https://www.longdom.org/open-access/pulmonary-haemorrhage-due-to-humpnosed-viper-bite-excellent-response-to-methyl-prednisolonecase-report-and-review-of-lit.pdf

Previously regarded as a mildly poisonous snake, hump-nosed Citation: Srirangan A, Pushpakumara J, Wanigasuriya K (2019) Pulmonary Haemorrhage due to Hump-Nosed Viper Bite; Excellent Response to Methyl Prednisolone-Case Report and Review of Literature. J Trop Dis 7: 309. doi:10.4172/2329-891X.1000309 Page 2 of 3 J Trop Dis, an open access journal ISSN:2329-891X Volume 7 • Issue 3 • 1000309 viper is now known to cause significant systemic toxicity and fatalities. Maduwage et al. demonstrated potent cytotoxic, weak procoagulant, neurotoxic, myotoxic and phospholipase A2 activities in all three Hypnale venoms in vitro [5].

metalloproteinases found in the snake venom can induce the release of inflammator\ mediators such as cytokines which intensify the inflammatory response.

https://www.news-medical.net/news/20210825/Enzyme-related-to-rattlesnake-neurotoxin-linked-with-COVID-19-infection-severity.aspx

sPLA2-IIA associated with high COVID-19 mortality: mechanism and implications.

Healthy individuals typically have sPLA2-IIA enzyme levels around half a nanogram per milliliter (mL) of blood,

but findings of the study showed that COVID-19 infection was lethal in 63% of patients who had severe COVID-19 and levels of sPLA2-IIA equal to or greater than 10 nanograms per mL of blood.

"Many patients who died from COVID-19 had some of the highest levels of this enzyme that have ever been reported," states Chilton.

https://www.medicalnewstoday.com/articles/covid-19-mortality-enzyme-that-shreds-membranes-implicated#Prognostic-indicator-and-therapeutic-target?

He and his team examined stored blood plasma samples from 127 hospitalized patients between May and July 2020 for levels of lipid metabolites and other biochemical substances to identify patterns associated with mortality from COVID-19.

The study found that people who had died from COVID-19 had sPLA2-IIA levels that were approximately 10 times higher than patients with mild disease and five times higher than patients who had survived severe COVID-19.

An sPLA2-IIA level of at least 10 nanograms per milliliter accurately predicted death from COVID-19 in 63% of patients in the study.

http://www.ijsrp.org/research-paper-0121/ijsrp-p10919.pdf

Phospholipase enzymes as potential biomarker for SARS CoV-2 virus

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 [

There are some evidence that elevated level of PLA2 is patients with lung infections and respiratory problems. Pulmonary surfactant is important to maintain alveolar stability by lowering surface tension along the alveolar epithelium. Destruction of this surface tension will result in lung injury (Acute Respiratory distress Syndrome ARDS) [44].

While both men and women have the same prevalence to SARS CoV-2 without any gender discrimination, men is more susceptible to face more complications and death [55]. Study [49] was evidenced the inverse correlation of sPLA2 activity with vitamin c concentration in covid 19 patients. Interestingly the vitamin C concentration in plasma is lower in males than

females [49]. It also links with the severity of covid 19 in males with the correlation of increasing sPLA2 activity and the decrease in vitamin C content.

Another study was revealed that Increasing rates of LpPLA2 were positively correlated with not only viral loads in patients with COVID-19 but also severity of pneumonia in non-COVID-19 patients. Therefore it could be suggested that increased levels of LpPLA2 in plasma could provide insights to higher mortality was seen in patients underlying comorbidities (e.g. hypertension, diabetes mellitus, cardiovascular disease) [62].

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7038244/

SURAMIN AS AN ANTIDOTE

Three of the many biological activities of suramin support its potential use as a protective agent: the inhibition of thrombin, the inhibition of phospholipase A2, and the inhibition of purinergic signaling. Several vipers possess toxins that mimic thrombin (70), perfidiously triggering the coagulation cascade in

mammalian blood. Suramin not only inhibits thrombin itself (71), but also the thrombin-like proteases of snake venom (72), and was therefore proposed as an antidote for snakebite. Other common constituents of metazoan venoms are phospholipases A2, which convert phospholipids into lysophospholipids. Again, suramin inhibits mammalian phospholipase A2 (73), as well as the orthologues from snake venom (74,–76) and bee venom (77), suggesting that it can act as an antidote. A certain degree of protection from venoms by suramin was confirmed in mouse models (77,–79). The potential use of suramin as an antidote is attractive, given the high global burden of snakebites (80) and the current shortage of antivenom (81).

