
# How To Beat ALL Long-Haulers COVID Symptoms,in 6 Days!

# Do You or Anyone You Know Still Suffer w/ Any of These Symptoms, Post-Covid

- Chronic fatigue
- Dizziness
- Can’t Take Deep Breathes
- Low-grade fever
- Loss of Taste/ Loss of Smell
- Memory lapses
- Muscle pain/weakness
- Diarrhea
- Vomiting
- Concentration difficulties
- Sleep difficulties
- Mood disorders
- Headache
- Chest tightness/pain
- Heart palpitations
- Cognitive impairment
- Motor deficits
- Exercise intolerance
- New onset of diabetes
- New onset of hypertension

# Do You or Anyone You Know Still Suffer w/ Any of These Symptoms, Post-Covid

"Its incidence is **estimated between 35%** (outpatients) (Tenforde et al. 2020) **and 87%** (inpatients) (Carfi et al. 2020) of **all individuals** experiencing SARS-CoV-2 infection. In addition, the duration of the symptoms is unpredictable (Yelin et al. 2020; Barker-Davies et al. 2020; Sawadogo et al. 2020); after six months, an average of 14 persistent symptoms is reported by subjects suffering from long-haul COVID (Carod Artal 2021)."

# According to Geneticists in China, BATS Are NOT the Origin of Covid-19's Virus: 1/2020

Received: 17 January 2020 | Accepted: 21 January 2020

DOI: 10.1002/jmv.25682

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]

[1]Department of Microbiology, Peking University Health Science Center School of Basic Medical Sciences, Beijing, China

[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

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



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



# 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 functi[illegible] as RNA processing, protein translation and protein foldin[illegible]. Codon usage bias reflects the origin, [illegible]mutation patterns and evolution of the species or genes. Inve[illegible]omes can reveal phylogenetic relationships between organisms, horizontal gene transfers, molecular evolution of genes and identify selective

