20th World Congress of the International Society on Toxinology
8-13 September, 2019. Buenos Aires, Argentina

"Toxinology in the 21st century: Public health impact from basic, translational and clinical sciences"
HISTORICAL PERSPECTIVE OF TOXINOLOGY IN THE AMERICAS:
A PERSONAL ACCOUNT

Gilberto B Domont  Proteomics Unit
gilberto@iq.ufrj.br
The first big challenge was to decide on what and how to include in the presentation.

So, I called my dear friend Tom asking him to help me to perform my *Impossible Mission*.

He wrote back in his direct way:

- Quit. It truly is a *Mission Impossible* !!! Tell Jay you will not do it. The sooner, the better.

- Why, I asked?

- Well, you´ll transform every friend you have in each lab, institution or country into foes. Each one you cite, will be a friend; each one you do not, will multiply into many enemies. Believe me, I know how to make enemies.

And, he added: - you´ll end up with so many and much more dangerous enemies than I ever have faced.
Finally, after jointly discussing pros and cons we came to the conclusion that it was better to sandwich them all !!!

Grumbling, he agreed that I should manage the presentation scaling down from societies to countries, institutions, laboratory and research groups pretending that this would probably do less harm

Secondly, I should do it through a wide selection of subjects:

- metalloproteinases, phospholipases/ neurotoxins, immunology/ antibodies, inhibitors etc

- snakes, spiders, scorpions, plants, microrganisms etc

- outstanding contributions (pioneers, priorities?)

Please, praise me for the hits and go after Tom for the faults. He knows how to survive enemies.
Countries, dependent territories and population

982,093 inhabitants

35 countries
20 dependent territories

Population

15 countries ≥ 10 millions:
USA, Brazil, Mexico, Colombia, Argentina, Canada, Peru, Venezuela, Chile, Guatemala, Ecuador, Bolivia, Cuba, Haiti, Dominican Republic

10 millions ≥ 10 ≥ 1 million
Costa Rica

30 ≤ 1 million
1954 - The idea of a society - this society - devoted to the study of naturally occurring animal poisons probably originated with Mrs Eleanor E. Buckley, Wyeth Laboratories, who organized and directed the 1st International Conference on Venoms, AAAS, Berkeley, CA

- Buckley invites Shannon, P. Boquet, E. Bogen and K. Slotta to meet for dinner (Bellevue Hotel, Berkeley, 28 December, 1954) to organize a group to advance the study of animal venoms and poisons. **This meeting marks the birth of IST**

- the proceedings of the meeting (Venoms, 1956) along with the paper of E. Kaiser and H Michl, *Die Biochemie der tierischen Gifte* (1958) marked the beginning of modern Toxinology

1961 -10th Pacific Science Congress: commitment is made to organize a society

1962 - Ambassador Hotel Atlantic City, 15 April, a group of scientists discuss the founding of a society and the first issue of Toxicon. The approved motion reads

*To advance our knowledge on the properties of the toxins derived from the tissues of plants and animals and to bring together scientists interested on these toxins through a common society and journal.*

Findlay E Russel. Toxicon 25: 3-21 (1987) [slightly modified version]
The Society has its first international meeting in 1966 in Atlantic City.

At this same meeting (1962)

Dr Findlay Russel is nominated for president by Dr Ghiretti: the voting was 11-1 Russel voting nay
Dr Paul R. Saunders is elected secretary-treasurer
Mrs Yvonne Majerus, is the corresponding secretary
Sectional co-chairman in the Americas: Moura Gonçalves

A Newsletter was circulates inviting a good team to start the Society
Boquet (France), Kaiser & Michl (Austria), Haberman (Germany), Pawlowsky (USSR), Stanic (Yugoslavia), Mohamed (Egypt), Efrati & Shulov (Israel), Gosh & Devi (India), Puranananda & Lee (Orient), Sotuhcott & Whitley (Australia), Gonçalves, Moussatché, Vieira & Diniz (Brazil), del Pozo (México) and Buckley, Klauber, Saunders, Halstead, Banner, Slotta, Nigrelli, van de Harreveld, Bogen, Keegan & Minton (USA).