Suramin's ability to block P2 purinergic, G protein-coupled receptors (82) may counteract the action of neurotoxins that trigger arachidonic acid signaling, e.g., via phospholipase A2 activity (83). A possible explanation is that suramin prevents the activation of ATP receptors at the motor nerve ending, which otherwise would depress Ca^{2+} currents and reduce acetylcholine release at the presynaptic membrane (84). Suramin was also proposed to serve as a neuroprotective agent (85, 86) and as an antidote for kidney toxicity during cancer chemotherapy (87) and, based on its antiapoptotic effect, to protect against liver failure (88). Suramin also inhibits connexin channels of the tight junction, thereby suppressing ATP release and protecting cells from pore-forming bacterial toxins, such as hemolysin (89). The suramin analogs NF340 and NF546 were cardioprotective in a mouse model for heart graft rejection, presumably via inhibition of the purinergic G protein-coupled receptor P2Y11 (90).

Go to:

FURTHER POTENTIAL USES OF SURAMIN

https://www.nature.com/articles/s41588-019-0559-8

The Indian cobra reference genome and transcriptome enables comprehensive identification of venom toxins

Ethics declarations

Competing interests

Employees of Genentech hold Roche shares/options, and employees of MedGenome hold MedGenome shares/options.

Genetech facility bought by Gilead in 2011
https://www.europeanpharmaceuticalreview.com/news/8538/gilead-sciences-to-purchase-biologics-process-research-and-clinical-manufacturing-facility-from-genentech/

https://www.linkedin.com/in/szu-wen-liu-39538391
researcher working for Gilead was with MedGenome

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086180/

Suramin inhibits the early effects of PLA_2 neurotoxins at mouse neuromuscular junctions: A twitch tension study

https://pubmed.ncbi.nlm.nih.gov/34743814/

SARS-CoV-2 spike protein causes blood coagulation and thrombosis by competitive binding to heparan sulfate

https://pubmed.ncbi.nlm.nih.gov/22268640/

Species identification from dried snake venom

https://newatlas.com/hydrogel-snake-venom-bleeding/40057/?itm_source=newatlas&itm_medium=article-body

Hydrogel infused with snake venom stops bleeding within seconds 2015

https://newatlas.com/medical/snake-venom-super-glue-stops-bleeding/

Snake venom-based surgical "super glue" plugs bleeding in seconds (nano hydrogel mentioned)

https://pubmed.ncbi.nlm.nih.gov/20384921/

Molecular identification of three Indian snake species using simple PCR-RFLP method

https://pubmed.ncbi.nlm.nih.gov/33166683/

Development of a PCR-RFLP method for detection of D614G mutation in SARS-CoV-2 Dec 2020

https://www.azernews.az/business/120722.html

Why Azerbaijan can't sell snake venom? Reason revealed Oct 19, 2017

https://www.azernews.az/nation/137109.html

Azerbaijan may export snake venom sept 5th 2018

https://www.researchgate.net/publication/273124353_Histopathological_Alterations_Induced_by_Naja_naja_Crude_Venom_on_Renal_Pulmonary_and_Intestinal_Tissues_of_Mice_Model

Results: Injection of cobra venom induced a range of histological changes in all envenomated mice comparing with their control. Results from the histopathological examination showed mainly inflammatory cellular infiltration, vacuolation in renal tubules, shrinking of glomeruli, raising space between the walls of Bowman's capsule in renal tissue and alveolar haemorrhage, inflammatory cellular infiltration and edema in pulmonary tissue
Check out the venom is prepared to be administered…
Methods: Twenty five mature female albino mice were divided mainly into two groups as control and envenomated group. Lyophilized Naja naja venom was dissolved in 0.9% NaCl solution and injected intraperitoneally into the mice of the envenomated group at dosages equivalent to LD 50 120 (0.25 mg/kg). Whereas the animals from control group were not received any venomous component

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

Moderna co-founder using mRNA technology to treat venomous snakebites

https://www.marketwatch.com/press-release/snake-antivenom-market-study-offering-deep-insight-related-to-growth-trends-until-2027-bioclon-institute-btg-plc-boehringer-ingelheim-pfizer-merck-group-csl-limited-2021-11-01

Snake Antivenom Market Study Offering Deep Insight Related to Growth Trends until 2027 | Bioclon Institute, BTG plc, Boehringer Ingelheim, Pfizer, Merck Group, CSL Limited

https://transcendingsquare.com/2021/06/18/snake-venom-toxin-in-the-spike-protein/

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.

