COVID DOCUMENTS & PROTOCOLS

SNAKE VENOM-RELATED ENZYME MAY DRIVE COVID-19 MORTALITY

AUGUST 26TH, 2021

POSTED BY ROSE BRANDT-ARIZONA

"This enzyme is trying to kill the virus, but at a certain point it is released in such high amounts that things head in a really bad direction, destroying the patient's cell membranes and thereby contributing to multiple organ failure and

Like Venom Coursing Through the Body: Researchers Identify Mechanism Driving COVID-19 Mortality

Researchers have identified what may be the key molecular mechanism responsible for COVID-19 mortality – an enzyme related to neurotoxins found in rattlesnake venom.

By Rosemary Brandt, College of Agriculture and Life Sciences

Aug. 24, 2021

BMJ Global Health

Snakebites and COVID-19: two crises, one research and development opportunity

Diogo Martins ,[1,2] Julien Potet ,[3] Isabela Ribeiro[4]

To cite: Martins D, Potet J, Ribeiro I. Snakebites and COVID-19: two crises, one research and development opportunity. *BMJ Global Health* 2021;**6**:e006913. doi:10.1136/bmjgh-2021-006913

Handling editor Soumyadeep Bhaumik

As the world battles COVID-19, other long-standing global health challenges continue to cause illness, suffering and death. Among them is the neglected crisis of snakebite envenoming (SBE): in the year after the COVID-19 pandemic was declared, an estimated 2.7 million SBE led to over 100 000 deaths and 400 000 long-term disabilities in the poorest and most rural communities

Summary box

- Despite inherent differences, Snakebite Envenoming and COVID-19 have much in common in terms of research and development (R&D) challenges and opportunities.
- Both crises require a diversified portfolio of R&D solutions, ranging from diagnostics to treatments, that can effectively work and be accessible in differ-

Caption

RESEARCH ARTICLE

REVISED Toxin-like peptides in plasma, urine and faecal samples from COVID-19 patients [version 2; peer review: 2 approved]

Carlo Brogna[1*], Simone Cristoni[2*], Mauro Petrillo[3*], Maddalena Querci[3], Ornella Piazza[4], Guy Van den Eede[5]

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v2 **First published:** 08 Jul 2021, **10**:550
https://doi.org/10.12688/f1000research.54306.1

Open Peer Review

Caption

Abstract

Background: SARS-CoV-2 that causes COVID-19 disease and led to the pandemic currently affecting the world has been broadly investigated. Different studies have been performed to understand the infection mechanism, and the involved human genes, transcripts and proteins. In parallel, numerous clinical extra-pulmonary manifestations co-occurring with COVID-19 disease have been reported and evidence of their severity and persistence is increasing. Whether these manifestations are linked to other disorders co-occurring with SARS-CoV-2 infection, is under discussion. In this work, we report the identification of toxin-like peptides in COVID-19 patients by application of the Liquid Chromatography Surface-Activated Chemical Ionization – Cloud Ion Mobility Mass Spectrometry.

Methods: Plasma, urine and faecal samples from COVID-19 patients and control individuals were analysed to study peptidomic toxins' profiles. Pr precipitation preparation procedure was used for plasma, to remove high molecular weight proteins and efficiently solubilize the peptide fraction; in the case of faeces and urine, direct peptide solubilization was employed.

Results: Toxin-like peptides, almost identical to toxic components of venoms from animals, like conotoxins, phospholipases, phosphodiesterases, zinc metal proteinases, and bradykinins, were identified in samples from COVID-19 patients, but not in control samples.

	1	2
version 2 (revision) 14 Oct 2021	✓ report	✓ report
version 1 08 Jul 2021	? report	? report

1. **Paolo Grumati**, Telethon Institute of Genetics and Medicine (TIGEM), Pozzuoli, Italy

2. **Moshe Arditi**, Cedars-Sinai Medical Center, Los Angeles, USA

Any reports and responses or comments on the article can be found at the end of the article.

UNIPROTKB CANDIDATE'S INFORMATION							TAXONOMY CANDIDATE'S INFORMATION			
AC	*ID*	*Status*	*Protein name*	*ENZYME EC*	*Other name(s)*	*Length (aa)*	*ID*	*Species*	*Phylum - Family*	*Organism's common name(s)*
Q8AY46	VKTHB_BUNCA	reviewed	Kunitz-type serine protease inhibitor homolog beta-bungarotoxin B1 chain	NA	-	85	92438	*Bungarus Candidus*	***Chordata*** *- Elapidae*	. Malayan krait
A6MEY4	PA2B_BUNFA	reviewed	Basic phospholipase A2 BFPA	EC 3.1.1.4	. Antimicrobial phospholipase A2 . Phosphatidylcholine 2-acylhydrolase (svPLA2)	145	8613	*Bungarus fasciatus*	***Chordata*** *- Elapidae*	. Banded krait . Pseudoboa fasciata
F5CPF1	PA235_MICAT	reviewed	Phospholipase A2 MALT0035C	EC 3.1.1.4	. Phospholipase A2 MALT0035C (svPLA2)	142	129457	*Micrurus altirostris*	***Chordata*** *- Elapidae*	. Uruguayan coral snake . Elaps altirostris
A8QL59	VM3_NAJAT	reviewed	Zinc metalloproteinase-disintegrin-like NaMP	EC 3.4.24.-	. Snake venom metalloproteinase (SVMP)	621	8656	*Naja atra*	***Chordata*** *- Elapidae*	. Chinese cobra
Q9I900	PA2AD_NAJSP	reviewed	Acidic phospholipase A2 D	EC 3.1.1.4	. svPLA2 . APLA . Phosphatidylcholine 2-acylhydrolase	146	33626	*Naja sputatrix*	***Chordata*** *- Elapidae*	. Malayan spitting cobra . Naja naja sputatrix
Q58L90	FA5V_OXYMI	reviewed	Venom prothrombin activator omicarin-C non-catalytic subunit	NA	. vPA . Venom coagulation factor Va-like protein *Cleaved into 2 chains*	1460	111177	*Oxyuranus microlepidotus*	***Chordata*** *- Elapidae*	. Inland taipan . Diemenia microlepidota
Q58L91	FA5V_OXYSU	reviewed	Venom prothrombin activator oscutarin-C non-catalytic subunit	NA	. vPA . Venom coagulation factor Va-like protein *Cleaved into 2 chains*	1459	8668	*Oxyuranus scutellatus*	***Chordata*** *- Elapidae*	. Coastal taipan
Q9W7J9	3S34_PSETE	reviewed	Short neurotoxin 4	NA	. SNTX4 . Alpha-neurotoxin 4	79	8673	*Pseudonaja textilis*	***Chordata*** *- Elapidae*	. Eastern brown snake
P23028	PA2AD_PSETE	reviewed	Acidic phospholipase A2 homolog textilotoxin D chain	NA	. svPLA2 homolog	152	8673	*Pseudonaja textilis*	***Chordata*** *- Elapidae*	. Eastern brown snake

UNIPROTKB CANDIDATE'S INFORMATION							TAXONOMY CANDIDATE'S INFORMATION			
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Q7SZN0	FA5V_PSETE	reviewed	Venom prothrombin activator pseutarin-C non-catalytic subunit	NA	. PCNS . vPA . Venom coagulation factor Va-like protein *Cleaved into 2 chains*	1460	8673	*Pseudonaja textilis*	***Chordata*** *- Elapidae*	. Eastern brown snake
Q2XXQ3	CRVP1_PSEPL	reviewed	Cysteine-rich venom protein ENH1	NA	. CRVP . Cysteine-rich secretory protein ENH1 (CRISP-ENH1)	239	338839	*Pseudoferania polylepis*	***Chordata*** *- Homalopsidae*	. Macleay's water snake . Enhydris polylepis
Q9PW56	BNP2_BOTJA	reviewed	Bradykinin-potentiating and C-type natriuretic peptides	NA	. Brain BPP-CNP . Evasin-CNP *Cleaved into the 12 chains*	265	8724	*Bothrops jararaca*	***Chordata*** *- Viperidae*	. Jararaca
A8YPR6	SVMI_ECHOC	reviewed	Snake venom metalloprotease inhibitor	NA	. 02D01 . 02E11 . 10F07 . Svmpi-Eoc7 *Cleaved into 15 chains*	308	99586	*Echis ocellatus*	***Chordata*** *- Viperidae*	. Ocellated saw-scaled viper
Q698K8	VM2L4_GLOBR	reviewed	Zinc metalloproteinase/ disintegrin [Fragment]	EC 3.4.24-	*Cleaved into 3 chains*	319	259325	*Gloydius brevicaudus*	***Chordata*** *- Viperidae*	. Korean slamosa snake . Agkistrodon halys brevicaudus
Q8AWI5	VM3HA_GLOHA	reviewed	Zinc metalloproteinase-disintegrin-like halysase	EC 3.4.24-	. Zinc metalloproteinase-disintegrin-like halysase . Snake venom metalloproteinase (SVMP) . Vascular apoptosis-inducing protein (VAP)	610	8714	*Gloydius halys*	***Chordata*** *- Viperidae*	. Chinese water mocassin . Agkistrodon halys
P82662	3L26_OPHHA	reviewed	Alpha-neurotoxin	NA	. Alpha-elapitoxin-Oh2b (Alpha-EPTX-Oh2b) . Alpha-elapitoxin-Oh2b . LNTX3 . Long neurotoxin OH-6A/OH-6B . OH-3	91	8665	*Ophiophagus hannah*	***Chordata*** *- Viperidae*	. King cobra . Naja hannah

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Q2PG83	PA2A_PROEL	reviewed	Acidic phospholipase A2 PePLA2	EC 3.1.1.4	. Phosphatidylcholine 2-acylhydrolase (svPLA2)	138	88086	*Protobothrops elegans*	***Chordata*** *- Viperidae*	. Elegant pitviper . Trimeresurus elegans
P06860	PA2BX_PROFL	reviewed	Basic phospholipase A2 PL-X	EC 3.1.1.4	. Phosphatidylcholine 2-acylhydrolase (svPLA2)	122	88087	*Protobothrops flavoviridis*	***Chordata*** *- Viperidae*	. Habu . Trimeresurus flavoviridis
P0C7P5	BNP_PROFL	reviewed	Bradykinin-potentiating and C-type natriuretic peptides	NA	. BPP-CNP *Cleaved into 6 chains*	193	88087	*Protobothrops flavoviridis*	***Chordata*** *- Viperidae*	. Habu . Trimeresurus flavoviridis
Q3C2C2	PA21_ACAPL	reviewed	Phospholipase A2 AP-PLA2-I	EC 3.1.1.4	. Phosphatidylcholine 2-acylhydrolase (svPLA2)	159	133434	*Acanthaster planci*	***Echinodermata*** *- Acanthasteridae*	. Crown-of-thorns starfish
D6C4M3	CU96_CONCL	reviewed	Conotoxin Cl9.6	NA	. Conotoxin Cl9.6	81	1736779	*Californiconus californicus*	***Mollusca*** *- Conidae*	. California cone - Conus californicus
D2Y488	VKT1A_CONCL	reviewed	Kunitz-type serine protease inhibitor conotoxin Cal9.1a	NA	-	78	1736779	*Californiconus californicus*	***Mollusca*** *- Conidae*	. California cone . Conus californicus
D6C4J8	CUE9_CONCL	reviewed	Conotoxin Cl14.9	NA	-	78	1736779	*Californiconus californicus*	***Mollusca*** *- Conidae*	. California cone . Conus californicus
P0DPT2	CA1B_CONCT	reviewed	Alpha-conotoxin ClB [Fragment]	NA	. C1.2	41	101291	*Conus catus*	***Mollusca*** *- Conidae*	. Cat cone
V5V893	CQG3_CONFL	reviewed	Conotoxin Fla16d	NA	. Conotoxin Fla16d *Cleaved into 2 chains*	76	101302	*Conus flavidus*	***Mollusca*** *- Conidae*	. Yellow Pacific cone
P58924	CS8A_CONGE	reviewed	Sigma-conotoxin GVIIIA	NA	. Sigma-conotoxin GVIIIA	88	6491	*Conus geographus*	***Mollusca*** *- Conidae*	. Geography cone . Nubecula geographus
P0DM19	NF2_CONMR	reviewed	Conotoxin Mr15.2	NA	. Conotoxin Mr15.2 (Mr094)	92	42752	*Conus marmoreus*	***Mollusca*** *- Conidae*	. Marble cone
P0C1N5	M3G_CONMR	reviewed	Conotoxin mr3g	NA	. Conotoxin mr3g (Mr3.6)	68	42752	*Conus marmoreus*	***Mollusca*** *- Conidae*	. Marble cone