A discussion about the size of the founding membership ensued: it was decided that the number should be held between 50 and 80 scientists

Finally, among the the 77 Founding Members were 33 scientists from the USA, 4 Brazilians, 1 Mexican and 2 Argentinians
1983 - Charlotte Ownby, Oklahoma, visits Gerd Habermehl and Dietrich Mebs in Frankfurt for advise to found a Panamerican Society of IST, similar to the European Section founded by Paul Boquet in 1975, Paris

1984 - A meeting is held in Stillwater, Oklahoma and a new section comes to light

2013 - Last track: XI Congress of the PanAmerican Section of the International Society on Toxinology together with the XII Congress of the Brazilian Society on Toxinology
1988 - Julia Prado-Franceschi leads the creation of the Brazilian Society on Toxinology during the XII Simpósio Anual da Academia de Ciências do Estado de São Paulo. The Symposium pays tribute to Oswaldo Vital Brazil.

- 2019 - XV Congress of the Brazilian Society on Toxinology - Toxins and Venomous Animals: Paths, Impacts and World Insertion, São Pedro, SP

2012 - Foundation of the North American Society of Toxinology (NAST), multidisciplinary organization dedicated to the advancement of the science of all things venomous

2005 - Venom Week I, Omaha

2018 - Venom Week VI, Kingsville, TX
Research mostly directed to pharmacological medical effects and use as tools than basic research on the characterization of venom components

MCGILL UNIVERSITY, MONTREAL

Department of Pharmacology

1988 - Maryka Quick & Svend Geertsen, alpha bungarotoxin

Sporadic publications by different authors, but not a group or laboratory dedicated to basic toxinology research (my search results)
Jay W Fox

- back in the early 80s, was one of the first to identify and characterize the metalloproteinases present in *Crotalus atrox* venom with impact on toxin structure and function

- continuing longstanding interests in elucidating novel molecular mechanisms associated with venom-induced wound morbidity

- recent focus in the interaction of host and tumor in carcinogenesis and metastasis and invasion
United States of America

TEXAS A & M UNIVERSITY, NATIONAL NATURAL TOXINS RESEARCH CENTER, INCEPTION, 1978

- animal and biological material resource center established in March 2000 to support basic and translational research on venomous snakes and their venoms

- dedicated to the advancement in the understanding of the therapeutic value of venom molecules and to training scientists in the field of toxinology performed using high-throughput genomic, proteomic recombinant DNA and screening techniques

John Perez

- founder and Director of NNTRC


  - main interests: animals that have a natural resistance to snake venom and venoms that are important in biomedical research

Elda Eliza Sánchez

- Running Director of NNTRC

  - main interests: isolation, characterization and cloning of components relevant in the treatment of strokes, heart attacks, cancers, and envenomations
UNIVERSITY OF NORTHERN COLORADO, GREELEY
Stephen Mackessy
- research on venomous snakes and their venoms ranging from functional biochemistry to population molecular genetics to natural history/ ecology

UNIVERSITY OF ARIZONA, TUCSON, College of Medicine, Pathology
Leslie V Boyer
- Centruroides, Buthus and Androctonus scorpion and Loxosceles as well as Crotalinae & Micrurus venoms & envenomation, diagnosis & treatment

UNIVERSITY OF NEW MEXICO
Steven Seifert
- emergency medicine, medical toxicologist, medical director of the New Mexico Poison and Drug Information Center
UNIVERSITY OF HAWAI

Carl-Wilhelm E Vogel
- uses cobra venom factor (CVF), a structural analog of the activated form of complement component C3, as a molecular tool to study the structure/function of human C3

Angel Yanagihara, at Manoa. Pacific Biosciences Research Center
- biochemical and pathophysiologcal characterization of novel toxins and bioactive compounds from venomous marine invertebrates of regional importance