"*Based on the clinical observation of low prevalence of smoking among hospitalized COVID-19 patients, we examined and identified a "toxin-like" amino acid (aa) sequence in the Receptor Binding Domain of the Spike Glycoprotein of SARS-CoV-2 (aa 375–390), which is homologous to a sequence of the Neurotoxin homolog NL1, one of the many snake venom toxins that are known*

to interact with nicotinic acetylcholine receptors (nAChRs)." (1)

https://www.sciencedirect.com/science/article/abs/pii/S0141813013000081

Inhibition of hyaluronidase by N-acetyl cysteine and glutathione: Role of thiol group in hyaluronan protection

The present study demonstrates the inhibitory efficacy of clinically accepted antioxidant N-acetyl cysteine (NAC) against hyaluronidase of serum, testis, and snake and bee venoms.

https://www.nature.com/articles/s41598-018-37435-4

L-amino acid oxidase from *Bothrops atrox* snake venom triggers autophagy, apoptosis and necrosis in normal human keratinocytes

Pharmacological inhibition by the antioxidant NAC (N-acetyl cysteine) prevented *B. atrox* venom-induced necrosis.

https://www.jpost.com/science/does-this-enzyme-raise-the-chance-of-covid-related-death-678710

Does this enzyme raise the chance of COVID-related death?

Researchers discovered an enzyme that is genetically related to a key enzyme in snake venom and was found in COVID-19 fatalities in doses 20 times the safe amount.

https://europepmc.org/article/MED/21682678

Inhibition of hemorrhagic activity of viper venoms by N-acetyl cysteine: involvement of N-acetyl and thiol groups.

The present study assessed the efficacy of N-acetyl cysteine (NAC) to inhibit gelatinase, hyaluronidase, hemorrhagic and defibrinogenating activities of Vipera russelli and Echis carinatus venoms. NAC inhibited these activities dosedependently, but it did not inhibit the PLA2, 5' nucleotidase, procoagulant and edema inducing activities of both the venoms

https://www.pnas.org/content/117/41/25254

Superantigenic character of an insert unique to SARS-CoV-2 spike supported by skewed TCR repertoire in patients with hyperinflammation

Further Examination of the Motif near PRRA Reveals Close Structural Similarity to the SEB Superantigen as well as Sequence Similarities to Neurotoxins and a Viral SAg.

The insertion PRRA together with seven sequentially preceding residues and succeeding R685 (conserved among β-CoVs) form a motif, Y_{674}QTQTNSPRRAR$_{685}$, homologous to those of neurotoxins from *Ophiophagus* (cobra) and *Bungarus genera*, as well as the neurotoxin-like regions from three RABV strains (20) (Fig. 2*D*). We further noticed that the same segment bears close similarity to the HIV-1 glycoprotein gp120 SAg motif F164 to V174.

https://comptes-rendus.academie-sciences.fr/biologies/item/CRBIOL_2020__343_1_33_0/

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

The recently published cryo-EM structure of the trimeric SARS-CoV-2 spike (S) protein [51, 52] revealed an insertion with respect to that of SARS-CoV-1, in a loop that is disordered in the reported structure, and which has a polybasic sequence that

corresponds to a furin site. Importantly, this exposed loop of the SARS-CoV-2 S protein also contains a motif that is homologous to that of snake neurotoxins and to the RABV neurotoxin-like region (Figure 1). This observation supports the hypothesis that SARS-CoV-2 virus itself is a nAChR blocker.