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D2DGD8	I361_CONPL	reviewed	Conotoxin Pu6.1	NA	-	83	93154	*Conus pulicarius*	***Mollusca*** *- Conidae*	. Flea-bite cone
P0C8U9	CA15_CONPL	reviewed	Alpha-conotoxin-like Pu1.5	NA	-	81	93154	*Conus pulicarius*	***Mollusca*** *- Conidae*	. Flea-bite cone
A1X8B8	CAl_CONQU	reviewed	Putative alpha-conotoxin Qc alphaL-1	NA	. QcaL-1	68	101313	*Conus quercinus*	***Mollusca*** *- Conidae*	. Oak cone
P58786	COW_CONRA	reviewed	Contryphan-R	NA	. Bromocontryphan *Cleaved into 2chains*	63	61198	*Conus radiatus*	***Mollusca*** *- Conidae*	. Rayed cone
P58811	CA1A_CONTU	reviewed	Rho-conotoxin TIA	NA	. Rho-TIA	58	6495	*Conus tulipa*	***Mollusca*** *- Conidae*	. Fish-hunting cone snail . Tulip cone
Q5K0C5	016A_CONVR	reviewed	Conotoxin 10	NA	-	79	89427	*Conus virgo*	***Mollusca*** *- Conidae*	. Virgin cone
B3FIA5	CVFA_CONVR	reviewed	Conotoxin Vi15a	NA	. Conotoxin Vi15.l	74	8765	*Conus virgo*	***Mollusca*** *- Conidae*	. Virgin cone

Caption

Venom Phospholipase A2- Found in **ONLY** the COVID-19 Patients

A6MEY4	PA2B_BUNFA	reviewed	Basic phospholipase A2 BFPA	EC 3.1.1.4	. Antimicrobial phospholipase A2 . Phosphatidylcholine 2-acylhydrolase (svPLA2)	145	8613	*Bungarus fasciatus*	***Chordata*** *- Elapidae*	. Banded krait . Pseudoboa fasciata
F5CPF1	PA235_MICAT	reviewed	Phospholipase A2 MALT0035C	EC 3.1.1.4	. Phospholipase A2 MALT0035C (svPLA2)	142	129457	*Micrurus altirostris*	***Chordata*** *- Elapidae*	. Uruguayan coral snake . Elaps altirostris
P23028	PA2AD_PSETE	reviewed	Acidic phospholipase A2 homolog textilotoxin D chain	NA	. svPLA2 homolog	152	8673	*Pseudonaja textilis*	***Chordata*** *- Elapidae*	. Eastern brown snake
Q2PG83	PA2A_PROEL	reviewed	Acidic phospholipase A2 PePLA2	EC 3.1.1.4	. Phosphatidylcholine 2-acylhydrolase (svPLA2)	138	88086	*Protobothrops elegans*	***Chordata*** *- Viperidae*	. Elegant pitviper . Trimeresurus elegans
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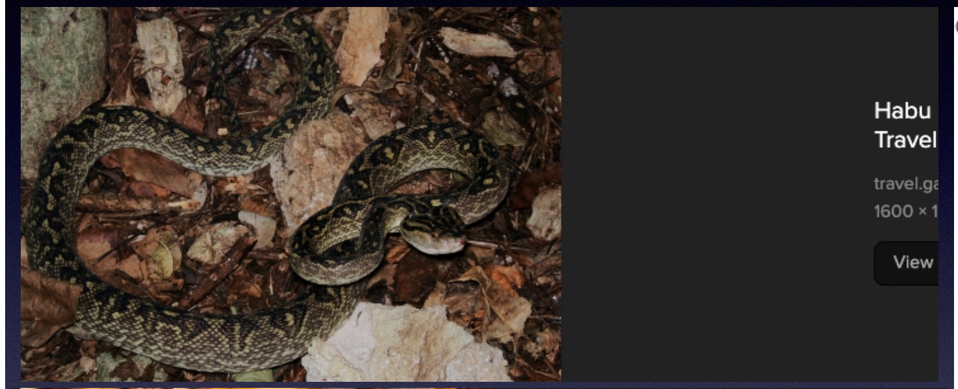
Q3C2C2	PA21_ACAPL	reviewed	Phospholipase A2 AP-PLA2-I	EC 3.1.1.4	. Phosphatidylcholine 2-acylhydrolase (svPLA2)	159	133434	*Acanthaster planci*	***Echinodermata*** *- Acanthasteridae*	. Crown-of-thorns starfish

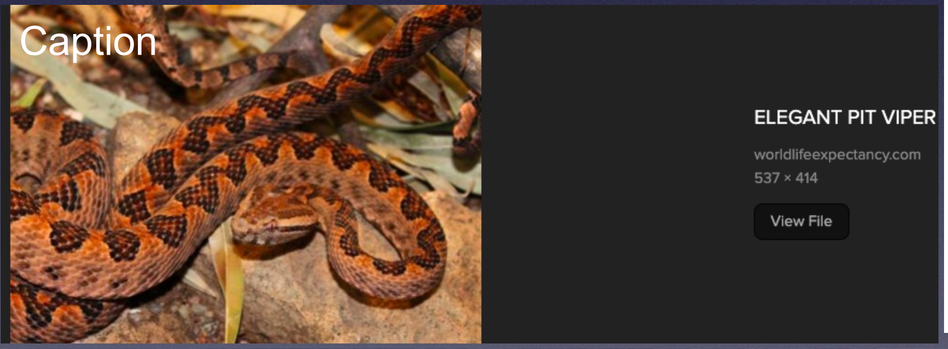
Caption

Venom Phospholipase A2- Found in **ONLY** the COVID-19

Banded Krait – Venomous – Deadly

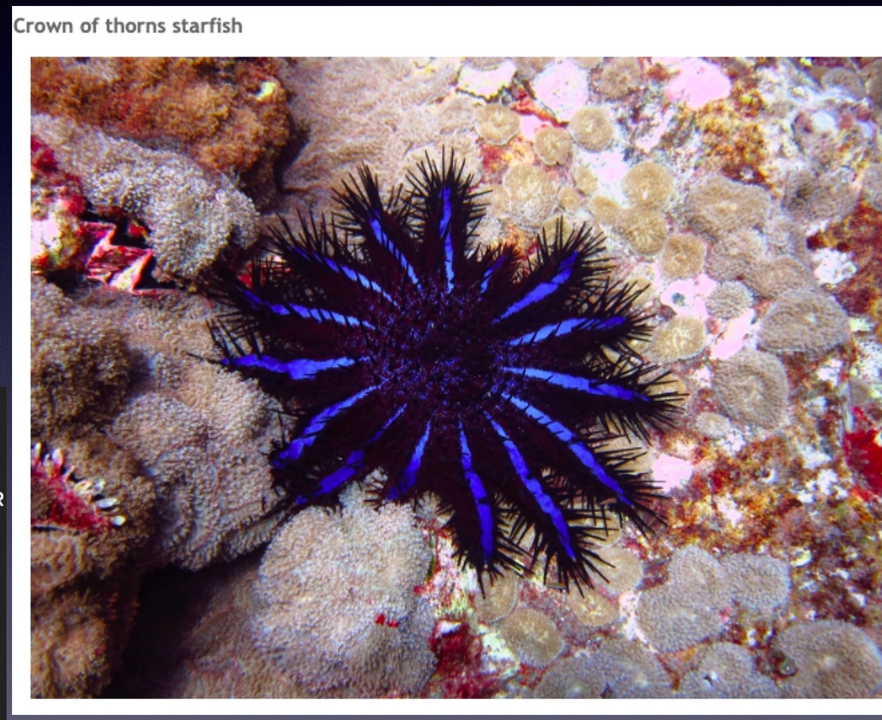


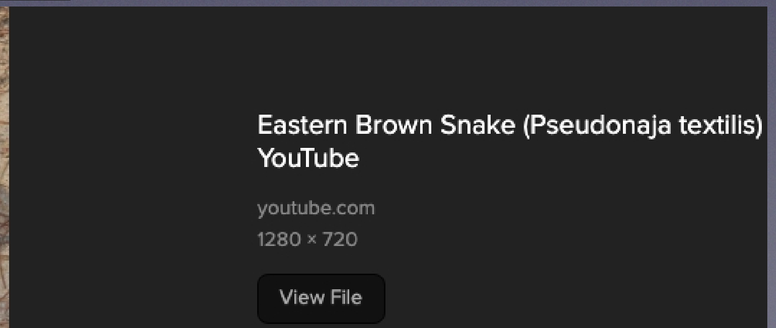
Caption



Caption

Uruguayan Coralsnake (*Micrurus altirostris*) More Photos





Like Venom Coursing Through the Body: Researchers Identify Mechanism Driving COVID-19 Mortality

Researchers have identified what may be the key molecular mechanism responsible for COVID-19 mortality – an enzyme related to neurotoxins found in rattlesnake venom.

By Rosemary Brandt, College of Agriculture and Life Sciences

Aug. 24, 2021

International Journal of Scientific and Research Publications, Volume 11, Issue 1, January 2021
ISSN 2250-3153

Phospholipase enzymes as potential biomarker for SARS CoV-2 virus

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Department of Chemistry, Faculty of Natural Sciences, The Open University of Sri Lanka

DOI: 10.29322/IJSRP.11.01.2021.p10919
http://dx.doi.org/10.29322/IJSRP.11.01.2021.p10919

Abstract-

Severe acute respiratory syndrome corona virus 2 (SARS CoV-2) is the responsible pathogenic RNA virus which is responsible for current ongoing pandemic covid 19. This review provides an updated summary of the current knowledge of phospholipase enzymes and its role on SARS CoV-2 virus, discussing the reported evidence as a potential bio marker and future directions that could be used to develop PLAs as a therapeutic target for covid 19 pandemic.

Index terms- bio marker, covid 19, LpPLA2, SARS CoV-2, sPLA2, therapeutic target

Caption

Researchers from the University of Arizona, in collaboration with Stony Brook University and Wake Forest School of Medicine, analyzed blood samples from two COVID-19 patient cohorts and found that circulation of the enzyme – secreted phospholipase A2 group IIA, or sPLA2-IIA, – may be the most important factor in predicting which patients with severe COVID-19 eventually succumb to the virus.

The sPLA2-IIA enzyme, which has similarities to an active enzyme in rattlesnake venom, is found in low concentrations in healthy individuals and has long been known to play a critical role in defense against bacterial infections, destroying microbial cell membranes.

When the activated enzyme circulates at high levels, it has the capacity to "shred" the membranes of vital organs, said **Floyd (Ski) Chilton**, senior author on the paper and director of the UArizona Precision Nutrition and Wellness Initiative in the university's **College of Agriculture and Life Sciences** (https://cals.arizona.edu/).