UNIVERSITY OF MINNESOTA, College of Pharmacy

Daniel E Keyler
- immunology, natural toxins, medical management of snakebites

UNIVERSITY OF CALIFORNIA, Riverside

Michael E Adams
- ion channels
United States of America

UNIVERSITY OF UTAH

Benedito Olivera and group (Grzegorz Bulaj & JS Imperial)
- conus toxins

UNIVERSITY OF OKLAHOMA

Eileen M Hotze
- bacterial toxins
Ashlee Rowe
- ion channels

DUKE UNIVERSITY

Charles Gerardo
- emergency medicine
Joao Ricardo Vissoci
- health, mental health reintegration
UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO
Instituto de Biotecnología
Lourival Domingos Possani Postay
- scorpion venoms and their components: structure, function, evolution
Alejandro Alagon
- improvement and development of antivenoms and physiopathology of envenomation
Gerardo Corzo
- structure and function of spider molecules and their voltage-gated ion channel receptors
Baltazar Becerril Lujan
- antibodies against scorpion toxins
Miguel Corona Villegas
- scorpion toxins
Cesar Vicente Ferreira Batista - Unidad Proteómica
- toxinology, scorpion venoms, mass spectrometry, Proteomics
INSTITUTO BUTANTAN

- Inauguration in 1899 as a laboratory for antiserum production attached to the Instituto Bacteriológico (now Instituto Adolpho Lutz). In 1901, became an autonomous institution called Instituto Serumtherápico, later Instituto Butantan

- First Director (1901-1919) and 1924-1927 - Vital Brazil Mineiro da Campanha. Pioneer in the investigation of toxins, developed anti-snake sera to treat bites or stings of poisonous animal (scorpions and spiders)

Afrânio Pompilio Gastos do Amaral
- herpetologist, worked in research and production of anti-venom serum, 450 published works

Jaime Arcoverde de Albuquerque Cavalcanti
- chemist and physician directed the Institute from 1938 - 1941, helped to create and named the first director of FAPESP

Articles on the memoirs of the Instituto Butantan are found in The Collection Cadernos de História da Ciência published by the Institution
Researchers in the last 50 years that deserve to be praised and are part of the scientific achievements of the Instituto

**Gastão Rosenfeld** - biochemistry of the action of snake venoms in humans

**Fayga Mandelbaum** - isolation and enzymatic characterization of metalloproteinases

**Ivan da Mota e Albuquerque** - immunology, characterization and regulation of IgE and IgG1

**Antonio Carlos Martins de Camargo** - animal toxins, mechanisms of action, biotechnology and pharmaceutics; peptides and processing enzymes

**Catarina de Fátima Pereira Teixeira** - inflammatory and antiinflammatory aspects, signaling pathways and applications of animal toxins

**Paulo Lee Ho** - development of vaccines, biotechnology, genomics, toxinology and cell biology

**Yara Cury** - mechanisms and pain control, physiopathology of pain and inflammation induced by animal toxins

**Denise Vilarinho Tambourgi** - influence of toxins on the immune system, complement system

**INSTITUTO BUTANTAN**
INSTITUTO BUTANTAN

Ana Maria Moura da Silva - focus on the structure, function and immunology of venom metalloproteinases

Solange Serrano - biological and structural characterization of proteolytic enzymes of snake venoms; Proteomics applied to the study of the structure and evolution of animal toxins

Ana Marisa Chudzinski-Tavassi - tissue repair, animal secretion molecules active in the hemostatic system and their characterization, biotechnology

Ignácio de Loiola Meirelles Junqueira de Azevedo - transcriptomics and genomics analyses of venom glands, animal toxins and molecular Evolution of proteins

Gisele Picolo - pain, analgesia, venoms and animal toxins

CENTRO DE ESTUDOS DE VENENOS E ANIMAIS PEÇONHENTOS, CEVAP

Benedito Barravieira - heterologous fibrin sealing and antiapilic serum

Rui Seabra Ferreira Junior - biochemical, pharmacological and enzymatic characterization of animal and plant toxins
UNIVERSIDADE DE CAMPINAS

Léa Rodrigues-Simioni - neuromuscular junction, venoms, miotoxins
Benedito Oliveira - venom toxins
Sergio Marangoni - phospholipase A2, inhibitors
Maria Alice da Cruz Hofling - spider and snake venoms action in the neuromuscular junction and the blood brain barrier

UNIVERSIDADE DE SÃO PAULO, Ribeirão Preto.

