CoVenom-19

Dr. Bryan Ardis D.C.

January 2020

HEALTH NEWS ✓ Fact Checked

Where Did the New Coronavirus Come From? Potentially a Bat, Snake, or Pangolin

Written by George Citroner on January 27, 2020 — Fact checked by Dana K. Cassell

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The new coronavirus was first detected in Wuhan, China. Getty Images

- Coronaviruses are named for their crown-like shape, and were first identified in the mid-1960s. The virus typically causes respiratory illnesses like the common cold.
- A new study found the virus may have originated in bats and then spread to humans via a snake or pangolin.
- Seven coronaviruses are known to infect humans.

January 2020

Shen Yongyi, a professor with the university and member of the research team, told the Xinhua news service that although previous research found the novel coronavirus originated in bats, the animals hibernate in winter, making it unlikely that they caused the current outbreak.

However, the actual study hasn't been published. So far, the university has only issued a press release.

Caption

January 2020

Snakes could be the source of the Wuhan coronavirus outbreak

THE CONVERSATION

By Haitao Guo, Guangxiang "George" Luo and Shou-Jiang Gao, The Conversation

Updated 2041 GMT (0441 HKT) January 24, 2020

January 2020

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(CNN) — Snakes -- the Chinese krait and the Chinese cobra -- may be the original source of the newly discovered coronavirus that has triggered an outbreak of a deadly infectious respiratory illness in China this winter.

The many-banded krait (Bungarus multicinctus), also known as the Taiwanese krait or the Chinese krait, is a highly venomous species of elapid snake found in much of central and southern China and Southeast Asia.

Related Article: Wuhan coronavirus death toll rises, as city imposes transport lackdown

The illness was first reported in late December 2019 in Wuhan, a major city in central China, and has been rapidly spreading. Since then, sick travelers from Wuhan have infected people in China and other countries, including the United States.

Using samples of the virus isolated from patients, scientists in China have determined the

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"recombination" of a viral protein that recognizes and binds to receptors on host cells. Such recognition is key to allowing viruses to enter host cells, which can lead to infection and disease.

Finally, the team uncovered evidence that the 2019-nCoV likely resided in snakes before being transmitted to humans. Recombination within the viral receptor-binding protein may have allowed for cross-species transmission from snake to humans.

"Results derived from our evolutionary analysis suggest for the first time that snake is the most probable wildlife animal reservoir for the 2019-nCoV," the authors wrote. "New information obtained from our evolutionary analysis is highly significant for effective control of the outbreak caused by the 2019-nCoV-induced pneumonia."

An accompanying editorial notes that although the ultimate control of emerging viral infections requires the discovery and development of effective vaccines and/or antiviral drugs, currently licensed antiviral drugs should be tested against the 2019-nCoV.

Concerned about this viral infection from China that may have originated in snakes and bats? Read

January 2020

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NEWS HEALTH & MEDICINE

No, snakes probably aren't the source of that new coronavirus in China

New research pinpoints the reptiles, but virus researchers aren't convinced

January 2020

sciencenews.org/article/snakes-probably-not-source-spread-new-coronavirus-outbreak-china

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Wei Ji, a microbiologist at Peking University Health Science Center School of Basic Medical Sciences in Beijing, and his colleagues analyzed codons used by 2019-nCoV. Codons, which are trios of DNA or RNA that dictate amino acids in a protein, tend to be similar between a virus and the animal it infects. The team compared 2019-nCoV's codons with those in potential animal reservoirs, including humans, chickens, bats, hedgehogs, pangolins and two snake species.

Based on similarities between the virus's codons and those of its potential animal hosts, "snake is the most probable wildlife animal reservoir for the 2019-nCoV," the researchers write. Wei and his team suggest a virus from the many-banded krait (*Bungarus multicinctus*) or Chinese cobra (*Naja atra*) may have combined with a bat virus and sparked the new outbreak.

But "coronaviruses tend to be found in mammals," says David Robertson, a virologist at the University of Glasgow in Scotland. So it's improbable the new virus came from snakes, he says.

January 2020 published Origin of Covid-19

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RESEARCH ARTICLE

JOURNAL OF MEDICAL VIROLOGY WILEY

Cross-species transmission of the newly identified coronavirus 2019-nCoV

Wei Ji[1] | Wei Wang[2] | Xiaofang Zhao[3] | Junjie Zai[4] | Xingguang Li[5]

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[2]Department of Spleen and Stomach Diseases, The First affiliated Hospital of Guangxi University of Chinese Medicine, Nanning, China

[3]Department of Science and Technology, Ruikang Hospital Affiliated to Guangxi

Abstract

The current outbreak of viral pneumonia in the city of Wuhan, China, was caused by a novel coronavirus designated 2019-nCoV by the World Health Organization, as determined by sequencing the viral RNA genome. Many initial patients were exposed to wildlife animals at the Huanan seafood wholesale market, where poultry, snake, bats, and other farm animals were also sold. To investigate possible virus

Caption

January 2020

onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25682

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other mammals.[27] Bootscanning plot analysis (data not shown) suggested that the major parents of the 2019-nCoV originated from Clade A (bat-SL-CoVZC45 and bat-SL-CoVZXC21) but formed a monophyletic cluster different from them. Overall, the ancestral origin of the 2019-nCoV was more likely from divergent host species rather than SARS-CoV.

The host range of some animal coronaviruses was promiscuous.[7] They caught our attention only when they caused human diseases

In summary, results derived from our evolutionary analysis suggest that 2019-nCoV has most similar genetic information with bat coronovirus and has most similar codon usage bias with snake. Additionally, a homologous recombination may occured within the viral receptor-binding spike glycoprotein, which may determine cross-species transmission. These novel findings warrant future investigation to experimentally determine if

November 2021

Epub 2021 Nov 25.

Codon usage bias

Sujatha Thankeswaran Parvathy [1], Varatharajalu Udayasuriyan [2], Vijaipal Bhadana [3]

