO to characterize venoms, the diversity among species still trumps understanding of venom components and their actions and renders antivenin development commercially difficult. These problems primarily affect developing nations. In Mexico and Central America, envenomation by *Bothrops asper* is the major offender but its effects on platelet activation and aggregation remain unknown and cannot be predicted by congeneric species which are known to promote or inhibit aggregation. **OBJECTIVES:** We aim to identify the role *B. asper* venom has on platelet activation and aggregation and to utilize 3 potential inhibitors of these actions to make inferences about mechanism of action in DIC-like syndrome and thrombocytopenia. **METHODS:** Dose-response effects on platelet aggregation by 5 doses of *B. asper* are assessed on platelet-rich plasma using standard methodology (Chrono-Log). Platelet activation by venom was determined by flow-cytometry (FacScan, Becton Dickinson) using gel-filtered platelets activated with dilutions of ADP or *B. asper* venom with monoclonal antibody to GPIIb/IIIa-FITC and to platelet activation marker CD62-PE. Platelet aggregation by venom was determined using 6 dilutions of 4 potential inhibitors: 1. polyvalent antibody gifted by Instituto Clodomiro Picado, San Jose, Costa Rico; 2. EDTA inhibitor of metalloproteins, 3. hirudin, a thrombin-specific inhibitor 4. PMSF, inhibitor of the general class of serine proteases or 5. controls (water or DMSO).**RESULTS:** *B. asper* venom activates platelets at surface proteins such as the GIIIb/IIa receptor which in turn contributes platelet aggregation. Aggregation is inhibited by EDTA, hirudin and polyvalent antivenin suggesting that metalloprotein and thrombin-like proteins may also have a role in platelet aggregation. PMSF trials failed due to failure of platelet aggregation in its solvent DMSO. **CONCLUSION:** According to this in vitro human model, B. asper activates and aggregates platelets. Aggregation may also be affected by metalloprotein and thrombin-like protein components of the venom since it was inhibited by DMSO and hirudin, respectively, as well as by antivenin. Treatment of potential thrombocytopenia should consider the role of these proteins.
**Keywords**: platelets, *Bothrops asper*, inhibitors

**343. The Short Course in Toxinology: Training the Trainers.**
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**Review:** Clinical toxinology is the medical discipline dealing with the diagnosis, treatment and prevention of toxin diseases caused by exposure to venomous animals and poisonous animals, plants and mushrooms. Currently there is no national or international organisation accrediting or training doctors in this discipline, but the IST is about to consider a major role in this area, the subject of a proposed revised Constitution. A few courses covering some aspects of clinical toxinology exist, either as very limited in extent, or with only a minor clinical focus, or with a very regional, rather than global focus. The only comprehensive clinical toxinology course is the one provided in Adelaide, Australia, running regularly since 1997. Hundreds of doctors from many nations have attended the Course since 1997. This course covers venomous animals, poisonous animals, plants and mushrooms, from a full global perspective, with an international faculty and an exit exam. Though lasting only one week, extensive pre-reading material is mandated. The current Course Handbook is about 500 pages. Emphasis is on clinically relevant information and is focussed on the needs of doctors treating cases. While it is expected that attendees will have, or acquire, direct experience managing cases of toxin disease and so will use the knowledge and skills gained in the Course in direct patient care, it is also expected that they will act as resource people in their home region/nation to promote up-skilling of the wider medical workforce in clinical toxinology. This Course may form the nucleus from which IST can develop a global accredited training scheme in clinical toxinology. Such a scheme will require input from diverse global regions and will be far more comprehensive and over a much longer time than the current Short Course, though likely will incorporate the Short Course in some way, or a derivative of it.
**Keywords**: training; snakebite; certification; venomous; poisonous; plants; mushrooms

**344. Introduction on Bacterial Toxins.** Cessare Montecucco

No abstract.

## Thursday, 12 July 2012

# International Society on Thrombosis & Haemostasis

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*Chairperson: Jan Rosing (NL)*

*Co-Chairperson: Kenneth Clemetson (CH); Manjunatha Kini (SG); Francis Markland Jr (US); Takashi Morita (JP); Mary Ann McLane (US); Ivo Francischetti (US)*

**Lunch Break** 12:35–12:45

SSC Session 12:40–1:45 Chairman: Manjunatha Kini

**Welcome and Introduction of new members** 12:45 – 12:55

**Minutes of the last meeting, Annual report and Publications of subcommittee** 12:55–1:05

**New inventories/activities** 1:05–1:15

A. **Educational program**
B. **Next international meeting on exogenous factors to be held in Amsterdam 2013**

**Functional genomics of salivary gland proteins** Ivo Francischetti 1:15–1:30

**Structural basis of coagulation factor V recognition for cleavage by RVV-V** Soichi Takeda 1:30–1:45

**Any other business and Next meeting** 1:40–1:50