"It's a bell-shaped curve of disease resistance versus host tolerance," said Chilton, a member of the university's **BIO5 Institute**(https:// other words, this enzyme is trying to kill the virus, but at a certain point it is released in such high amounts that things head in a really bad direction, destroying the patient's cell membranes and thereby contributing to multiple organ failure and death."

Caption

Senior Projects

Fall 2021–2022
Fall 2020–2021
Fall 2019–2020
Fall 2018–2019
Fall 2017–2018
Fall 2016–2017

Synthetic Snake Venom
The Novel Creation of *Crotalid* Phospholipase A2 Using Genetic Engineering

Taylor Anderson | Emily Jesgarz | Richard Klein | Andrew Merkley | Alaric Siddoway

Introduction

Antivenin is listed as one of the World Health Organization's Essential Medicines, and as such, it is integral to a modern health care system. Antivenin is currently developed through a process of milking venomous animals, in this case, snakes, concentrating the venom, inoculating animals, and isolating antibodies found in their plasma. The aim of this project is to genetically engineer an organism to overexpress common proteins found in snake venom, thereby lowering the cost of antivenin.

Antivenin Manufacturing and Facts

Design Criteria and Objectives

To genetically engineer an organism, several steps are performed, including: PCR, obtaining the desired DNA, DNA transformation, cell culturing, and DNA extraction. The outlined criteria down below guided our design.

Design Objectives

1. Introduce the DNA for PLA_2 into an organism
2. Express PLA_2 production and secretion in an organism
3. Ensure the functionality of PLA_2
4. Evaluate and improve the economic viability of the process

Caption

Economic Evaluation and Viability -- When produced in a bench-top system, PLA_2 from crotalid venom can be produces for $0.60 per unit. More data is needed in order to scale up this operation, but currently the average purchasing price for PLA_2 is $0.60 per unit. Although crotalid PLA_2 is more expensive, since there is no commercial source for crotalid PLA_2 currently, it is reasonable to expect a much higher retail rate.

Conclusions and Future Work

The final design must be compared to the design criteria determined at the beginning of the design process.

Satisfaction of Design Criteria

1. The final gene was successfully cloned into *E. coli* using molecular cloning standards
2. Overexpression of PLA_2 was achieved in BL_{21} *E. coli*. The concentration was calculated using data from the Bradford Assay and the SDS-PAGE Gel and was found to me 2 mg/L
3. An activity assay showed positive results by exhibiting increasing fluorescence over time, indicating that the synthesized proteins' activity was unaffected by the isolation mechanism
4. The process developed reliably produces one unit of crotalid PLA_2 for $0.60, compared to the industry standard of one unit of PLA_2 (non-crotalid) for $0.60

The overexpression of phospholipase A2 by recombinant assembly and insertion into *E. coli* provides a reliable source for active phospholipase A2. In addition, the recombinant assembly allowed for the creation of an isolation mechanism durable enough to survive sonication, yet small enough not to affect the activity of the product.

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Protein on Demand™ Kunitz-type serine protease inhibitor homolog beta-bungarotoxin B2a chain Recombinant Protein (Malayan krait) (OPCA298869)

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Caption

Q8AY46	VKTHB_BUNCA	reviewed	Kunitz-type serine protease inhibitor homolog beta-bungarotoxin B1 chain	NA	-	85	92438	*Bungarus Candidus*	***Chordata*** *- Elapidae*	. Malayan krait

Protein on Demand™ Kunitz-type serine protease inhibitor homolog beta-bungarotoxin B2a chain Recombinant Protein (Malayan krait) (OPCA298869)

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Select Your Size *

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Price:

$1,488.00

15 **Conotoxins** Found In **ONLY** COVID-19 Patients

D2Y488	VKT1A_CONCL	reviewed	Kunitz-type serine protease inhibitor conotoxin Cal9.1a	NA	-	78	1736779	*Californiconus californicus*	***Mollusca*** *- Conidae*	. California cone . Conus californicus
D6C4J8	CUE9_CONCL	reviewed	Conotoxin Cl14.9	NA	-	78	1736779	*Californiconus californicus*	***Mollusca*** *- Conidae*	. California cone . Conus californicus
P0DPT2	CA1B_CONCT	reviewed	Alpha-conotoxin ClB [Fragment]	NA	. C1.2	41	101291	*Conus catus*	***Mollusca*** *- Conidae*	. Cat cone
V5V893	CQG3_CONFL	reviewed	Conotoxin Fla16d	NA	. Conotoxin Fla16d *Cleaved into 2 chains*	76	101302	*Conus flavidus*	***Mollusca*** *- Conidae*	. Yellow Pacific cone
P58924	CS8A_CONGE	reviewed	Sigma-conotoxin GVIIIA	NA	. Sigma-conotoxin GVIIIA	88	6491	*Conus geographus*	***Mollusca*** *- Conidae*	. Geography cone . Nubecula geographus
P0DM19	NF2_CONMR	reviewed	Conotoxin Mr15.2	NA	. Conotoxin Mr15.2 (Mr094)	92	42752	*Conus marmoreus*	***Mollusca*** *- Conidae*	. Marble cone
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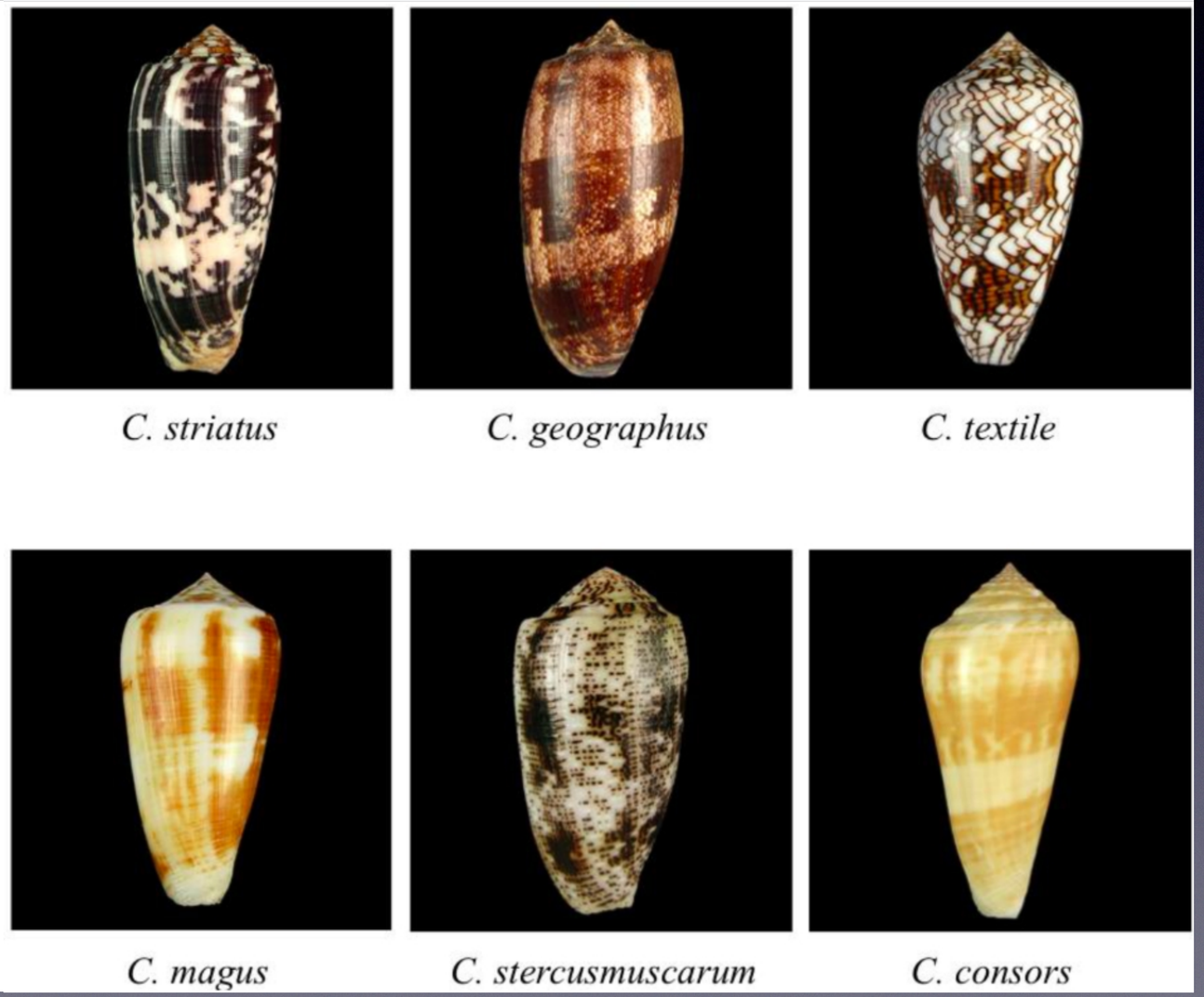
P0C8U9	CA15_CONPL	reviewed	Alpha-conotoxin-like Pu1.5	NA	-	81	93154	*Conus pulicarius*	***Mollusca*** *- Conidae*	. Flea-bite cone
A1X8B8	CAI_CONQU	reviewed	Putative alpha-conotoxin Qc alphaL-1	NA	. QcaL-1	68	101313	*Conus quercinus*	***Mollusca*** *- Conidae*	. Oak cone
P58786	COW_CONRA	reviewed	Contryphan-R	NA	. Bromocontryphan *Cleaved into 2chains*	63	61198	*Conus radiatus*	***Mollusca*** *- Conidae*	. Rayed cone
P58811	CA1A_CONTU	reviewed	Rho-conotoxin TIA	NA	. Rho-TIA	58	6495	*Conus tulipa*	***Mollusca*** *- Conidae*	. Fish-hunting cone snail . Tulip cone
Q5K0C5	016A_CONVR	reviewed	Conotoxin 10	NA	-	79	89427	*Conus virgo*	***Mollusca*** *- Conidae*	. Virgin cone
B3FIA5	CVFA_CONVR	reviewed	Conotoxin Vi15a	NA	. Conotoxin Vi15.l	74	8765	*Conus virgo*	***Mollusca*** *- Conidae*	. Virgin cone

15 **Conotoxins** Found In **ONLY** COVID-19 Patients

Cone snail drug 1000x more potent than morphine

By AAP with AG Staff • March 17, 2014

Australian cone snail (Conus textile), with proboscis extended and poised for attack. Image credit: AAP Image/Melbourne University/David Paul



US005969096A

United States Patent [19]

Shon et al.

[11] **Patent Number: 5,969,096**

[45] **Date of Patent: Oct. 19, 1999**

[54] CONOTOXIN PEPTIDES

[75] Inventors: **Ki-Joon Shon**, Shaker Heights, Ohio; **William R. Gray**, Salt Lake City, Utah; **John Dykert**, Vista, Calif.; **Doju Yoshikami**, Salt Lake City, Utah; **Maren Watkins**, Salt Lake City, Utah; **David R. Hillyard**, Salt Lake City, Utah; **Jean E. F. Rivier**, La Jolla, Calif.; **Baldomero M. Olivera**, Salt Lake City, Utah

[73] Assignees: **The Salk Institute for Biological Studies**, La Jolla, Calif.; **University of Utah Research Foundation**, Salt Lake City, Utah

[21] Appl. No.: **09/105,715**

[22] Filed: **Jun. 26, 1998**

OTHER PUBLICATIONS

Shon, et al., "A Non–competitive Inhibitor of the Nicotinic Acetlcholine Receptor fron *Conus purpurascens*Venom" Biochemistry 1997, 36, 9581.

Shon, et al., "Three–Dimensional Solution Structure of α–Conotoxin MII, an $\alpha_3\beta_2$ Neuronal Nicotinic Acetylcholine Receptor–Targeted Ligand", Reprinted from *Biochemistry*, vol. 36(50):15693–15700 (1997).