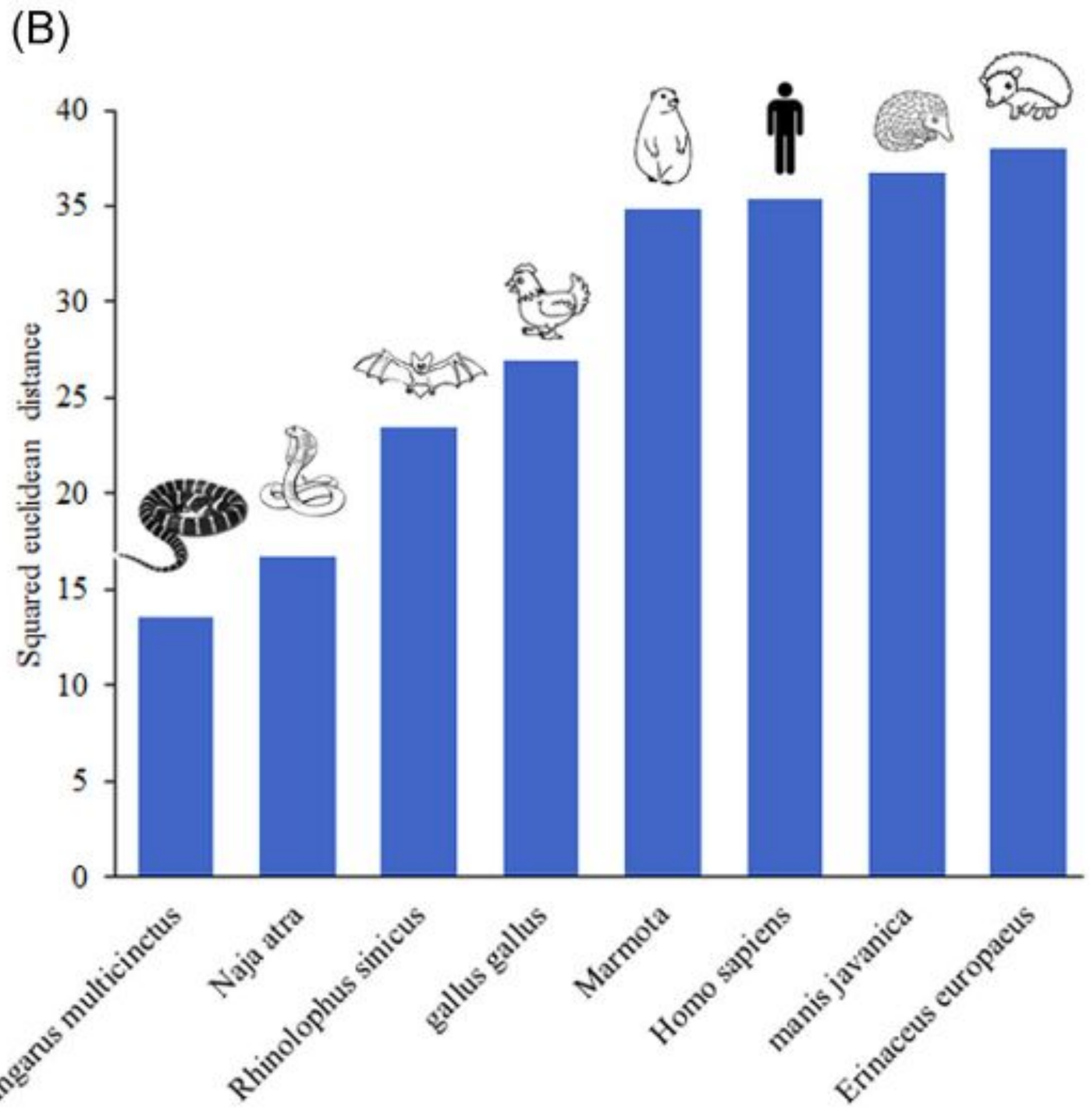
Affiliations + expand

PMID: 34822069 PMCID: PMC8613526 DOI: 10.1007/s11033-021-06749-4

Free PMC article

Abstract

Codon usage bias is the preferential or non-random use of synonymous codons, a ubiquitous phenomenon observed in bacteria, plants and animals. Different species have consistent and characteristic codon biases. Codon bias varies not only with species, family or group within kingdom, but also between the genes within an organism. Codon usage bias has evolved through mutation, natural selection, and genetic drift in various organisms. Genome composition, GC content, expression level and length of genes, position and context of codons in the genes, recombination rates, mRNA folding, and tRNA abundance and interactions are some factors influencing codon bias. The factors shaping codon bias may also be involved in evolution of the universal genetic code. Codon-usage bias is critical factor determining gene expression and cellular function by influencing diverse processes such as RNA processing, protein translation and protein folding. Codon usage bias reflects the origin, mutation patterns and evolution of the species or genes. Investigations of codon bias patterns in genomes can reveal phylogenetic relationships between organisms, horizontal gene transfers, molecular evolution of genes and identify selective forces that drive their evolution. Most important application of codon bias analysis is in the design of transgenes, to increase gene expression levels through codon optimization, for development of


(B)
Squared euclidean distance
0
5
10
15
20
25
30
35
40
Bungarus multicinctus
Naja atra
Rhinolophus sinicus
gallus gallus
Marmota
Homo sapiens
manis javanica
Erinaceus europaeus

April 2020

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News and events

A nicotinic hypothesis for Covid-19 with preventive and therapeutic implications

Jean-Pierre Changeux [1]; Zahir Amoura [2, 3]; Felix A. Rey [4]; Makoto Miyara [2, 5]

Caption

April 2020

Full text

Symptomatic Covid-19 disease (as caused by SARS-CoV-2 virus) is observed in 2.5 percent of infected individuals [2] indicating an individual variability in the clinical presentation. Among the epidemiological and clinical features of Covid-19, the following features are of special interest for understanding the patho-physiolology, namely: (1) in outpatients with favorable outcome : neurological/psychiatric disorders, especially loss of sense of smell which is specific of the disease and (2) in hospitalized older patients with a poor prognosis : systemic hyperinflammatory syndrome with increased levels of circulating cytokines and atypical acute respiratory distress syndrome with loss of neurological control of lung perfusion regulation and hypoxic vasoconstriction [3]. This raises the issue of the basis of inter-individual variability for the susceptibility to infection.

The nAChR appears as a hypothetical clue for the main clinical manifestations of Covid-19. It is accepted that the angiotensin converting enzyme 2 (ACE2), represents the principal receptor molecule for SARS-CoV-2 [4, 5, 6]. ACE2 is expressed at the transcriptomic level in the lung, the small intestine and colon, in the kidney, in the testis, in the heart muscle and in the brain, yet the protein is not detected in the lung [7]. In the brain, ACE2 is expressed in both neurons and glia and particularly present in the brain stem and in the regions responsible for the regulation of cardiovascular functions, including the subfornical organ, paraventricular nucleus, nucleus of the tractus solitarius, and rostral ventrolateral medulla [8]. Additional receptors or co-receptors are, however, not excluded. The relationship between nicotine and ACE2 has been explored in the framework of cardiovascular and pulmonary diseases [9]. Accordingly, in the ACE/ANG II/AT1R arm, nicotine increases the expression and/or activity of renin, ACE and AT1R, whereas in the compensatory ACE2/ANG-(1–7)/MasR arm, nicotine down regulates the expression and/or activity of ACE2 and AT2R, thus suggesting a possible contribution of acetylcholine receptors in ACE2

Caption

April 2020

relationship between nicotine and ACE2 has been explored in the framework of cardiovascular and pulmonary diseases [9]. Accordingly, in the ACE/ANG II/AT1R arm, nicotine increases the expression and/or activity of renin, ACE and AT1R, whereas in the compensatory ACE2/ANG-(1–7)/MasR arm, nicotine down regulates the expression and/or activity of ACE2 and AT2R, thus suggesting a possible contribution of acetylcholine receptors in ACE2 regulation. This possibility has not yet been explored in the framework of viral neuroinfections.

There is strong evidence for a neurotropic action of SARS-CoV-2 infection. It has been demonstrated that β-coronaviruses to which the SARS-CoV-2 belongs, do not limit their presence to the respiratory tract and have been shown to frequently invade the CNS [10]. This propensity has been convincingly documented for the SARS-CoV-1, MERS-CoV and the coronavirus responsible for porcine hemagglutinating encephalomyelitis (HEV 67N). In light of the high similarity between SARS-CoV-1 and SARS-CoV-2, it is quite likely that SARS-CoV-2 also possesses a similar potential. Neuroinfection has been proposed to potentially contribute to the pathophysiology and clinical manifestations of Covid-19 [10] with the neuroinvasive potential of SARS-CoV-2 suggested to play a role in the respiratory failure of Covid-19 patients [11, 12]. Our nicotinic hypothesis proposes that the virus could enter the body through neurons of the olfactory system and/or through the lung leading to different clinical features with different outcome, and contrasts with the currently accepted view that ACE2 is the principal receptor of SARS-CoV-

Caption

April 2020

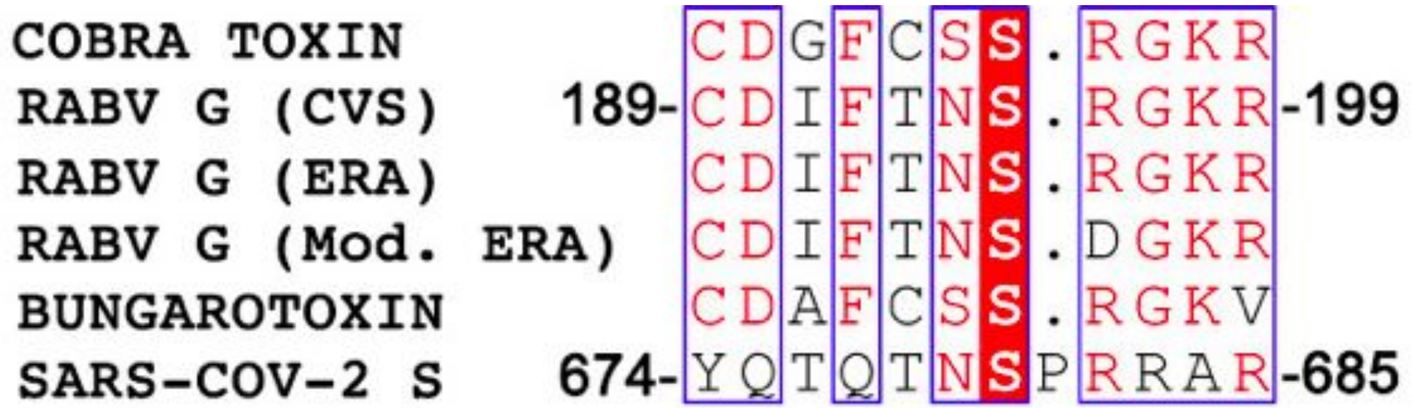

Figure 1.