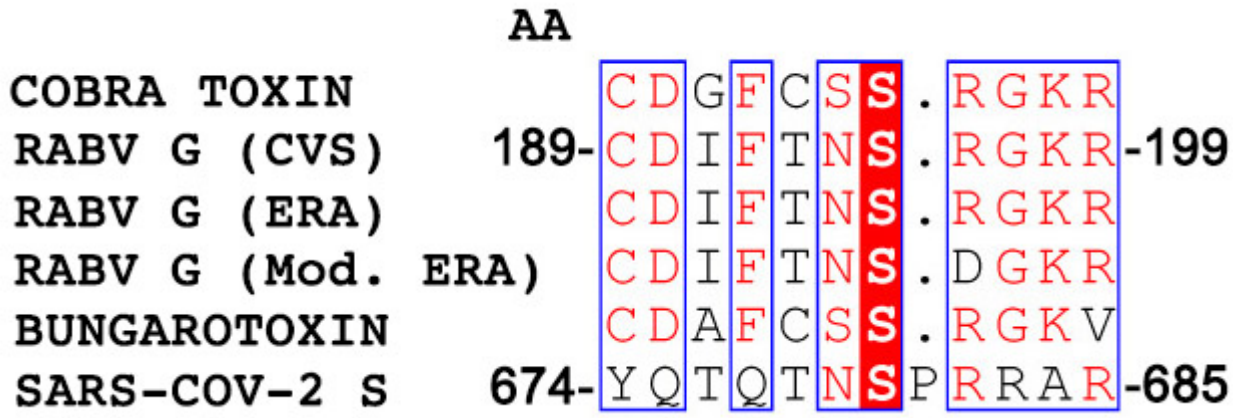

Figure 1.
The neurotoxin motifs. Amino acid sequence alignment of the motifs found in toxins from snakes of the Ophiophagus (cobra) and Bungarus genera, in G from three RABV strains and in S from SARS-CoV-2.

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.

https://www.bbc.com/news/world-us-canada-52568716
Bing Liu: Chinese-born professor dies in US murder-suicide

By Zhaoyin Feng
BBC Chinese Service, Washington

Published
7 May 2020

Can we trust the swabs used in the US?

https://www.newscentermaine.com/article/news/health/all-swabs-will-be-thrown-out-following-trump-visit-puritan-says/97-2777a555-dc39-4088-b597-3a1a367ca3ed

All swabs will be thrown out following Trump visit, Puritan says

Why would trump need to visit the cotton swab plant?

https://www.newscentermaine.com/article/news/health/coronavirus/755-million-partnership-will-double-production-of-coronavirus-covid-19-testing-swabs-in-maine-create-150-jobs/97-23b0fcfe-dd01-4cd3-9e35-d61c68e6fdee

$75.5 million partnership will double production of coronavirus, COVID-19 testing swabs in Maine, create 150 jobs

Puritan was awarded $75.5 million through the CARES Act, which included $1 billion for the Defense Production Act in order to increase domestic production capacity for materials necessary to combat COVID-19.

https://www.inc.com/magazine/202012/alex-bhattacharji/puritan-medical-products-company-of-the-year-best-in-business-2020.html

This Century-Old Family Company Became the Most Important Manufacturer in the World in 2020

Presenting Inc.'s Company of the Year: A medical supplier in remote Maine executed a lightning-fast expansion to meet an historic challenge.

Notes Copan Diagnostics in Italy sued Purtian, over swab rights, and mentions the family that owns Puritan.

https://sg.news.yahoo.com/coronavirus-testing-gears-specialized-swabs-000619262.html?guccounter=1&guce_referrer=aHR0cHM6Ly9kdWNrZHVja2dvLmNvbS8&guce_referrer_sig=AQAAAEWIFZmETBpgRSWsNxHWwLFJzCHXBnHspVc-jlXsQNrMxEc-WEnTxR7c_X8o4JHzFDRnCTA-WQENf8DqUH1lV_oz7L3dIqZsnfn_KNCUNKFSlXpK_7lh2s

KtG7u1P0EcLkPAGFGc_wpeAaZu04z5C6m1--SRB04I_szHtne-c1bw

As Coronavirus Testing Gears Up, Specialized Swabs Running Out (march 2020)

They must be made of synthetic fiber and cannot have a wooden shaft. Nor can they contain calcium alginate, a substance typically used for swab tips in wound care, as that can kill the virus, according to the Centers for Disease Control and Prevention (CDC).

https://www.scientzbio.com/info/how-to-make-snake-venom-lyophilized-powder-33070726.html
how to freeze dry snake venom

https://pmj.bmj.com/content/78/919/276

Krait snake bite hospital treatment, requires ventilation bc of paralysis of the diaphragm in neurotoxin.

http://toxicology.ucsd.edu/Snakebite%20Protocols/Naja2.htm

Cobra snake bite hospital treatment and ventilator reference..