José Roberto Giglio - protein chemistry of toxins
Alexandre Corrado - pharmacology
Mauricio Rocha e Silva, Sergio Henrique Ferreira and Wilson Beraldo - bradykinin
José Moura Gonçalves - protein toxins
Carlos Ribeiro Diniz - broad studies

UNIVERSIDADE ESTADUAL PAULISTA, Rio Claro

Mario Sergio Palma - proteomics, structural biology, toxins
Carlos Ribeiro Diniz, pioneer
- recovered the Institute for research and technology
- pioneered scorpion and spider venom research

Consuelo Latorre Fortes-Dias - characterization of proteins and peptides of animal venoms and natural inhibitors

Marcelo Ribeiro Vasconcelos Diniz - molecular characterization of toxic peptides and proteins from venomous animals

Eladio Oswaldo Flores Sanchez - structure/function of snake venom proteins active in hemostasis and cell interaction
UNIVERSIDADE FEDERAL DE MINAS GERAIS

Maria Elena de Lima Perez Garcia - arthropodes venoms: spiders, scorpions
Paulo Sergio Lacerda Beirão - mechanism of action of toxins on ion channels
Carlos Delfin Chávez-Olórtegui - immunochemistry of venoms
Adriano Monteiro de Castro Pimenta - structure and function of peptides and criptides, proteomics, toxins

FUNDAÇÃO INSTITUTO OSWALDO CRUZ, FIOCRUZ, RJ

Pioneer = Haiti Moussatché - natural inhibitors of hemorrhagic snake venom enzymes

Jonas Perales - natural immunity: animal resistance to toxic effects of snake venoms
Ana Gisele Costa Neves Ferreira - protein chemistry & proteomics of peptide and protein toxins, XL

Richard Hemmi Valente - toxinology and natural immunity; proteomics technologies, HDX.
Brazil

UNIVERSIDADE FEDERAL DO RIO DE JANEIRO

Russolina Zingali - anti-thrombotic proteins, Proteomics of biological fluids including venoms
Paulo de Assis Melo - venom pharmacology
Gilberto Barbosa Domont - proteomics applied to biological systems

INSTITUTO VITAL BRASIL, RJ

Anibal Rafael Melgarejo Gimenez - herpetologist, biological characterization of snake venoms

UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

Celia Regina Ribeiro da Silva Carlini - protein structure and biological activity relationship of plant and microorganism toxins
Jorge de Almeida Guimarães - peptides and enzymes in hemostasis and thrombosis from snake venoms, insects and plants
Brazil

UNIVERSIDADE DE BRASILIA

Lauro Morhy - University, Higher Education, Science & Technology; protein chemistry

Elisabeth Nogueira Ferroni Schwartz - ion channel neurotoxins, pharmacological tools

Carlos Alberto Schwartz - cellular electrophysiology of ion channel toxins

Mariana de Souza Castro - purification and characterization of polypeptides from frogs and snakes

Osmindo Rodrigues Pires Junior - pharmacological and structural characterization of low MW compounds

EMBRAPA

Carlos Bloch - structure and function of amphibian peptides and proteins with biological activity; mass spectrometry

Maura Vianna Prates - bioactive peptides, proteomics

UNIVERSIDADE FEDERAL DO PARANÁ

Silvio Sanchez Veiga - spider venom and biological effects
INSTITUTO CLODOMIRO PICADO

Scientific/technological investigation and social action on the prevention and handling of envenomations. Antiserum production.