The neurotoxin motifs. Amino acid sequence alignment of the motifs found in toxins from snakes of the Ophiophagus (cobra) and Bungarus genera, in G from three RABV strains and in S from SARS-CoV-2.

Nicotine may be suggested as a potential preventive agent against Covid-19 infection. Both the epidemiological/clinical evidence and the in silico findings may suggest that Covid-19 infection is a nAChR disease that could be prevented and may be controlled by nicotine. Nicotine would then sterically or allosterically compete with the SARS-CoV-2 binding to the nAChR. This legitimates the use of nicotine as a protective agent against SARS-CoV-2 infection and the subsequent deficits it causes in the CNS. Thus, in order to prevent the infection and the retro-propagation of the virus through the CNS, we plan a therapeutic assay against Covid-19 with nicotine (and other nicotinic agents) patches or other delivery methods (like sniffing/chewing) in hospitalized patients and in the general population.

April 2020

Figure 1.

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In conclusion, we propose, and try to justify, the hypothesis that nAChRs play a critical role in the pathophysiology of SARS-CoV-2 infection and as a consequence propose nicotine and nicotinic orthosteric and/or allosteric agents as a possible therapy for SARS-CoV-2 infection. Interestingly, ivermectin, which has been recently shown to inhibit the replication of SARS-CoV-2 in cells in vitro [53], is a positive allosteric modulator of α7 nAChR [54]. The nicotinic hypothesis might be further challenged by additional clinical studies and by experimental observations determining whether SARS-CoV-2 physically interacts with the nAChR in vitro, for instance by

June 2021

JUNE 18, 2021 BY JENNY

Snake venom toxin in the spike protein?

Unusual gene insertions within the SARS-CoV-2 viral gene sequence were found that resemble the protein structure and genetic code of a snake venom toxin. That is the bad news. The good news is that an anti-clotting snake venom anti-toxin medication was found helpful in the treatment of patients with severe COVID19. The anti-clotting medication is Tirofiban/Aggrastat, see image, and Dr. Fauci was emailed about the success of the treatment on April 27, 2020. It would have been nice of Dr. Fauci to let the rest of us know the good news last year.

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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.

The information reported in Table 1 has been retrieved from the UniprotKB database and from the NCBI Taxonomy database[20], after confirmation by BLAST sequence comparison analysis[18].

SANIST was set to perform the database search considering all potential protein points and post-translational modifications, and to consider proton rearrangements. No enzyme cutting rules were specified, but all the protein subsequence combinations were considered. Database search calculation was performed by means of General Processing Graphic Processing Units (GPGPU).

The MS data are available on the ZENODO platform[16] (see section *Data availability*).

Results and discussion

The presence of (oligo-)peptides characterised as toxic components of animal venoms was observed in plasma and urine samples from SARS-CoV-2 infected patients and never in plasma, urine and faecal samples from control individuals. Examples of SACI-CIMS chromatograms are reported in Figure 1 and Figure 2 (panels a and b), showing the spectra acquired

The types of toxic-like peptides found resemble known conotoxins, phospholipases A2, metalloproteinases, prothrombin activators, coagulation factors, usually present in animal venoms, which are known to have high specificity and affinity towards human ion channels, receptors, and transporters of the nervous system, like the nicotinic acetylcholine receptor. Cheng *et al.*[21] reported the discovery of a superantigen-like motif in the S1 Spike protein, as well as two other neurotoxin-like motifs that have peptide similarities to neurotoxins from *Ophiophagus* (cobra) and Bungarus genera. They conclude that neurotoxin-like motifs are present in SARS-CoV-2 protein products, acting as neurotoxin-like peptides. We checked in the full set of peptides we got (here we report only 36 examples), and we identified, in plasma and faecal samples, toxin-like peptides mapping on kappa 1a-bungarotoxin, Kappa 1b-bungarotoxin from Malayan krait, kappa-2-bungarotoxin and alpha-bungarotoxin from many-banded krait (Uniprot Accession Numbers Q8AY56, Q8AY55, P15816, and P60615, respectively), which were reported by Cheng and colleagues. Furthermore, we looked at the amino acid changes currently reported in GISAID data[22], analysed by CoV-GLUE-Viz (update 15/09/2021)[23], and

Table 1. Overview of candidate proteins on which toxin-like peptides have been mapped. Thirty-six candidate protein sequences on which the identified toxin-like peptides have been mapped are here reported, together with information retrieved from UniprotKB and NCBI Taxonomy databases. The table is split in three sections according to the phylum of the reported species: *Chordata* (green), *Echinodermata* (pink), *Mollusca* (azure).

Caption

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

AC	ID	Status	Protein name	ENZYME EC	Other name(s)	Length (aa)	ID	Species	Phylum - Family	Organism's common name(s)
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-	91	8665	*Ophiophagus hannah*	***Chordata*** *- Viperidae*	. King cobra . Naja hannah

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)***
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 Flal6d *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

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)***
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

January 2007

pubmed.ncbi.nlm.nih.gov/17979732/

Review > Curr Pharm Des. 2007;13(28):2872-86. doi: 10.2174/138161207782023775.

Snake venom components affecting blood coagulation and the vascular system: structural similarities and marked diversity

Yasuo Yamazaki [1], Takashi Morita

Affiliations + expand

PMID: 17979732 DOI: 10.2174/138161207782023775

Abstract

In studies of blood coagulation and the vascular system, snake venom toxins have been indispensable in elucidating the complex physiological mechanisms that govern coagulation and the vascular system in mammals, given their potency and highly specific biological effects. The various components of snake venom toxins can be classified according to their mechanism of action, for example, serine proteases, metalloproteinases, Kunitz-type protease inhibitors, phospholipases A(2), (L)-amino acid oxidases, C-type lectin(-like) proteins, disintegrins, vascular endothelial growth factors, three-finger toxins, and cysteine-rich secretory proteins. Although the molecular structures of most toxins are not unique to snake venom toxins, venom proteins often

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

D.V.D. Hemalika
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."

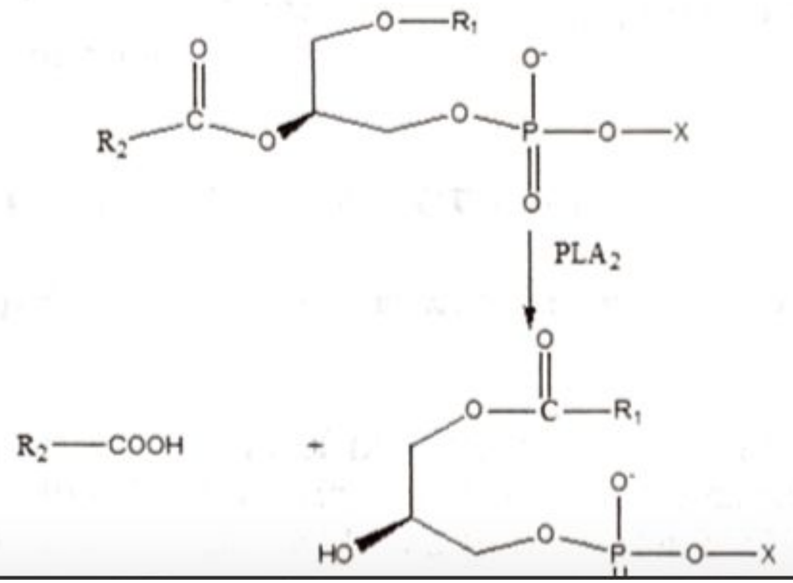
Caption

6. AdPLA2 - adipose PLA2

Among them, sPLA2 is the first discovered group of PLA2 enzymes, which was discovered as a component of cobra venom [22]. PLA2 has been identified as one of the main components of animal venom. Elapidae and Viperidae family snakes having sPLA2 group IA, IIA or IIB as the main component in snake venom [23]. Snake venom PLA2s induce pathophysiological alterations in the victim by hydrolyzing phospholipids in membranes [23].