General Considerations:

A. It is important that the patient be placed at rest, kept warm, and avoids unnecessary movement.
B. The onset of dangerous **Neurotoxic symptoms** can be rapid and subtle. In addition, they are more rapidly reversed in their early stages than when fully developed. It may be necessary to wake the patient and perform a brief neurologic check every hour or so to assure that breathing and other neurological functions are not impaired. Carefully note the progress of any paralysis which maybe present.
C. **Respiratory obstruction and failure** are the greatest immediate concerns. Should the patient develop difficulties in breathing or airway management, respiratory support will be required. If the tongue, jaw or pharynx become paralyzed, insert an oral airway; intubation may be required. Make sure adequate suction equipment is available and operative.

https://pubmed.ncbi.nlm.nih.gov/17506264/

[Venomous and poisonous animals. III. Elapidae snake envenomation]

Artificial ventilation is necessary in case of dyspnea

https://www.sciencedirect.com/science/article/abs/pii/S0022510X15020213

HCQ can stop the inflammatory actions and cytokine storm elements of PLA2
While its precise mode of action in these diseases is uncertain it is notable that **HCQ** can inactivate macrophage **phospholipase A2 and** reduce production of pro-inflammatory cytokines by macrophages and lymphocytes [13], [14]. In addition to immunological actions, **HCQ** has antithrombotic, lipid-lowering and other metabolic actions [10], [11].

https://www.healthbiotechpharm.org/article_138021_bdedc0af9095b30f181f3b31379c3fbc.pdf
HCQ reduces PLA2 Sept 2021
Major antiinflammatory and anti-viral functions for HCQ include suppression of phospholipase A2, [12] decreased expression of IL-1 and IL6 cytokines by macrophages, TNF-α inhibition, prevention of toll-like receptor signals, and inhibition of T and B cell receptors [13,14].

http://covid19newscenter.com/2021/08/29/covid-19-is-like-getting-a-rattlesnake-bite-study/

COVID-19 Is Like Getting A Rattlesnake Bite: Study

AUG 29, 2021

https://www.medscape.com/answers/2085111-196749/how-are-elevated-d-dimer-levels-interpreted

Interpreting Elevated D-dimer levels

“snake venom”

https://www.sciencedirect.com/science/article/pii/B9780123756886100489

Chapter 48 - Extracts of Cowhage (*Mucuna pruriens*) Seeds and Anti-Snake Venom Effects (this could be the answer for all covid vaccinated includes Cobra venom

April 2011

It can be concluded that pretreatment with *Mucuna pruriens* seed extract was able to significantly inhibit the venom-induced myotoxic and cytotoxic effects and the elevation of D-dimer levels.

Aguiyi and colleagues (Aguiyi et al., 2001, Guerranti et al., 2001) also investigated the effect of MPE pretreatment on venom-induced elevation of the serum enzymes lactate dehydrogenase, glutamate pyruvic transaminase, and creatine kinase, as well as increased prothrombin time and

levels of D-Dimer (a parameter associated with disseminated intravascular coagulation). They concluded that pretreatment with MPE (21 mg/kg, one injection 24 hours before venom challenge; or three weekly injections) was able to significantly inhibit the venom-induced myotoxic and cytotoxic effects and the elevation of D-Dimer levels. The pretreatment also decreased the clotting time of mice injected with the venom. The data could be partially explained by inhibition of the venom phospholipase A_2 following MPE pretreatment, as phospholipase A_2 is known to exhibit myotoxic (Zhou *et al.*, 2008) and anticoagulant activities.

https://www.mja.com.au/journal/2010/193/5/changes-serial-laboratory-test-results-snakebite-patients-when-can-we-safely

Changes in serial laboratory test results in snakebite patients: when can we safely exclude envenoming?