PIONEERS

Roger Bolaños Herrera - catedrático de la Facultad de Microbiología de la Universidad de Costa Rica
Jesús María Giménez Porras - pharmacology and biochemistry of snake venom
José María Gutiérrez - biochemical and toxicological characterization of snake venoms: myotoxins, metalloproteinases, technological development of antivenoms and public health of envenomings

Alberto Alape-Girón - snake venom and bacterial toxins

Bruno Lomonte - immunological and biochemical characteristics of snake venoms and isolated toxins

Teresa Escalante Muñoz - local and systemic pathology induced by snake venoms, mainly hemorrhagic metalloproteinases

Yamilé Angulo - biochemical characterization and mechanism of action of snake venom phospholipases A2 and their inhibitors

Alexandra Rucavado Romero - mechanisms of action and the pathological effects of metalloproteinase of snake venoms
Venezuela

INSTITUTO VENEZOLANO DE INVESTIGACIONES CIENTÍFICAS

Founded in 1959 is a research institute and graduate training center

Gina D´Suze - effects of venoms on human physiology

Carlos Sevcik - biochemical and biophysisc actions of scorpion toxins

Carmen Arocha-Piñango - venoms and hematology

Belsy Auxiliadora Guerrero-Guerrero - physiological effects of animal venoms

Jonas Perales & Haiti Moussatché
HISTORY OF TOXINOLOGY IN THE AMERICAS

Colombia

UNIVERSIDAD DE ANTIOQUIA

Grupo de Investigación Ofidismo Escorpionismo

Pioneer

Rafael Otero-Patiños - biochemical and biological characterization of venoms
UNIVERSIDAD DE CHILE

Urra Felix - toxins and cancer

UNIVERSIDAD DE TALCA

David Ramirez - computational biophysics, toxins, ion channels
Ecuador

UNIVERSIDAD REGIONAL AMAZÓNICA IKIAM

José Rafael de Almeida - biochemistry of snake venom toxins

Saulo Luís da Silva - biochemistry of snake venom phospholipases
The enormous toxinology community of sponsors, researchers, technicians as well as students from all American countries for their outstanding not-mentioned and anonymous contributions.
HISTORY OF TOXINOLOGY IN THE AMERICAS

JANUS
GOD OF BEGINNINGS AND TRANSITIONS

OF PRIMITIVE LIFE AND CIVILIZATION
Looking far back Janus would find research on snake venoms focused on identifying lethal species and venom components responsible for the lethality.

Closer, He sees the focus changing to the isolation and characterization of toxins and the examination of the efficacy of antivenoms.

Looking to the right at the last two decades, He finds how Proteomics techniques, especially nLC-mass spectrometry help in the characterization of whole venoms and isolated toxins.
Janus would be astonished by the PubMed statistics entries revealing the size of our work in numbers

Venoms in PubMed - entries up to Sept 04, 2019

- 24,878 plant toxins, 1947
- 18,992 snake venom entries from 1945
- 4,692 scorpions, 1946
- 3,0240 spiders, 1946
- 2,520 microorganism toxins, 1919
Toxins in PubMed - entries up to Sept 04, 2019

- metalloproteinases = 1,672 from 1957; metalloproteases = 1,451 from 1957
- phospholipases = 4,429,1947
- hemostasis = 2,640,1946
- electrophysiology = 1,312,1963
- natural immunity = 354,1950
- myotoxins = 193,1980
- biotechnology
  - anti serum & venoms = 3,512,1945
Then, what is the IMPACT of our work to Science and Society?

Science
- to better understand the molecular basis of toxin structure, interaction, activity, functionality and action

Society
- immunotherapy, new treatments as well as the discovery of new drugs

IF WE ACCEPT THAT THE ONLY GOAL OF SCIENCE IS TO RELIEVE US FROM THE BURDEN OF LIVING

THEN, THE TOXINOLOGY COMMUNITY HAS TO BE VERY PROUD OF ITS ACHIEVEMENTS

LIVES WERE SAVED, MORBIDITIES WERE AVOIDED OR MINIMIZED
My heart leaps up when I behold
A rainbow in the sky:
So was it when my life began,
So is it now I am a man,
So be it when I shall grow old
Or let me die!
The child is father of the man:
And I could wish my days to be
Bound each to each by natural piety

*William Wordsworth (1770-1850)*