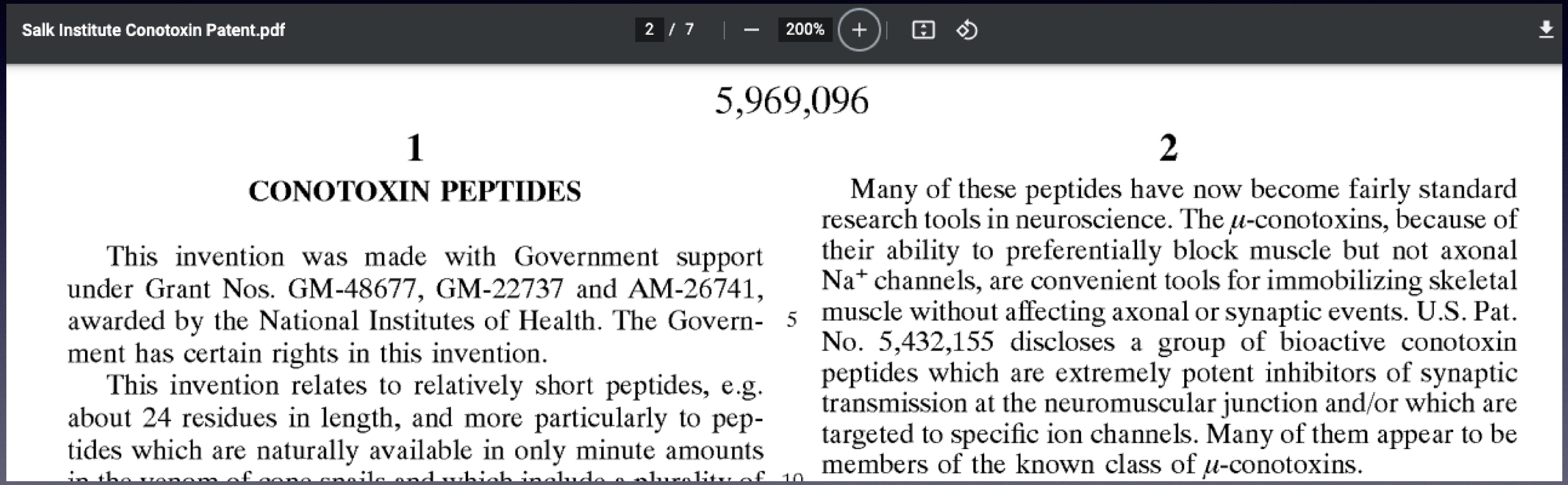
Advance ACS Abstract, Jul. 1, 1997, K. Shoen, et al., "Society for Neuroscience", 27th Annual Meeting, 1997.

Shon, et al., "A Noncompetitive Peptide Inhibitor of the Nicotinic Acetylcholine Receptor from *Conus purpurascens* Venom", *Biochemistry*, 36:9581–9587, 1997.

Primary Examiner—Cecilia J. Tsang
Assistant Examiner—Fabian A. Jameison
Attorney, Agent, or Firm—Fitch, Even, Tabin & Flannery

[57] ABSTRACT

Guess Who Has Rights To Salk Institutes Conotoxin Peptides?



CONOTOXIN PEPTIDES

This invention was made with Government support under Grant Nos. GM-48677, GM-22737 and AM-26741, awarded by the National Institutes of Health. The Government has certain rights in this invention.

This invention relates to relatively short peptides, e.g. about 24 residues in length, and more particularly to peptides which are naturally available in only minute amounts in the venom of cone snails and which include a plurality of

Many of these peptides have now become fairly standard research tools in neuroscience. The μ-conotoxins, because of their ability to preferentially block muscle but not axonal Na^+ channels, are convenient tools for immobilizing skeletal muscle without affecting axonal or synaptic events. U.S. Pat. No. 5,432,155 discloses a group of bioactive conotoxin peptides which are extremely potent inhibitors of synaptic transmission at the neuromuscular junction and/or which are targeted to specific ion channels. Many of them appear to be members of the known class of μ-conotoxins.

Caption

Google Patents

A kind of method of yeast bio synthesis conotoxin

Abstract

The invention discloses a kind of biology preparation methods of Yeast expression conotoxin.Conotoxin maturation peptide gene optimizes genetic codon preferences according to Pichia pastoris, artificial synthesized mature peptide gene is cloned into the expression vector with sfGFP, obtains the Yeast engineering bacteria for expressing conotoxin after being transferred to yeast, prepares conotoxin.The yeast expression system that the present invention uses expresses biologically active conotoxin, and safety is high, and expression product can be used for the diseases potential drug such as nerve, has many advantages, such as lower production costs, it can be achieved that large-scale production.

Classifications

A61P25/00 Drugs for disorders of the nervous system

View 5 more classifications

CN110358770A
China

Download PDF | Find Prior Art | Similar

Other languages: Chinese

Inventor: 伍炳华, 缪颖, 郑磊

Current Assignee : Fujian Agriculture and Forestry University

Worldwide applications

2019 • CN

Application CN201910685519.0A events

2019-07-27 • Application filed by Fujian Agriculture and Forestry University

2019-07-27 • Priority to CN201910685519.0A

2019-10-22 • Publication of CN110358770A

Caption

marine drugs

MDPI

Review

Conotoxin Patenting Trends in Academia and Industry

Noemi Sanchez-Campos [1], Johanna Bernaldez-Sarabia [1] and Alexei F. Licea-Navarro [1,2,*]

[1] Biomedical Innovation Department, Scientific Research Center and Higher Education from Ensenada (CICESE), Carretera Ensenada-Tijuana 3918, Zona Playitas, Ensenada 22860, BC, Mexico
[2] Innovation and Development Office, Scientific Research Center and Higher Education from Ensenada (CICESE), Carretera Ensenada-Tijuana 3918, Zona Playitas, Ensenada 22860, BC, Mexico
* Correspondence: alicea@cicese.mx

Abstract: Sea snails of the genus *Conus* produce toxins that have been the subjects of numerous studies, projects, publications, and patents over the years. Since *Conus* toxins were discovered in the 1960s, their biological activity has been thought to have high pharmaceutical potential that could be explored beyond the limits of academic laboratories. We reviewed 224 patent documents related to conotoxins and conopeptides globally to determine the course that innovation and development has

Caption

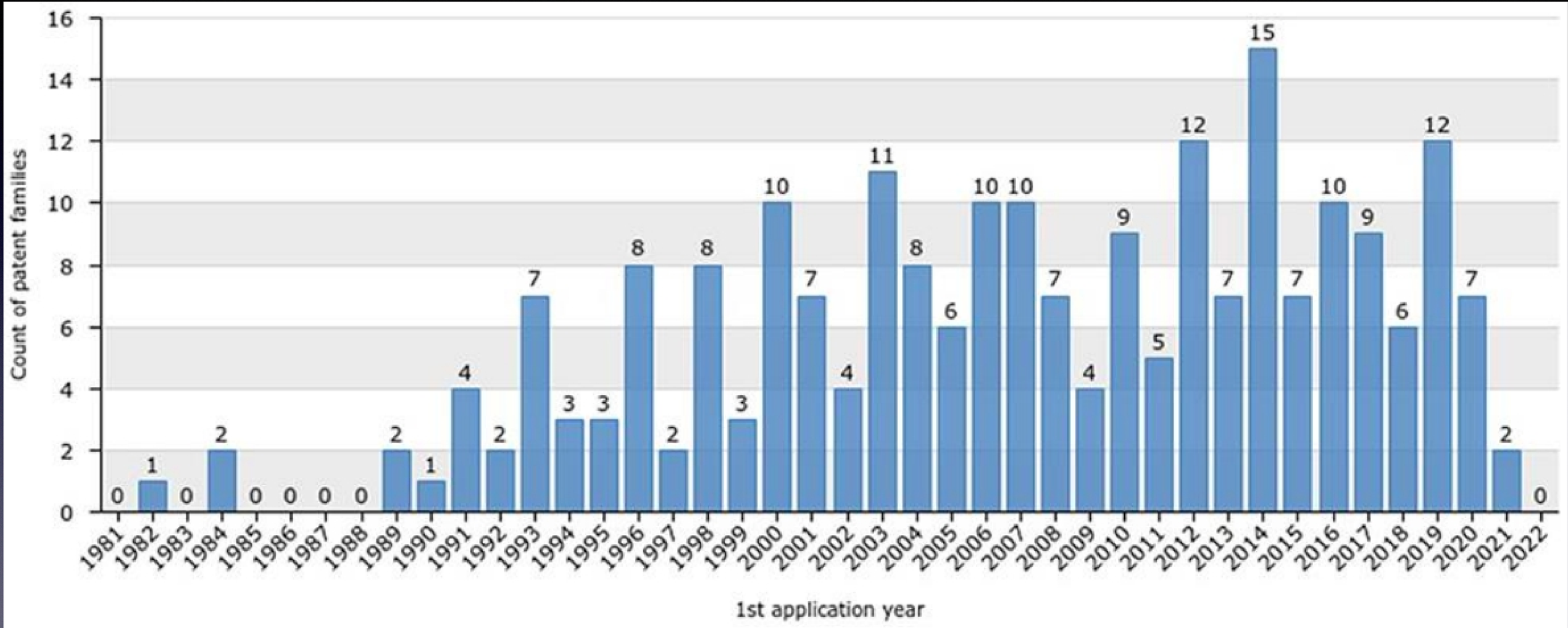
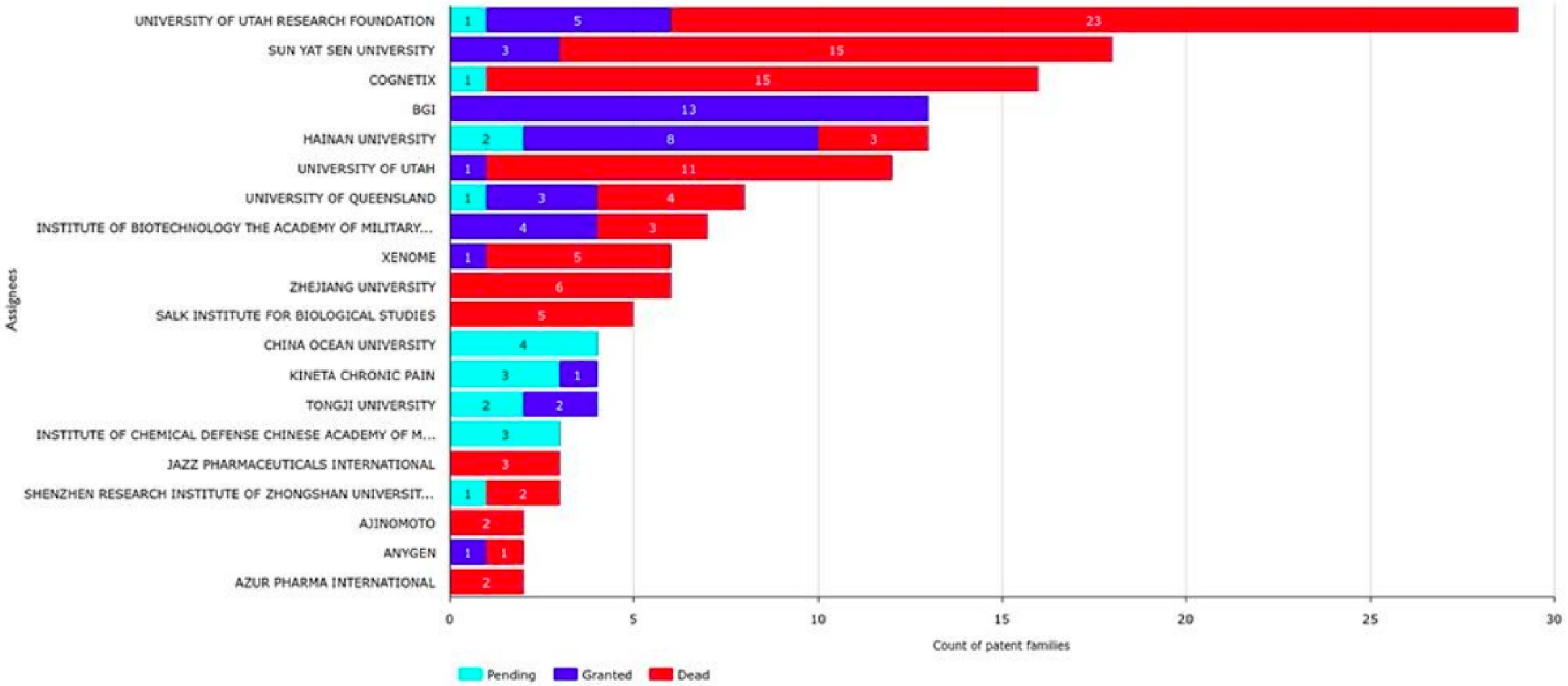


Figure 1. Conotoxin patent applications overview for the last 41 years.