Severe envenoming was defined as any of the following:

- Venom-induced consumption coagulopathy (VICC): evidence of a complete consumption coagulopathy, indicated by either an undetectable fibrinogen level or a raised D-dimer level (at least 10 times the assay

cut-off or > 2.5 mg/L), with an international normalised ratio (INR) > 3.0.

- Myotoxicity: a creatine kinase (CK) level > 1000 U/L, with myalgia and/or muscle tenderness.
- Neurotoxicity: with either two nerve groups (eg, ocular and bulbar) involved, respiratory muscle paralysis, or requirement for intubation or mechanical ventilation.
- Thrombotic microangiopathy: defined as the presence of intravascular haemolysis on the blood film, thrombocytopenia and an abnormal creatinine level with or without acute renal failure.13

Thrombotic microangiopathies (TMA) are clinical syndromes defined by the presence of hemolytic anemia (destruction of red blood cells), low platelets, and organ damage due to the formation of microscopic blood clots in capillaries and small arteries. The kidneys are commonly affected, although virtually any organ may be involved.

OMG: https://modernaofficial.com/about-us/

https://montreal.citynews.ca/2021/07/06/fresh-off-vaccine-success-moderna-co-founder-sets-sights-on-venomous-snakebites/

Ophirex and holy crap…. Wellcome Trust

https://www.ophirex.com/20200302-ophirex-receives-wellcome-trust-award

> https://finance.yahoo.com/video/darpa-seeded-ground-rapid-covid-214655580.html

REGINA DUGAN: Sure. Well, you should know that DARPA was formed after Sputnik in 1958 with the goal of preventing and creating strategic surprise. So big questions about risks and vulnerabilities and new capabilities that we might create were routine at DARPA.

And what I remember was a pivotal moment in 2010. So we were contemplating new programs, and a program manager by the name of Dan Wattendorf asked too big what ifs. He said, what if we have a global pandemic and it's a novel pathogen? That will be catastrophic. We can't wait the normal 3 to 10 years for a vaccine. And what if instead we could use mRNA to create a vaccine in days and weeks instead of the normal year-long timelines, 3 to 10 years?

> https://pubmed.ncbi.nlm.nih.gov/22879897/

Unusual stability of messenger RNA in snake venom reveals gene expression dynamics of venom replenishment

> August 2012

https://pubmed.ncbi.nlm.nih.gov/27280729/

Stabilising the Integrity of Snake Venom mRNA Stored under Tropical Field Conditions Expands Research Horizons

June 2016

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5267563/

Exploration of immunoglobulin transcriptomes from mice immunized with three-finger toxins and phospholipases A_2 from the Central American coral snake, *Micrurus nigrocinctus*

Micrurus nigrocinctus. Although exploratory in nature, our indicate results showed that only low frequencies of mRNA encoding IgG isotypes, the most relevant isotype for therapeutic purposes, were present in splenocytes of five mice immunized with 6 doses of the two types of toxins over 90 days

https://www.nature.com/articles/s41598-020-70565-2

Kinetic analysis of effects of temperature and time on the regulation of venom expression in *Bungarus multicinctus 2020*

Venom toxins mRNA has been shown to increase abruptly in snake after venom expenditure

https://watermark.silverchair.com/gkr586.pdf?token=AQECAHi208BE49Ooan9kkhW_Ercy7Dm3ZL_9Cf3qfKAc485ysgAAAsIwggK-BgkqhkiG9w0BBwagggKvMIICqwIBADCCAqQGCSqGSIb3DQEHATAeBglghkgBZQMEAS4wEQQM1H_OWgUWJnWy4hyBAgEQgIICdVcOJFhuher0B24PPA85jO90XLzvMAV2LQgvJXjyGpgSc4Sen8PjarC2fzERp_VTRAaYFLwYgTxT4sLXDSG_kyQw3-u91YVaAa9U2TCxRmQ9uLC2O_wUODy3ilqMlMkKKLkCgsFQ_0mWt8mrrWRBChjDItsXE4QxxeSbzLd6VoI9WQmgLQnL-BOShysOpnesGG68nXpTXzx53ZuVDizwd8CIAvVCsPA2AMBhcHe-7pwGbqt6Xb4x5K_jd9HhZhuGrbpUfcu3tqKgp6JwrJW6YO1RXEhy1vGoRlLz26BiAM23ESg4dnDHYn6wiu0BtMB42LxOZbNi3gMz9VJhDUzOt3-adNcZ-6xBmOsHFcMCh3xhk5-kthWrUizA9Gk4MB-5gH_h30G5WSoFqCMAjR1h9hjX6MzeuX8_hx-k11AjicpyK8BTjhVpXNtc7af3LAZLcSiAL15Rd7T8JXzRp0XE3vq6DbbTvrmJVA26UY8qAcFkaBk69xI1OP1TEO2fs3obuxF_1dvkqzRao12WbwlBnlM7YhEHYJXUzuTJ1f9zg52Fe9CE3DsAhGSm-