Among all existing isoforms of phospholipase enzymes, sPLA2 mainly play a major role in developing drug target as inhibitors since it involves in many inflammatory conditions [24].

Studies about this sPLA2 enzyme and its function, hold great importance since PLA2 catalyzes the release of arachidonic acid, which is believed to be the rate-limiting event in the generation of pro-inflammatory lipid mediators (prostaglandins, leukotrienes, lipoxins) and platelet-activating factor [25]. Release of these mediators initiates the pain, swelling, and other unpleasant symptoms we experience as part of an inflammatory response [26].



Caption

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

August 2021

SNAKE VENOM-RELATED ENZYME MAY DRIVE COVID-19 MORTALITY

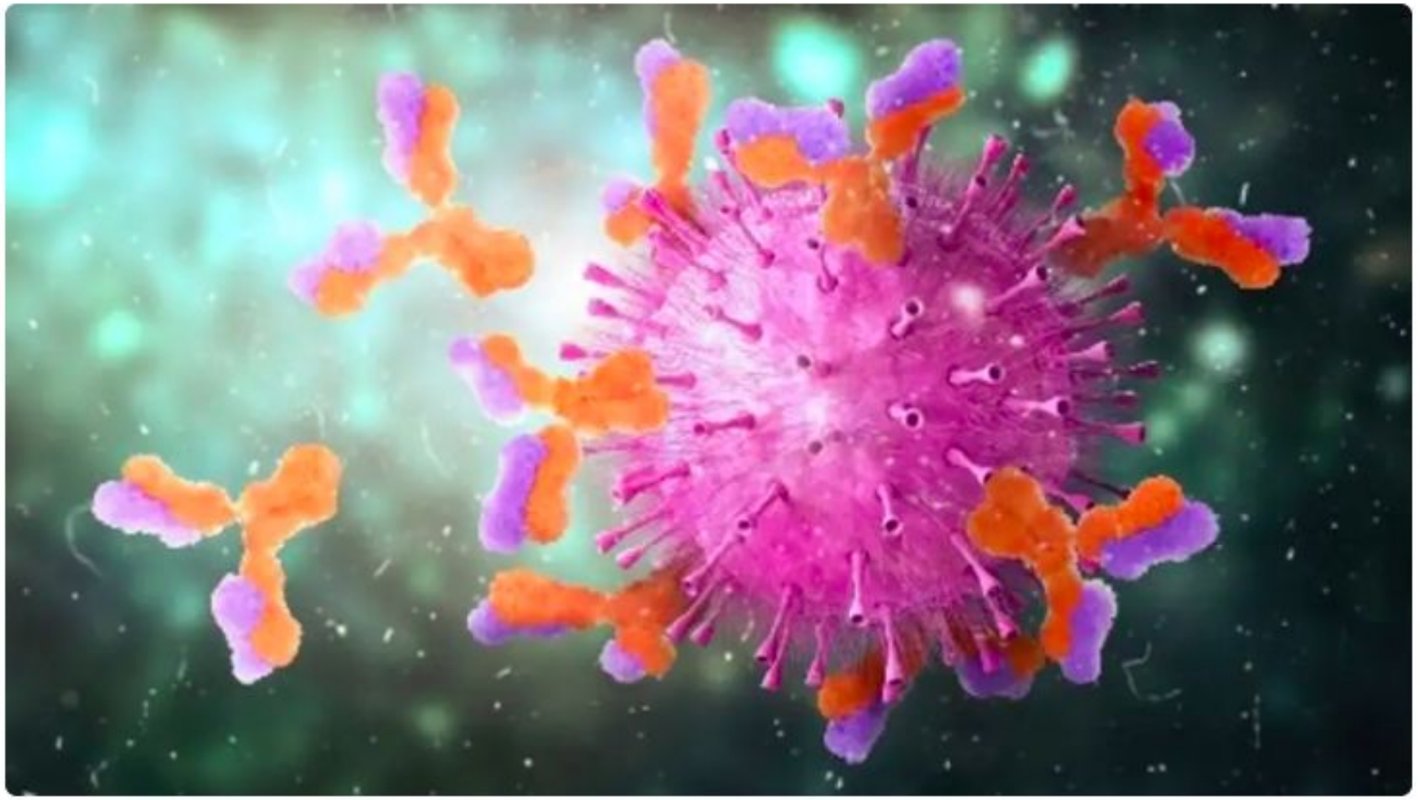
AUGUST 26TH, 2021

POSTED BY ROSE BRANDT-ARIZONA

"This enzyme is trying to kill the virus, but at a certain point it is released in

Scientists Decode Molecular Mechanism Responsible for COVID-19 Mortality

By IANS · 25 August, 2021 · TWC India



Representative Image

(IANS)

A team of researchers has identified what may be the key molecular mechanism responsible for COVID-19 mortality—an enzyme related to neurotoxins found in rattlesnake venom.

Study finds link between COVID-19 deaths and snake venom

University of Arizona researchers find certain enzyme that could be driving COVID deaths.

JAN

12

Dr. Charles Hoffe Issues Dire Warning About MRNA 'Vaccines', Points To D-Dimer Blood Test And Negative Impact Of 'Clot Shots' - Public Health England PHE Reports That Fully Vaccinated People Are 885% More Likely To Die From Covid-19 Than Those Who Are Jab Free And Pure Blooded - Billionaire Great Reset Promises, Promises

Dr. Charles Hoffe Issues Dire Warning About MRNA 'Vaccines', Points To D-Dimer Blood Test And Negative Impact Of 'Clot Shots' - Public Health England PHE Reports That Fully Vaccinated People Are 885% More Likely To Die From Covid-19 Than Those Who Are Jab Free And Pure Blooded - Billionaire Great Reset Promises, Promises

Caption

How are elevated D-dimer levels interpreted?

Updated: Nov 18, 2019 | Author: Reka G Szigeti, MD, PhD; Chief Editor: Eric B Staros, MD more...

References

Answer

D-dimer is the degradation product of crosslinked fibrin; therefore, it reflects ongoing activation of the hemostatic system. Since there is constant minimal physiologic fibrin formation and degradation in vivo, healthy individuals have a minimal D-dimer level.

Elevated D-dimer levels reflect ongoing activation of the hemostatic and thrombolytic system, providing clinical utility in the following:

- Evaluation of thrombus formation
- Ruling out DVT (discussed further below)
- Monitoring anticoagulative treatment (a decreasing value indicates effective treatment)
- Disseminated intravascular coagulation (DIC)
- Snake venom poisoning

Media Toolkit

Penn mRNA Scientists Drew Weissman and Katalin Karikó Receive 2021 Lasker Award, America's Top Biomedical Research Prize

Weissman and Karikó's mRNA technology is recognized for enabling rapid development of highly effective COVID-19 vaccines

September 24, 2021

November 2009

Mol Ther. Author manuscript; available in PMC 2009 Nov 10.

Published in final edited form as:

Mol Ther. 2008 Nov; 16(11): 1833–1840.