Caption

the Institute of Chemical Defense Chinese Academy of Military Science have all of their applications still pending. The most recent pending applications belong to Kineta and the Institute of Chemical Defense of the Chinese Academy of Military Sciences (Figure 5).



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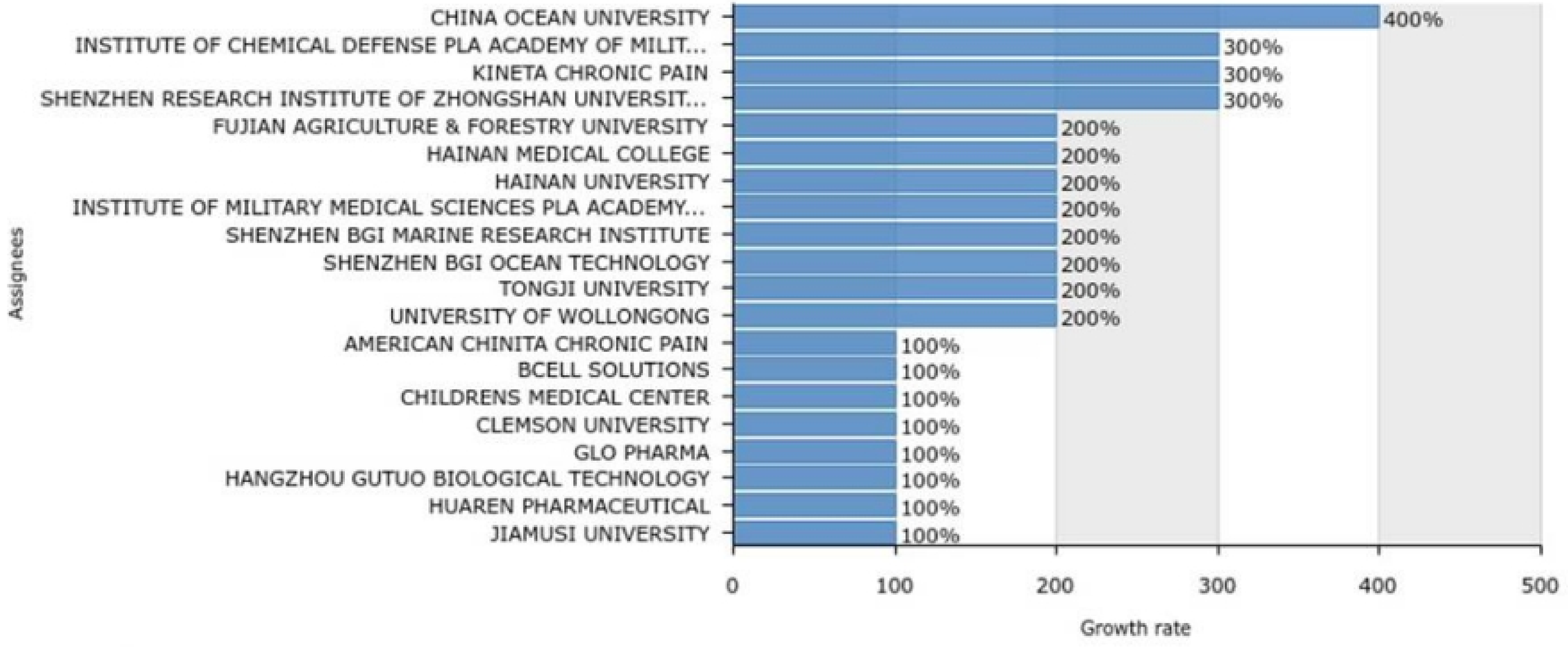


Figure 17. Assignees with the highest growth rates over the last six years (2016–2022), based on the number of filings per year.

Caption

(3), Taiwan (3), and Iceland (2; Figure 13). Between 2016 and 2022, the countries/territories that submitted the most patent applications for conotoxin inventions were: China (29), the United States (9), Canada (6), Australia (6), and Japan (6), Brazil (5), India (4), Korea (4), Israel (3), Singapore (3), Hong Kong (2), Mexico (2), Russia (2), United Arab Emirates (1), Switzerland (1), Chile (1), Colombia (1), and Costa Rica (1; Figure 14).

Captio

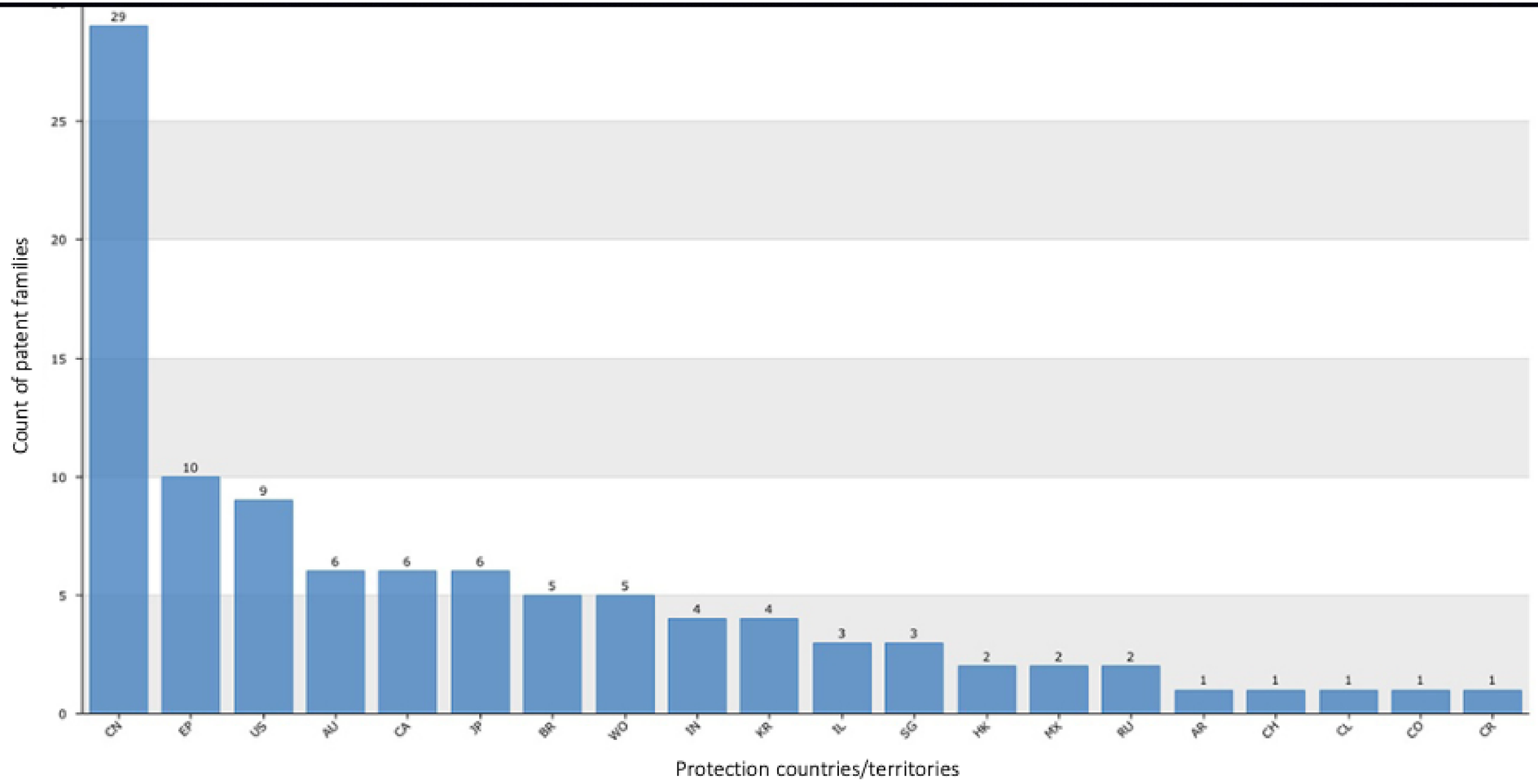
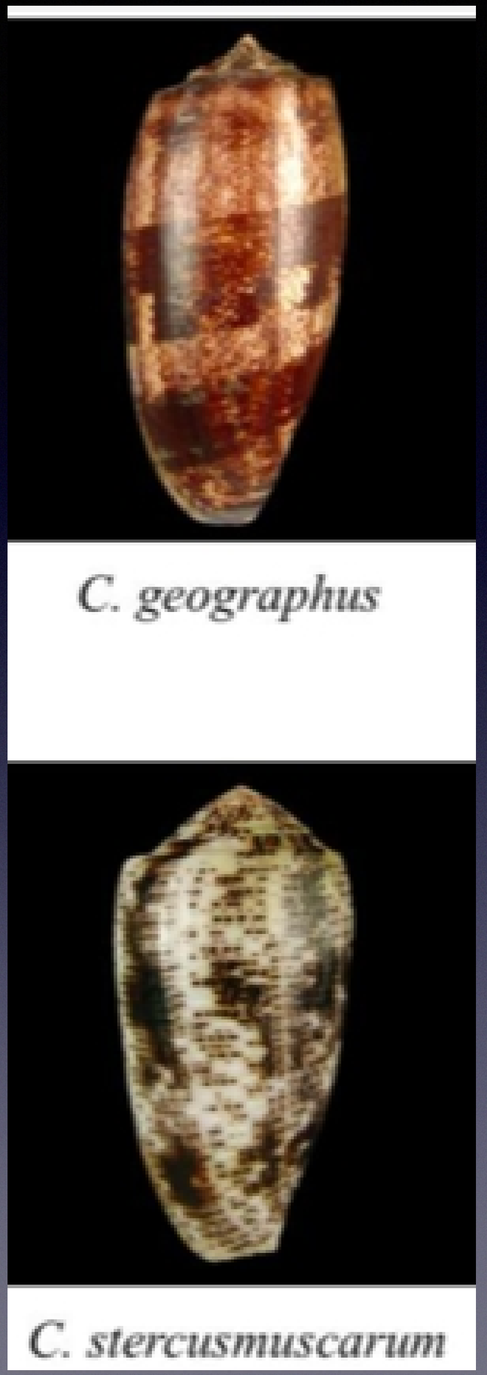


Figure 14. Top 20 countries/territories where the assignees have submitted conotoxin patent applications between 2016 and 2022.

Caption



Caption

Conotoxins: Potential Weapons From the Sea

NCJ Number: 240750
Journal: *Bioterrorism & Biodefense* Volume: 3 Issue: 3 Dated: 2012 Pages: 1-4
Author(s): Peter D. Anderson; Gyula Boker
Date Published: 2012
Length: 4 pages

Annotation
Cone snails are predatory marine animals that kill their prey with powerful venom.