Uw6OC329fwDDRshYMvLFbePrSSqjg7fn-Vduk0TydSXcQGgNc-AsuPb6pRViokr1Z_N3NmelHdjMAuirdm975jkgP6QSf9JsHgnnR8bIcw0BKsCd313kuKxcZm_GuneYve-OdqoBFTzZGdAuhmaS5h9JDNgN1cxwUUsvPysnm5kSRVGvp5QrFfBZMgK_CqGgWfGq0aTTpqy0LoGFPN6BxOS7fH9c5RsetfXiW0AdGJodnCHXWsLtU2XfSj40ZuVlWxTuLFCOn-xTCwW

Two mRNA vaccine founders produce study on mRNA in 2011 includes terms, dynabeads, and luciferase and snake venom

RNA containing 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 -RNA with reduced efficiency (37) last paragraph on page 9335

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.

https://www.pennmedicine.org/news/news-releases/2021/september/penn-mrna-scientists-drew-weissman-and-katalin-kariko-receive-2021-lasker-award

Messenger RNA innovators **Drew Weissman, MD, PhD**, the Roberts Family Professor of Vaccine Research in Penn's Perelman School of Medicine, and **Katalin Karikó, PhD**, an adjunct professor of Neurosurgery at Penn and a senior vice president at BioNTech, are honored with what is widely regarded as America's top biomedical research prize for the discovery of a therapeutic technology based on the modification of mRNA that makes it remarkably safe and effective.

Editor's Note: The Pfizer/BioNTech and Moderna COVID-19 mRNA vaccines both use licensed University of Pennsylvania technology. As a result of these licensing relationships, Penn, Dr. Weissman and Dr. Karikó have received and may continue to receive significant financial benefits in the future based on the sale of these products. BioNTech provides funding for Dr. Weissman's research into the development of additional infectious disease vaccines.

https://www.freepatentsonline.com/5466786.html

Gilead Sciences Patent includes snake venom in description US Patent number 5466786

The stability of the oligomers to nucleases can be determined using any convenient assay, but is conveniently assessed using the snake venom assay illustrated hereinbelow. This assay is conducted as follows: The assay buffer is 0.5M Tris HCl, pH 8.0, containing 100 uM/$MgCl_2$. Commercially available phosphodiesterase isolated from Croatalus durissus is obtained from Boehringer Mannheim as a 50% (v/v) solution in glycerol, pH 6, with a specific activity of approximately 1.2 U/mg. One ul of the phosphodiesterase-containing solution is added to 100 ul buffer, and oligomers are tested by reconstituting 0.15 OD of oligomer in the 100 ul buffer/venom prepared above. Degradation is monitored by observing the disappearance of the 260 nm absorption of the oligomer at its characteristic retention time on HPLC, and measuring the appearance of degradation products.

The oligomers of the invention which contain at least one nucleotide residue containing the 2' substituent are more stable to nuclease as judged by the foregoing assay than the corresponding oligomer containing an unsubstituted 2' position in place of the substituted positions in the

invention compounds. By comparing the rate of hydrolysis in the snake venom assay with the invention compound, with that of the corresponding oligomer which is not derivatized in the 2' position, it can be assessed whether the presence of the 2' substituent(s) stabilized the oligomer to cleavage by nucleases.

Rattlesnake venom from German company Boehringer Mannheim

https://www.bioz.com/result/snake%20venom%20phosphodiesterase%20svp/product/Boehringer%20Mannheim
Must read description

https://www.freepatentsonline.com/result.html?sort=relevance&srch=top&patents_us=on&query_txt=gilead+sciences+snake+venom&search=Search

1st patent lists venom of snake as prothrombin pro coagulate

Echis carinatus venom