Published online 2008 Sep 16. doi: 10.1038/mt.2008.200

PMCID: PMC2775451

NIHMSID: NIHMS156788

PMID: 18797453

Incorporation of Pseudouridine Into mRNA Yields Superior Nonimmunogenic Vector With Increased Translational Capacity and Biological Stability

Katalin Karikó,[1] Hiromi Muramatsu,[1] Frank A Welsh,[1] János Ludwig,[2] Hiroki Kato,[3] Shizuo Akira,[3] and Drew Weissman[4]

Author information | Copyright and License information | Disclaimer

Caption

November 2009

ncbi.nlm.nih.gov/pmc/articles/PMC2775451/

Tube | Maps | Dropbox - TruLab... | Dietary Suppleme... | DuckDuckGo — P... | AHA: Mrna COVID... | Natural Immunity

A likely contributing factor to the enhanced translation observed with Ψ modification is an increase in biological stability of the mRNAs (Figure 4d). Indeed, higher resistance to hydrolysis by phosphodiesterases from snake venom and spleen has been reported when uridine was replaced with Ψ in dinucleotide substrates.19 Previous studies have also demonstrated that Ψ stabilizes RNA secondary structures by promoting base stacking,20 which could slow degradation. However, stability of mRNAs containing either uridines or pseudouridines was the same when tested by *in vitro* assays using human skin–associated RNases21 (data not shown). Enhanced translation might be another factor that improves stability by protecting the RNA with high ribosome occupancy.

Caption

November 2009

ncbi.nlm.nih.gov/pmc/articles/PMC2775451/

YouTube Maps Dropbox - TruLab... Dietary Suppleme... DuckDuckGo — P... AHA: Mrna COVID... Natural Immunity Rem

ACKNOWLEDGMENTS

Go to:

This work was supported by the National Institutes of Health (NIH) grants NIAID AI-050484, NHLBI HL87688, and NINDS NS-29331. H.M. was supported by Ruth L. Kirschstein National Research Service Awards postdoctoral fellowship. We thank Houping Ni for technical assistance. K.K. and D.W. have formed a small biotech company that receives funding from the NIH to explore the use of nucleoside-modified mRNA for gene therapy.

Caption

November 2009

ncbi.nlm.nih.gov/pmc/articles/PMC2775451/

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Caption

August 2011

Published online 3 August 2011

Nucleic Acids Research, 2011, Vol. 39, No. 21 ***9329–9338***
doi:10.1093/nar/gkr586

Nucleoside modifications in RNA limit activation of 2′-5′-oligoadenylate synthetase and increase resistance to cleavage by RNase L

Bart R. Anderson[1], Hiromi Muramatsu[2], Babal K. Jha[3], Robert H. Silverman[3], Drew Weissman[1] and Katalin Karikó[2,*]

[1]Department of Medicine, 3610 Hamilton Walk, 522B Johnson Pavilion, University of Pennsylvania, Philadelphia, PA 19104, [2]Department of Neurosurgery, 371 Stemmler Hall, University of Pennsylvania, Philadelphia, PA 19104 and [3]Department of Cancer Biology NB40, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA

Received April 17, 2011; Revised June 27, 2011; Accepted June 30, 2011

Caption

August 2011: mRNA study continues

The presence of Ψ has been shown to enhance the stability of RNA secondary structures, but has not previously been demonstrated to cause resistance to nucleases. RNA containing Ψ was cleaved efficiently by RNase A, RNase H (36), RNase T1, RNase T2, nuclease P1 and snake venom phosphodiesterase, although there is some indication that pancreatic diesterase and snake venom phosphodiesterase may cleave Ψ-RNA with reduced efficiency (37). A previous report based on cleavage of a $C_{11}N_2C_7$ oligo RNA showed that RNA containing 2′-deoxy-2′-α-fluorouridine was bound by RNase L but cleaved slowly, whereas RNA containing 2′-*O*-methyluridine was not bound by RNase L (38). Here, we used a similar approach and demonstrated that purified RNase L readily cleaved

Caption

August 2011

FUNDING

National Institutes of Health (R01AI50484 and R21DE019059 to D.W.; T32GM07229, T32DK07748 and T32RR007063 to B.R.A.; R01NS029331 and R42HL87688 to K.K.; R01CA044059 to R.H.S). Funding for open access charge: National Institutes of Health (grant R42HL87688 to K.K.).

Conflict of interest statement. K.K. and D.W. have formed a small biotech company RNARx that receives funding from the National Institutes of Health to explore the use of nucleoside-modified mRNA for gene therapy.

Snake Venom Phosphodiesterase I Purified Lyophilized

IDBRPDEILY100UN

Innovative Research

$133.00

Volume

100 un

Quantity

1

ADD TO CART

Snake Venom Phosphodiesterase I Purified lyophilized from Innovative Research is prepared by process of Williams, Sung and Laskowski, JBC, 236, 1130 (1961) and

Quantity

1

ADD TO CART

Snake Venom Phosphodiesterase I Purified lyophilized from Innovative Research is prepared by process of Williams, Sung and Laskowski, JBC, 236, 1130 (1961) and treated to inactivate contaminating 5'-nucleotidase activity according to Sulkowski and Laskowski, Biochim. Biophys. Acta, 240, 443 (1961). This is a lyophilized in vials with a concentration of 20 Units/mg dry weight.

This product is useful successively hydrolyzing 5'-mononucleotides from 3'-OH-terminated riboand deoxyribo-oligonucleotides. The enzyme has an optimal pH range of 9.8-10.4 and a molecular weight of 115 kDa. Phosphodiesterase is inhibited by reducing agents such as glutathione, The enzyme has an optimal pH range of 9.8-10.4 and a molecular weight of 115 kDa. It is inhibited by reducing agents such as glutathione, cysteine and ascorbic acids and completely inhibited by 5 mM EDTA. ATP, ADP and AMP are partial inhibitors. The enzyme has an absolute requirement for Mg^{2+}

Caption

January 2022

CONVERSATIONS ON HEALTH CARE

CONVERSATIONS ON HEALTH CARE

Pediatrician Dr. Peter Hotez Creates New Vaccine; Gives Advice for Families With Young Children Staying Safe During Surge

January 6, 2022 10:39 am < a min read

This content is provided by Community Health Center, Inc.

January 2022

Microbiologist Maria Bottazzi, her colleague Peter Hotez and their team at the Texas Children's Hospital's Center for Vaccine Development last month unveiled Corbevax, "the world's COVID-19 vaccine", and doctors say it could be a game changer.


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What Does India’s Biological E. Manufacture?

I am sure this is just coincidental… don’t you?

February 2022

PRODUCT LIST

Biological E. Limited
Celebrating Life Every Day

SERA

ANTI-SNAKE

1. Product : **SNAKE ANTIVENIN (Polyvalent) IP**
   (Enzyme Refined Equine Globulins)

   Label Composition : Each mL of Antiserum Neutralizes :

   - Cobra Venom *(Naja naja)* ..... 0.60 mg
   - Common Krait Venom *(Bungarus caeruleus)* ..... 0.45 mg
   - Russell's Viper Venom *(Vipera russelli)* ..... 0.60 mg
   - Saw Scaled Viper Venom *(Echis carinatus)* ..... 0.45 mg
   - Preservative : Phenol IP ..... ≤ 0.25% w/v

   Pack : Liquid & Lyophilized 10 mL Vial

   Indication : Passive Immunization against Snake bite

February 2022

PRODUCT LIST

Biological E. Limited
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VACCINES & BIOLOGICS