Abstract
Conotoxins are a pharmacologically and chemically diverse group of toxins found in the venom. A number of species of cone snails, such as Conus geographus, are deadly to humans. Conotoxins affect numerous neurotransmitter receptors and ion channels in the body. The receptors impacted include nicotinic, adrenergic, NMDA, and serotonergic. Ion

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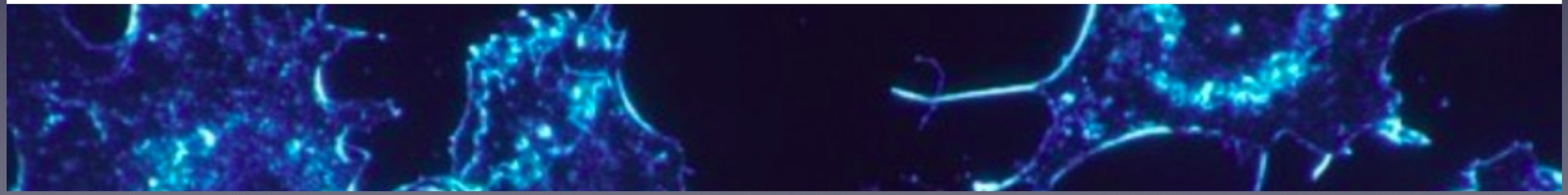
IMPROVING THE STATE
OF THE WORLD

FOURTH INDUSTRIAL REVOLUTION

How can killer snails improve the state of the world?

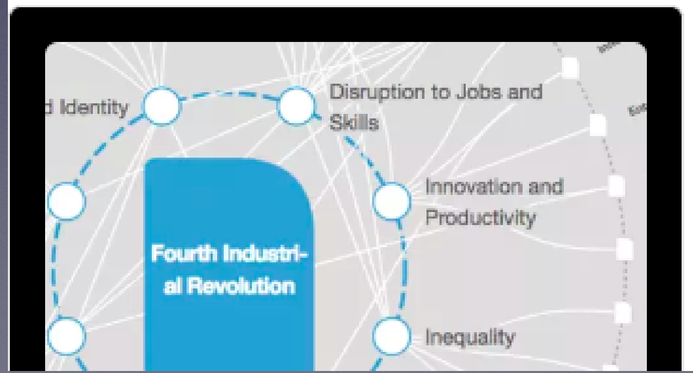
Sep 11, 2015



Caption

Mandë Holford

Associate Professor of Chemical Biology, Hunter College, City University of New York (CUNY)



This post is part of a blog series with Young Scientists, who attended the Annual Meeting of the New Champions 2015, which took place in Dalian, China, from 9-11 September. In this blog, Mande Holford, Assistant Professor of Chemical Biology at Hunter College in New York, discusses using venomous marine snails as tools for manipulating cell signalling in the nervous system.

How can killer snails help improve the state of the world?

Most people wouldn't think of snails as venomous creatures, but just like snakes, scorpions and spiders they have an extraordinary potential to contribute to medical science.

Venom is potent, fast-acting and extremely efficient. In short, it has all the makings of a successful drug. The venom of conoidean snails – or killer snails, as I lovingly refer to them – allows these slow-moving predators to feed on an agile prey by shutting down a fish's normal functions, preventing them from escaping. The same venomous peptides that switch off cellular function can be used to stop cancerous cells from multiplying and forming malignant tumours, or turn off neuronal impulses such as chronic pain.

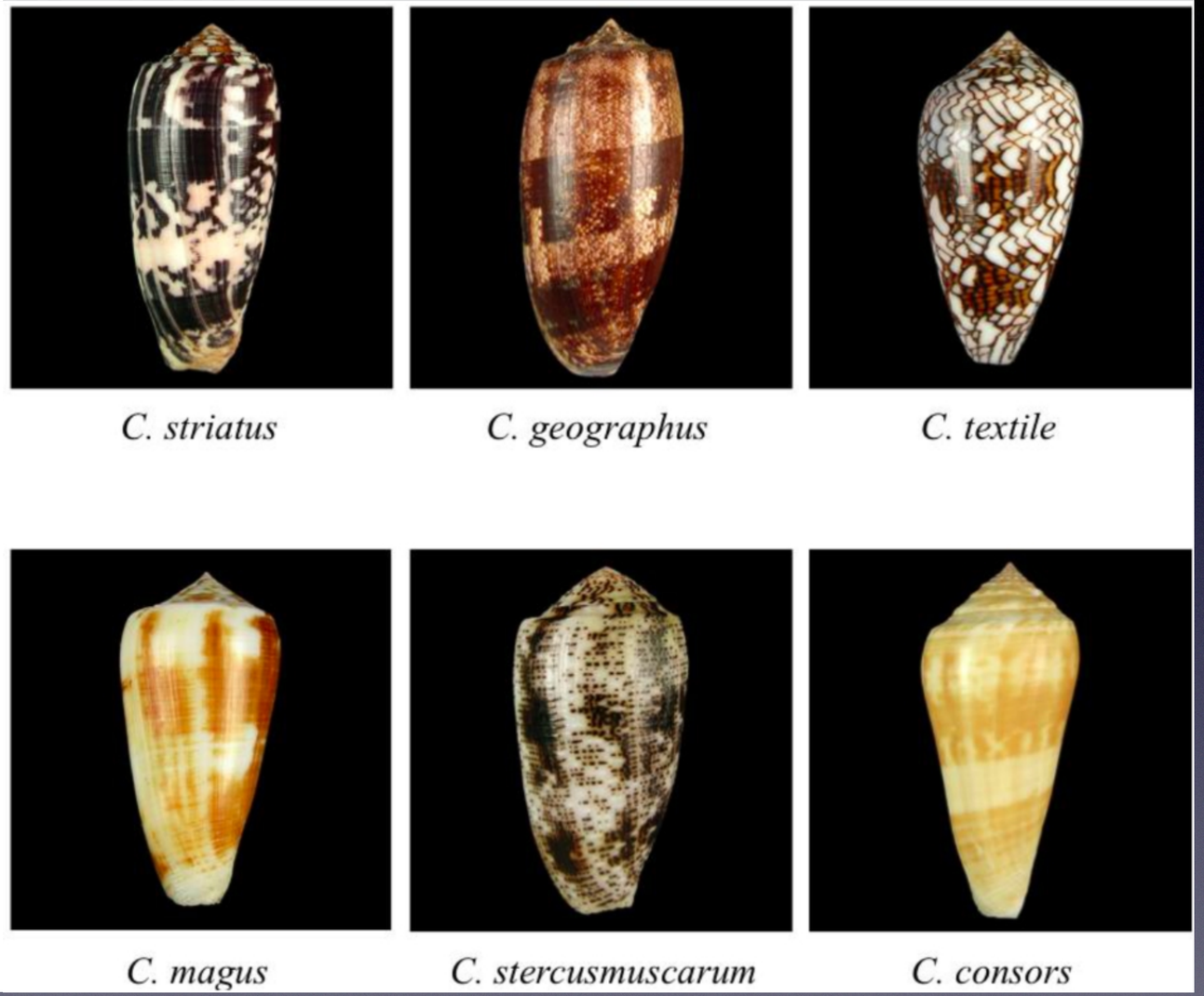
15 **Conotoxins** In COVID-19 Patients

Cone snail drug 1000x more potent than morphine

By AAP with AG Staff • March 17, 2014

Australian cone snail (Conus textile), with proboscis extended and poised for attack. Image credit: AAP Image/Melbourne University/David Paul

Caption



Caption

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Cone snail drug 1000x more potent than morphine

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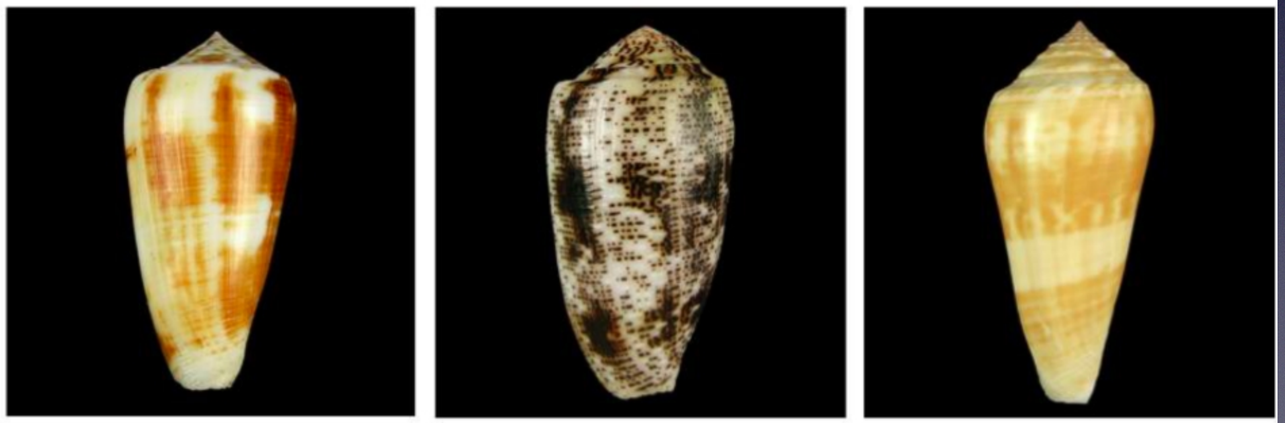
Australian cone snail (Conus textile), with proboscis extended and poised for attack. Image credit: AAP Image/Melbourne University/David Paul

C. striatus *C. geographus* *C. textile*



C. magus *C. stercusmuscarum* *C. consors*

Caption

Conotoxin Cl9.6	NA	. Conotoxin Cl9.6	81	1736779	*Californiconus californicus*

Conotoxin Cl9.6	NA	. Conotoxin Cl9.6	81	1736779	*Californiconus californicus*

Caption

Conotoxin Cl9.6	NA	. Conotoxin Cl9.6	81	1736779	Californiconus californicus

Caption

Conus californicus Conotoxin Cl9.6-Yeast

Filters

Technique

Supplier

Species

Label

Isotype

Host

Tissue

Virus

Disease

Catalog number	GEN1186700.Yeast
Supplier	MBS Recombinant
Price	2103.77 USD
Size	1000ug