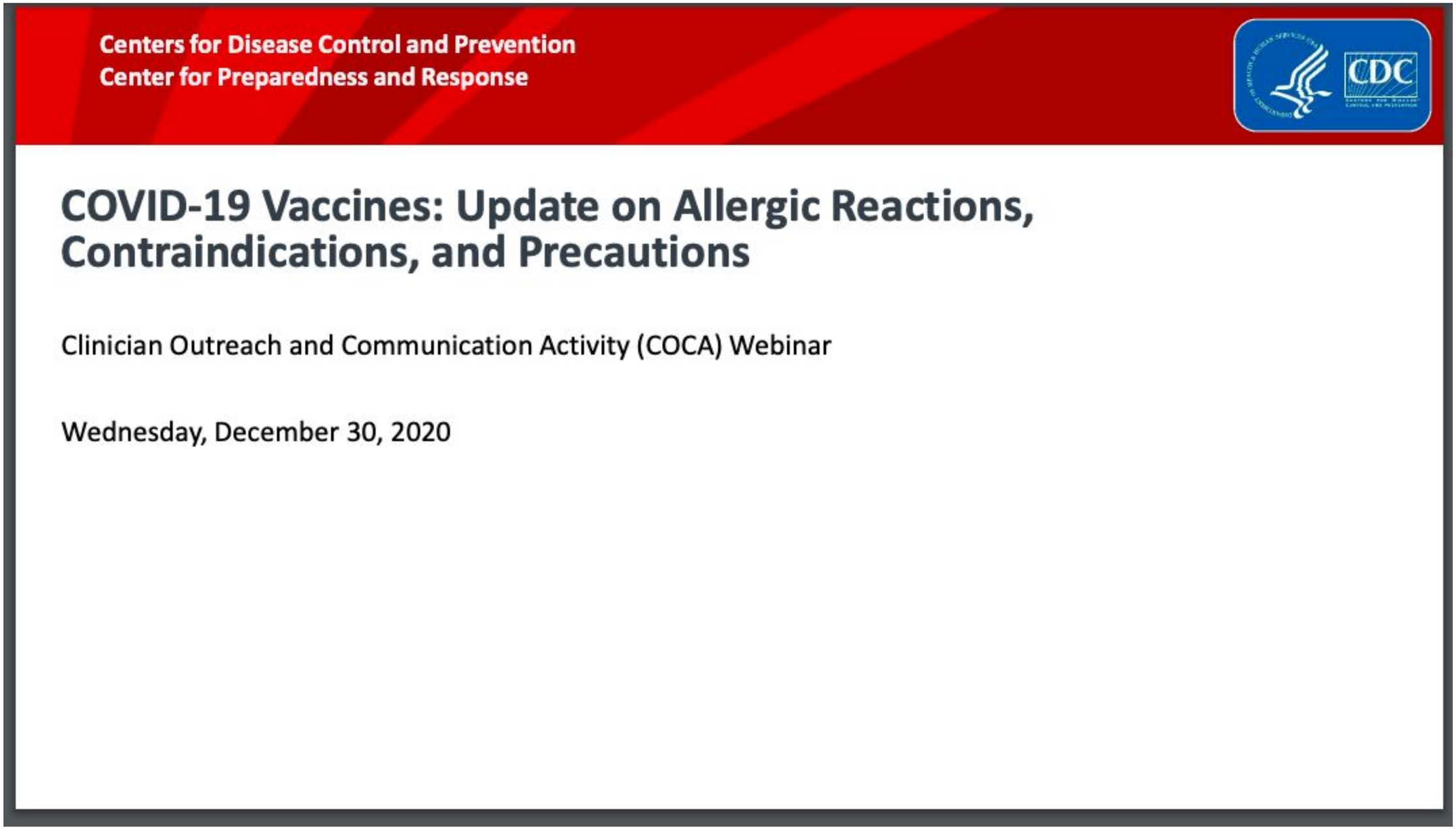
CORBEVAX™ GETS DCGI APPROVAL

CORBEVAX™ is India's 1st indigenously developed protein sub-unit COVID-19 Vaccine

- CORBEVAX™ is a "recombinant protein sub-unit" vaccine, developed from a component of the spike protein on the virus's surface, which helps the body build the immune response against the virus
- The vaccine has the Receptor Binding Domain (RBD) protein as an antigen, and also an optimum adjuvant consisting of Dynavax (DVAX) CpG 1018 and alum
- CORBEVAX™ is accorded Emergency Use Authorization as a COVID-19 vaccine and is available for consumption only in India via authorized channels

Click on the following for

Fact Sheet | SmPC | Package Insert | FAQs


Centers for Disease Control and Prevention
Center for Preparedness and Response
CDC
COVID-19 Vaccines: Update on Allergic Reactions, Contraindications, and Precautions
Clinician Outreach and Communication Activity (COCA) Webinar
Wednesday, December 30, 2020

Caption

Contraindications and Precautions to mRNA COVID-19 vaccination

Caption

Neither contraindications nor precautions to vaccination

Pfizer-BioNTech and Moderna COVID-19 vaccines

- History of allergic reactions not related to vaccines, injectable therapies, components of mRNA COVID-19 vaccines, or polysorbates, including:
  - Food
  - Pet dander
  - Venom
  - Environment
  - Oral medications
  - Latex
  - Eggs
  - Gelatin

Caption

Remember COVID-19 shots and the strange Magnetic Phenomenon

Dynabeads by Thermo Fisher Scientific

August 2011

Published online 3 August 2011

Nucleic Acids Research, 2011, Vol. 39, No. 21 ***9329–9338***
doi:10.1093/nar/gkr586

Nucleoside modifications in RNA limit activation of 2′-5′-oligoadenylate synthetase and increase resistance to cleavage by RNase L

Bart R. Anderson[1], Hiromi Muramatsu[2], Babal K. Jha[3], Robert H. Silverman[3], Drew Weissman[1] and Katalin Karikó[2,*]

[1]Department of Medicine, 3610 Hamilton Walk, 522B Johnson Pavilion, University of Pennsylvania, Philadelphia, PA 19104, [2]Department of Neurosurgery, 371 Stemmler Hall, University of Pennsylvania, Philadelphia, PA 19104 and [3]Department of Cancer Biology NB40, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA

Received April 17, 2011; Revised June 27, 2011; Accepted June 30, 2011

Caption

August 2011

RNA stability in rabbit reticulocyte lysate

Equal mass (25 ng/μl) or equal molar (40 μM) mRNAs-encoding firefly and *Renilla* luciferases were incubated in 15 μl rabbit reticulocyte lysate (RRL) (Promega) at 30°C. At the indicated times, a 2 μl aliquot was removed and the RNA was recovered using Trizol for subsequent detection by northern blotting.

RNA stability in cell culture

HEK293T, WT MEF or RNase $L^{-/-}$ MEF cells were nucleofected with 5 μg mRNA using nucleofector program T-020 and nucleofector V kit (Lonza). After 15 min recovery in RPMI, cells were plated in complete media and incubated at 37°C. At the indicated time, RNA was recovered from cells using Trizol for subsequent detection by northern blotting.