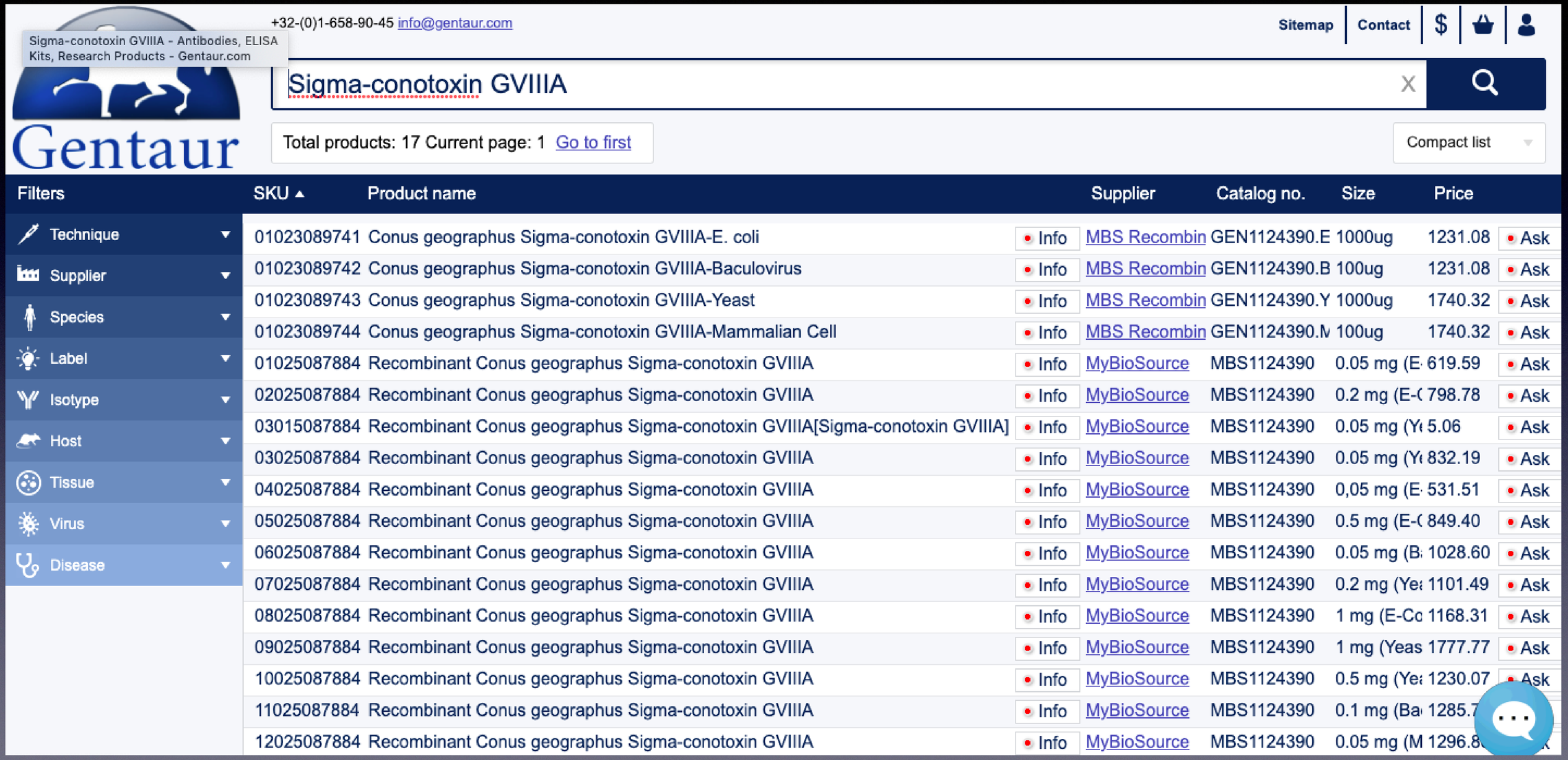
Contact us | Ask Conus californicus Conotoxin Cl9 6-Yeast selection audit

+ Add to compare

Quantity: − 1 +

Add to cart

Long name	Recombinant Conus californicus Conotoxin Cl9.6
Alternative names	Conotoxin Cl9.6;
Gene name	N/A
General description	Conotoxin Cl9.6 is a recombinant protein expressed in Yeast . The protein can be with or without a His-Tag or other tag in accordance to customer's request. All of our recombinant proteins are manufactured in strictly controlled facilities and by using well established technology which guarantees full batch-to-bact consistency and experiment reproducibility.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Price
01023089741 Conus geographus Sigma-conotoxin GVIIIA-E. coli Info MBS Recombin GEN1124390.E 1000ug 1231.08 Ask
01023089742 Conus geographus Sigma-conotoxin GVIIIA-Baculovirus Info MBS Recombin GEN1124390.B 100ug 1231.08 Ask
01023089743 Conus geographus Sigma-conotoxin GVIIIA-Yeast Info MBS Recombin GEN1124390.Y 1000ug 1740.32 Ask
01023089744 Conus geographus Sigma-conotoxin GVIIIA-Mammalian Cell Info MBS Recombin GEN1124390.M 100ug 1740.32 Ask
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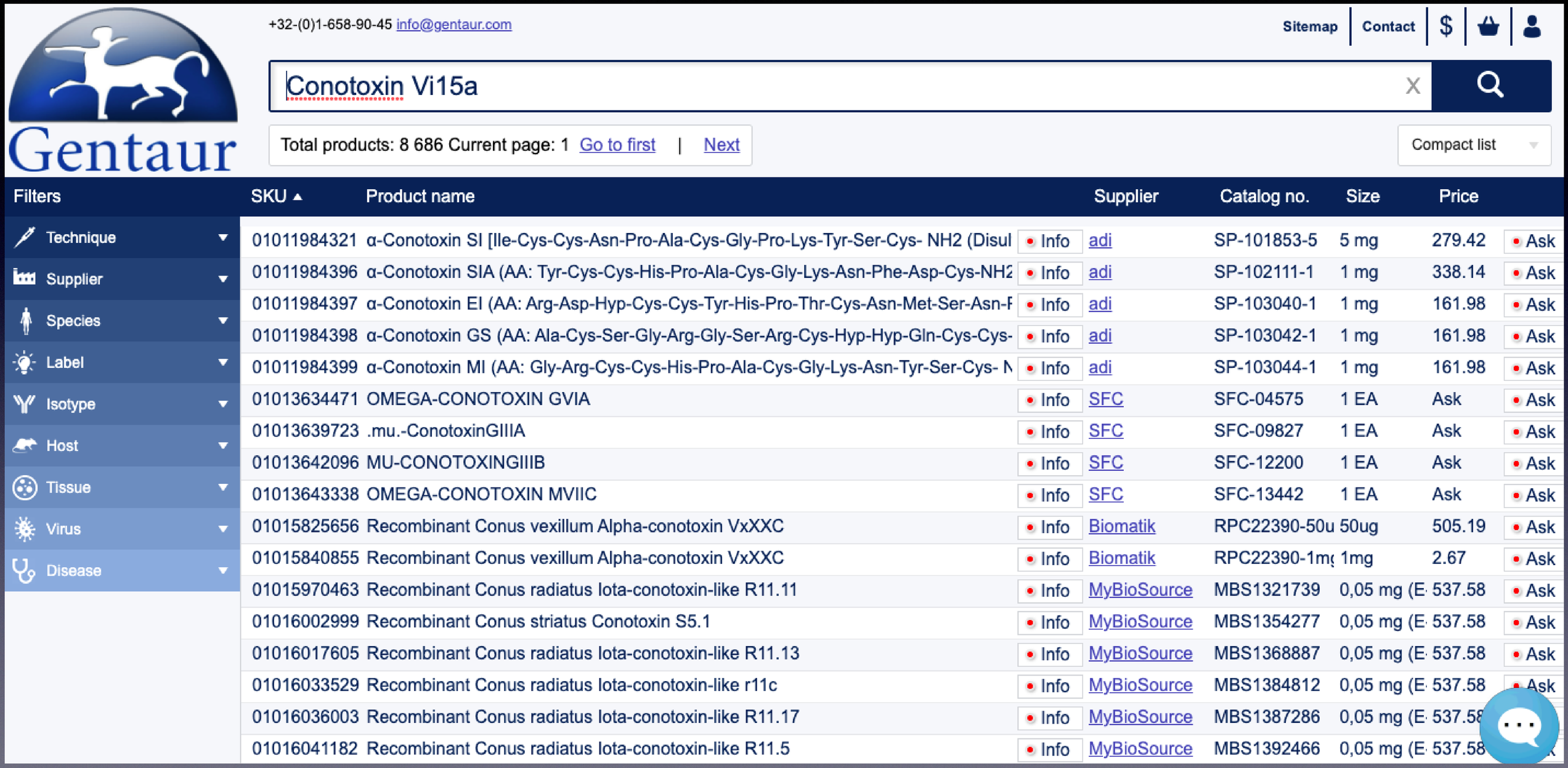
Caption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Technique
Supplier
Species
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Isotype
Host
Tissue
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Disease
SKU ▲ Product name Supplier Catalog no. Size Price
01011984321 α-Conotoxin SI [Ile-Cys-Cys-Asn-Pro-Ala-Cys-Gly-Pro-Lys-Tyr-Ser-Cys- NH2 (Disul Info adi SP-101853-5 5 mg 279.42 Ask
01011984396 α-Conotoxin SIA (AA: Tyr-Cys-Cys-His-Pro-Ala-Cys-Gly-Lys-Asn-Phe-Asp-Cys-NH2 Info adi SP-102111-1 1 mg 338.14 Ask
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01016002999 Recombinant Conus striatus Conotoxin S5.1 Info MyBioSource MBS1354277 0,05 mg (E 537.58 Ask
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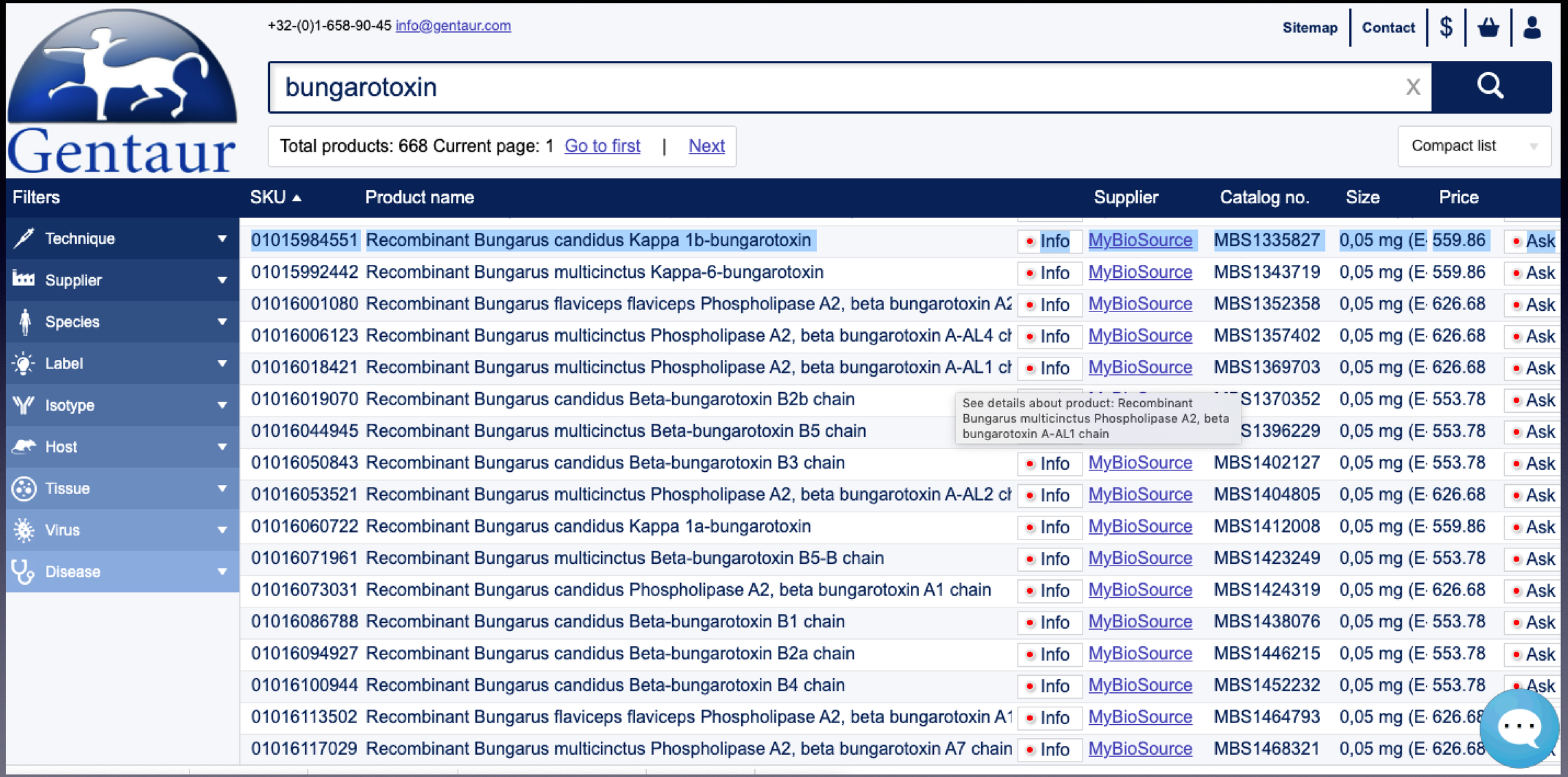
Caption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Catalog no.
Size
Price
01015984551 Recombinant Bungarus candidus Kappa 1b-bungarotoxin Info MyBioSource MBS1335827 0,05 mg (E 559.86 Ask
01015992442 Recombinant Bungarus multicinctus Kappa-6-bungarotoxin Info MyBioSource MBS1343719 0,05 mg (E 559.86 Ask
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01016019070 Recombinant Bungarus candidus Beta-bungarotoxin B2b chain S1370352 0,05 mg (E 553.78 Ask
See details about product: Recombinant Bungarus multicinctus Phospholipase A2, beta bungarotoxin A-AL1 chain
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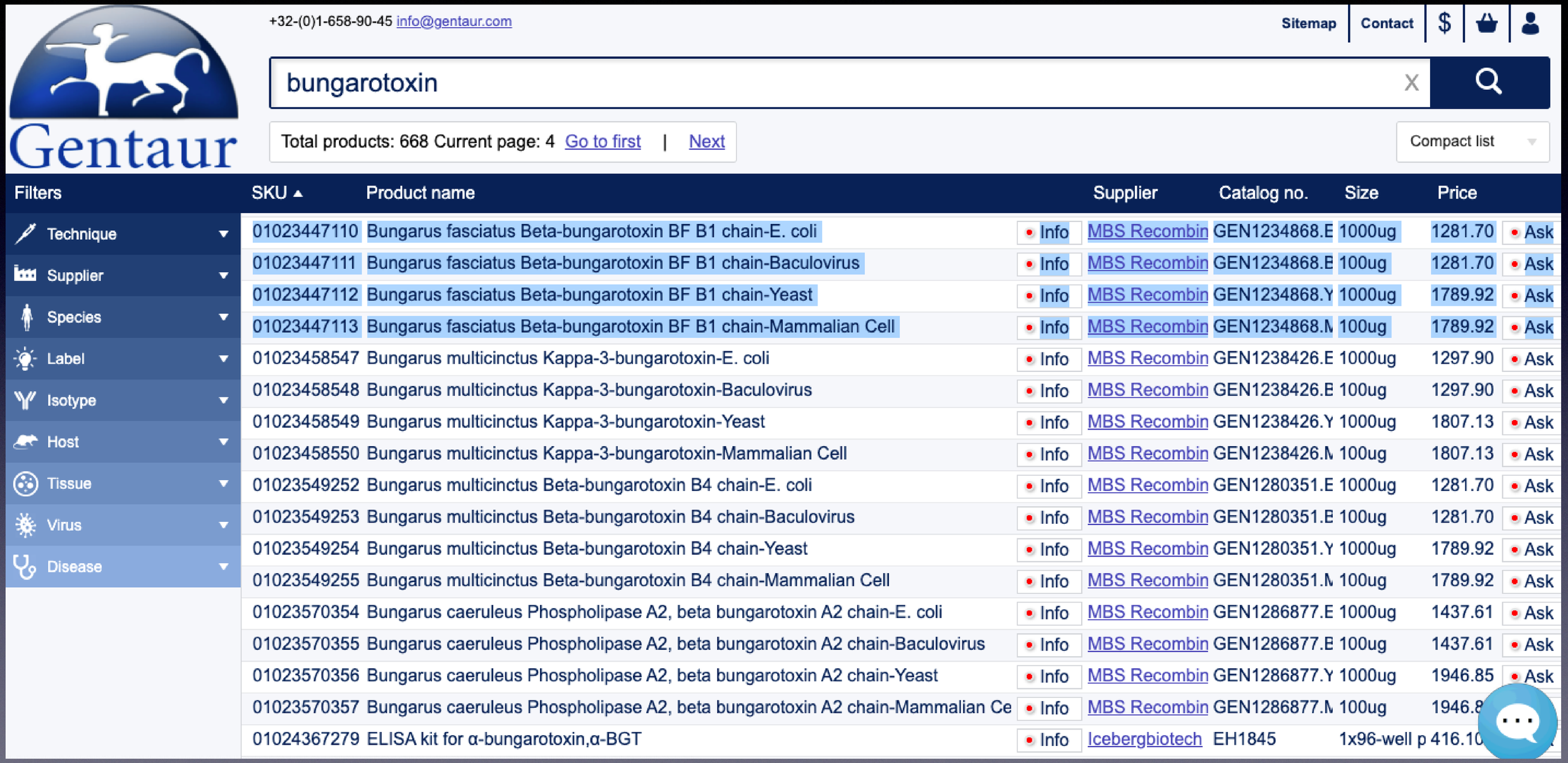
01016071961 Recombinant Bungarus multicinctus Beta-bungarotoxin B5-B chain Info MyBioSource MBS1423249 0,05 mg (E 553.78 Ask
01016073031 Recombinant Bungarus candidus Phospholipase A2, beta bungarotoxin A1 chain Info MyBioSource MBS1424319 0,05 mg (E 626.68 Ask
01016086788 Recombinant Bungarus candidus Beta-bungarotoxin B1 chain Info MyBioSource MBS1438076 0,05 mg (E 553.78 Ask
01016094927 Recombinant Bungarus candidus Beta-bungarotoxin B2a chain Info MyBioSource MBS1446215 0,05 mg (E 553.78 Ask
01016100944 Recombinant Bungarus candidus Beta-bungarotoxin B4 chain Info MyBioSource MBS1452232 0,05 mg (E 553.78 Ask
01016113502 Recombinant Bungarus flaviceps flaviceps Phospholipase A2, beta bungarotoxin A1 Info MyBioSource MBS1464793 0,05 mg (E 626.68
01016117029 Recombinant Bungarus multicinctus Phospholipase A2, beta bungarotoxin A7 chain Info MyBioSource MBS1468321 0,05 mg (E 626.68

Caption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bungarotoxin
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SKU ▲ Product name Supplier Catalog no. Size Price
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01023458549 Bungarus multicinctus Kappa-3-bungarotoxin-Yeast Info MBS Recombin GEN1238426.Y 1000ug 1807.13 Ask
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01023549254 Bungarus multicinctus Beta-bungarotoxin B4 chain-Yeast Info MBS Recombin GEN1280351.Y 1000ug 1789.92 Ask
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01023570357 Bungarus caeruleus Phospholipase A2, beta bungarotoxin A2 chain-Mammalian Ce Info MBS Recombin GEN1286877.M 100ug 1946.8
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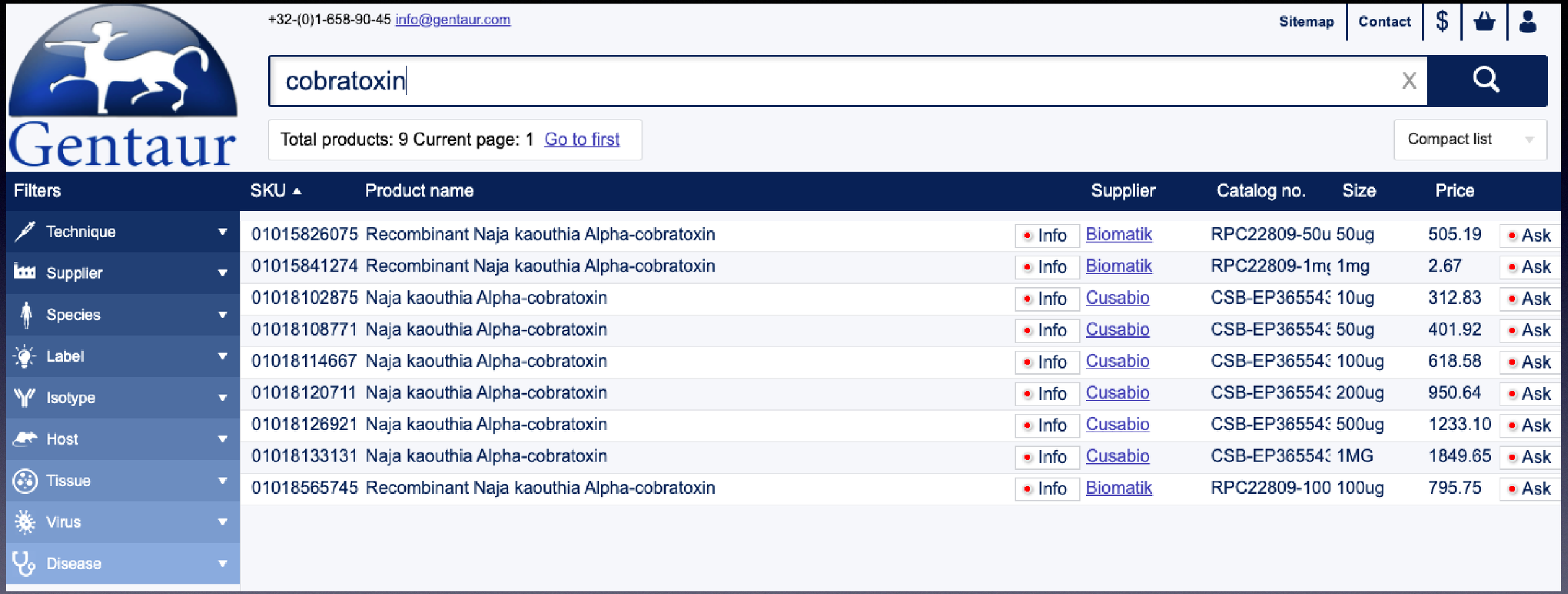
Caption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SKU ▲ Product name Supplier Catalog no. Size Price
01015826075 Recombinant Naja kaouthia Alpha-cobratoxin Info Biomatik RPC22809-50u 50ug 505.19 Ask
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01018102875 Naja kaouthia Alpha-cobratoxin Info Cusabio CSB-EP36554 10ug 312.83 Ask
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01018120711 Naja kaouthia Alpha-cobratoxin Info Cusabio CSB-EP36554 200ug 950.64 Ask
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01018565745 Recombinant Naja kaouthia Alpha-cobratoxin Info Biomatik RPC22809-100 100ug 795.75 Ask

Caption

Senior Projects

Fall 2021–2022
Fall 2020–2021
Fall 2019–2020
Fall 2018–2019
Fall 2017–2018
Fall 2016–2017

Synthetic Snake Venom
The Novel Creation of *Crotalid* Phospholipase A2 Using Genetic Engineering

Taylor Anderson | Emily Jesgarz | Richard Klein | Andrew Merkley | Alaric Siddoway

Introduction

Antivenin is listed as one of the World Health Organization's Essential Medicines, and as such, it is integral to a modern health care system. Antivenin is currently developed through a process of milking venomous animals, in this case, snakes, concentrating the venom, inoculating animals, and isolating antibodies found in their plasma. The aim of this project is to genetically engineer an organism to overexpress common proteins found in snake venom, thereby lowering the cost of antivenin.

Antivenin Manufacturing and Facts

Design Criteria and Objectives

To genetically engineer an organism, several steps are performed, including: PCR, obtaining the desired DNA, DNA transformation, cell culturing, and DNA extraction. The outlined criteria down below guided our design.

Design Objectives

1. Introduce the DNA for PLA_2 into an organism
2. Express PLA_2 production and secretion in an organism
3. Ensure the functionality of PLA_2
4. Evaluate and improve the economic viability of the process

Caption


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