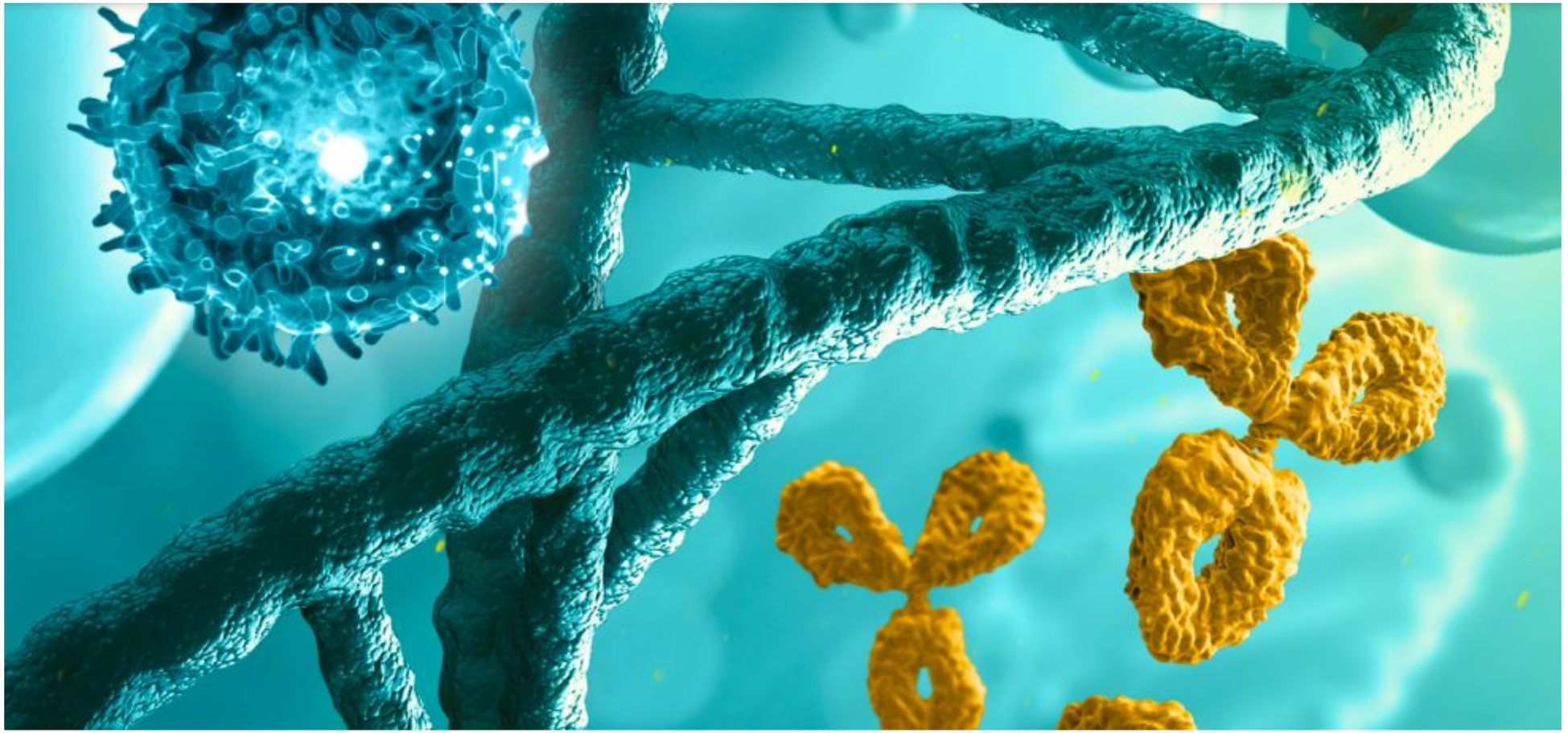
Northern blotting

RNA was isolated from RRL or cells using Trizol.

Immunoprecipitation

HEK293T cells were seeded into 96-well plates at a density of 5.0×10^4 cells/well 1 day prior to transfection. Cells were exposed to 50 μl DMEM containing lipofectin-complexed RNA (0.25 μg) for 1 h, which was then replaced with complete medium and further cultured. Cells were incubated in methionine/cysteine-free medium (Invitrogen) for 1 h, then pulsed with complete medium supplemented with ^{35}S-methionine/cysteine (140 mCi/ml) (PerkinElmer) for 3 h prior to lysis in 50 μl RIPA buffer supplemented with protease inhibitor cocktail (Sigma). *Renilla* luciferase was immunoprecipitated from lysates using an anti-*Renilla* luciferase antibody (PM047, Medical & Biological Laboratories) and protein G-coated Dynabeads (Invitrogen) and separated by 15% polyacrylamide gel electrophoresis. Gels containing the labeled samples were treated with 1 M sodium salicylate, dried and a fluorogram was generated by exposure to BioMax MS film (Kodak).

Caption



Dynabeads magnetic beads

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What are Dynabeads?

Since the 1980s, Invitrogen™ Dynabeads™ technology has pioneered magnetic separation of biological materials. Today, Dynabeads products support a staggering range of applications within the life sciences, biotechnology, and health care. They continue to provide the most gentle and efficient separation, helping to ensure reliable and reproducible results.

That's why, when it matters most, scientists trust Dynabeads products for their research.

What are Dynabeads?

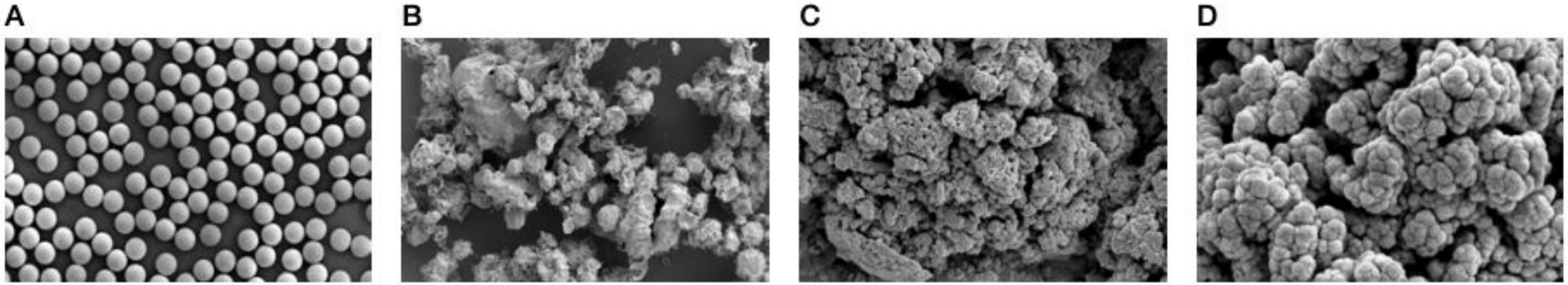


Figure 1. The magnetic bead you choose will affect your results. Dynabeads magnetic beads have a defined surface to carry out the necessary binding, with no inner surface to trap unwanted proteins. **(A)** Dynabeads products are the most uniform, monodispersed superparamagnetic beads, manufactured with highly controlled product quality to help ensure the highest degree of reproducibility. **(B–D)** Magnetic particles from alternative suppliers have variable shapes and sizes that trap impurities, resulting in lower reproducibility and increased nonspecific binding.

It began in space

Notable events in the history of Dynabeads magnetic beads

July 2021

Moderna co-founder using mRNA technology to treat venomous snakebites

By **Salmaan Farooqui** · **The Canadian Press**

Posted July 6, 2021 5:49 am · Updated July 6, 2021 5:52 am

July 2021

Gmail YouTube Maps Dropbox - TruLab... Dietary Suppleme... DuckDuckGo — P... AHA: Mrna COVII

Moderna co-founder using mRNA technology to treat venomous snakebites

In one interview, he mentioned offhand that mRNA could have more uses than vaccines, such as for antisera used to treat venomous snakebites.

That comment caught the attention of scientists in the snakebite community, and eventually led him to become an adviser for a company called Ophirex, which is working on a pill that could help save people's lives immediately after a snakebite.

Ophirex founder Matthew Lewin said many people die from snakebites on their way to hospital, since those most at risk of venomous snakebites are sometimes days away from the nearest hospital — and because antisera is

July 2021

globalnews.ca/news/8005422/moderna-cofounder-mrna-snakebotes/

Gmail YouTube Maps Dropbox - TruLab... Dietary Suppleme... DuckDuckGo — P... AHA: Mrna COVID

Moderna co-founder using mRNA technology to treat venomous snakebites

To combat that, Ophirex is working on a pill that targets a specific enzyme found in the venom of many snakes, and which is particularly harmful to the human body.

Lewin and Rossi say the pill could be the difference between someone dying en route to the hospital or making a full recovery.

“Seventy-five per cent of the deaths (from snakebites) occur before patients even get help,” said Lewin, who is based just north of San Francisco.

“For me, the idea that you could have something that could act as a bridge to survival on top of having a better outcome in the cases is really compelling.”

Ophirex Is a Public Benefit Corporation

As a registered Delaware public benefit corporation, Ophirex pursues its business in a manner that advances our vision to deliver potentially life-saving medical treatments and also serves the financial interests of our shareholders.

Our shareholders to date have been predominantly individual investors. These individuals invested in Ophirex in large part because of our commitment to address the medical need presented by snakebite — especially in under-resourced areas — as well as diseases and conditions with related mechanisms of illness and injury, to the extent we are capable.

In recognition of our development efforts, we have also won multiple grants from the U.S. Department of Defense and an award from the Wellcome Trust.

wellcome

Ophirex Receives Wellcome Trust Award to Advance Clinical Development of Novel Snakebite Treatment

— Wellcome Award Funds Manufacture of Clinical Supply for Upcoming Ophirex Trials —

Corte Madera, Calif., Monday, March 2, 2020 — Ophirex, Inc., a public-benefit biotechnology company working to improve outcomes for global victims of snakebite, announced today that it has received a $2.5 million award from the Wellcome Trust's £80 million (approximately $100 million) commitment to improve treatment of snakebite. The award will fund manufacturing of oral and IV varespladib, Ophirex's lead drug candidate, for use in Ophirex's upcoming, potentially pivotal clinical trial studies.

Ophirex is developing varespladib as a first-in-class, toxin-targeting antidote for snakebite, with the ultimate goal of safe and rapid administration to snakebite victims in the out-of-hospital setting where — without immediate access to antivenom — most snakebite deaths occur. By inhibiting the progression of a key venom component called "sPLA2," varespladib could mitigate many of the most common,

Caption

The World Health Organization (WHO) reinstated snakebite envenoming to its list of neglected tropical diseases in 2017 and, more recently, has outlined strategies to reduce the death and disability toll from snakebite —currently approximately 500,000 people per year — by half by 2030. In early 2019, the WHO Snakebite Envenoming Working Group specifically identified Ophirex's drug as a priority for accelerated study.1

1. Williams DJ, Faiz MA, Abela-Ridder B, Ainsworth S, Bulfone TC, Nickerson AD, Habib AG, Junghanss T, Fan HW, Turner M, Harrison RA, Warrell DA. Strategy for a globally coordinated response to a priority neglected tropical disease: Snakebite envenoming. Gutiérrez JM, ed. *PLoS Negl Trop Dis*. 2019;13(2):e0007059. doi:10.1371/journal.pntd.0007059.

2. Surugue L. Why is it so hard to stop people dying from snakebite? 2019. https://mosaicscience.com/story/snakebite-antivenom-crisis-Africa-Togo/.

Caption

Varespladib

A repurposed molecule with an extensive development and safety record

Varespladib blocks secretory phospholipase-A2 (sPLA2), an enzyme fundamental to the functioning of many organisms' innate immune response. In many animals, including venomous snakes, sPLA2 has evolved into a deadly poison.

As the most enzymatically active of the major classes of snake venom toxins, sPLA2 plays a critical, direct role in life-threatening tissue destruction,

Responding to the COVID-19 pandemic

As the coronavirus pandemic surged in 2020, Ophirex reviewed earlier data to evaluate varespladib's potential as an effective therapy for Acute Respiratory Distress Syndrome (ARDS), a primary cause of death in COVID-19 patients.

Our hypothesis is that varespladib may be able to address two critical mechanisms of ARDS — by stabilizing disregulated inflammatory response and by preventing lung surfactant degradation. If so, varespladib could quickly become a valuable tool for global treatment of COVID-19–associated ARDS in both advanced and low-resource health systems.

Caption

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

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

February 2022

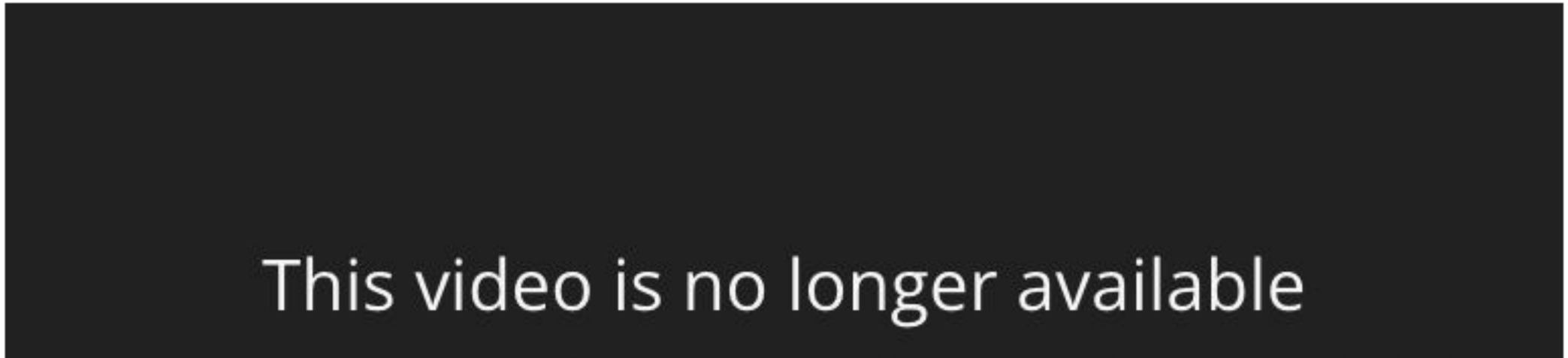
CHANNEL 3000 NEWS WEATHER SPORTS OBITS MORE

CDC unveils its latest weapon in Covid-19 detection: wastewater

By Brenda Goodman, CNN

Posted: February 3, 2022 9:44 PM

Updated: February 19, 2022 12:59 PM



February 2022

Data from anywhere with a sewer connection

SARS-CoV-2, the virus that causes Covid-19, is encased in an oily envelope. After it invades our bodies and begins to furiously clone itself, some of those copies are shed into our intestines, where the fatty parts of the virus stick to the fats in stool. When we poop, genetic material from the virus gets flushed down the toilet into the wastewater stream, where it can be detected by the same kinds of tests labs use to detect the virus from nasal swabs: real time polymerase chain reaction tests, or RT-PCR.

This kind of testing is highly sensitive. It can pick up the presence of the virus when just one person out of 100,000 in a given area, or sewershed, is infected.

And because wastewater testing doesn't depend on people to realize they're sick and seek out a test, or even to have symptoms at all, it's often the earliest warning a community has that wave of Covid-19 infections is on the way.

The CDC estimates that it takes five to seven days after a toilet flushes to get the wastewater data to its COVID Tracker, and and the samples typically turn positive in an area four to six days before clinical cases show up.

February 2022

CHANNEL 3000 NEWS WEATHER SPORTS OBITS MORE

Wastewater-based epidemiology has proven to be so reliable in dozens of pilot projects across the US that the government has invested millions to create the National Wastewater Surveillance System, or NWSS, a network of 400 testing sites spread across 19 states that is coordinated by the US Centers for Disease Control and Prevention.

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Wednesday, April 13, 2022 by: Mike Adams

Tags: Big Pharma, biosciences, Bryan Ardis, conspiracy theory, covid-19, drug development, goodscience, king cobra, medical science, phafmaceuticals, snake venom, toxins, vaccines, venom, VenomTech

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Venomtech

Caption

Nanocarriers can stabilize snake venom peptides for delivery via water

In response to Dr. Ardis' revelations about the possibility of snake venom peptide delivery via water systems, there has been almost derision from certain influencers who claim that snake venom wouldn't be stable in municipal water systems. In effect, **they are absurdly claiming that tap water is anti-venom**.

If that were true, all snake bites could simply be treated by drinking tap water.

In truth, the National Library of Medicine has published a study that reveals the existence of "nanocarriers" which can stabilize snake venom peptides in order to achieve delivery via water systems.

Entitled, "Nanoparticles Functionalized with Venom-Derived Peptides and Toxins for Pharmaceutical Applications," the study abstract explains the mechanism by which snake venom peptides are stabilized in water and other solutions: (emphasis added)

Venom-derived peptides display diverse biological and pharmacological activities, making them useful in drug discovery platforms and for a wide range of applications in medicine and pharmaceutical biotechnology. Due to their target specificities, venom peptides have the potential to be developed into biopharmaceuticals to treat various health conditions

U.S.

Snake Venom in Drinking Water Causing Covid Is Latest Conspiracy Theory

BY ROBYN WHITE ON 4/22/22 AT 11:23 AM EDT

Caption


COVID - 19
Vaccine
Injection only
COVENOM19
A HEALTH SECRET FILM