Caption

# 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

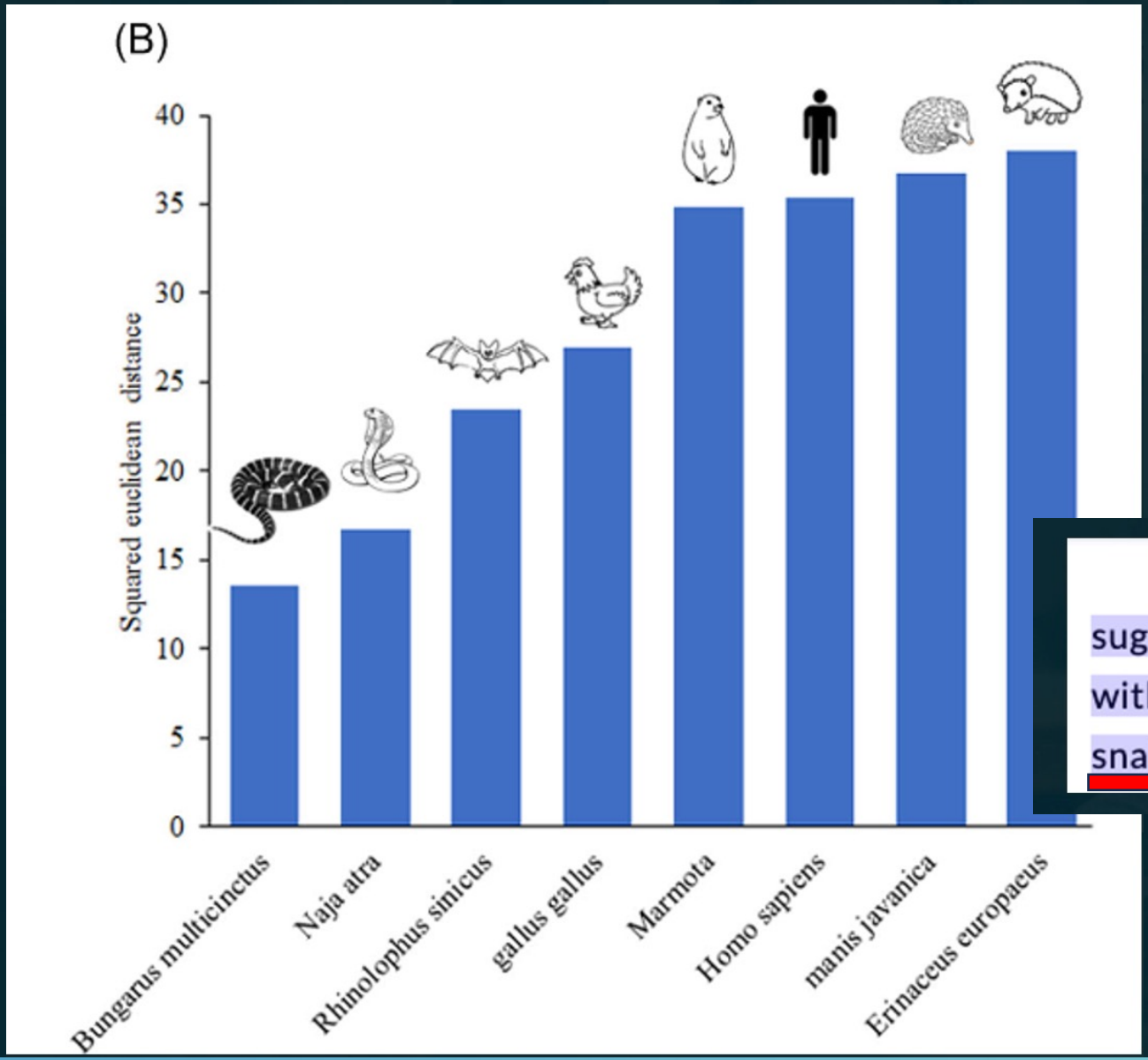
Free PMC article

## Abstract

Codon usage bias is the preferential or non-random use of synonymous codons, a ubiquitous phenomenon observed in bacteria, plants and animals. Diffe
characteristic codon biases. Codon bias varies not only with
kingdom, but also between the genes within an organism. C
mutation, natural selection, and genetic drift in various orga
content, expression level and length of genes, position and
recombination rates, mRNA folding, and tRNA abundance ar
influencing codon bias. The factors shaping codon bias may
universal genetic code. Codon-usage bias is critical factor determining gene expression and
cellular functi
h as RNA processing, protein translation and
protein foldin
. Codon usage bias reflects the origin,
mutation patterns and evolution of the species
or genes. Inve
omes can reveal phylogenetic relationships
between organisms, horizontal gene transfers, molecular evolution of genes and identify selective

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

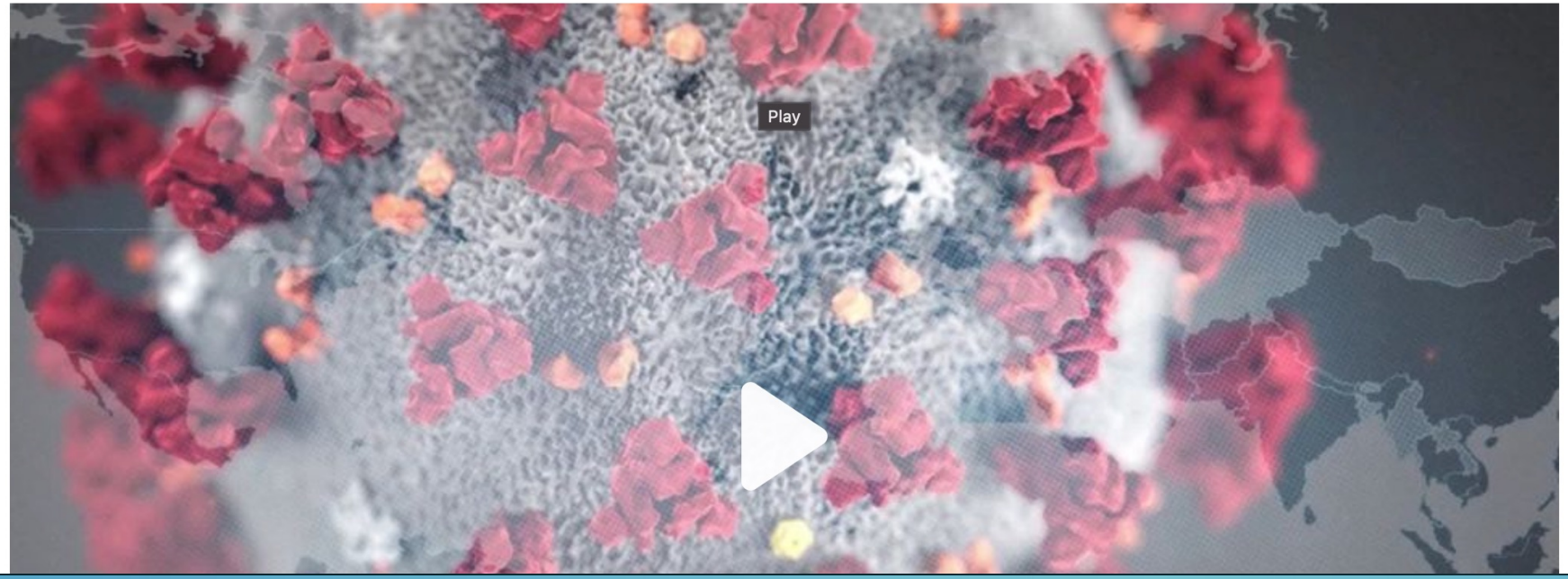
Caption




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

# 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 3:41 PM EST, Fri January 24, 2020



# Snakes could be the source of the Wuhan coronavirus outbreak

CNN health Life, But Better Fitness Food Sleep Mindfulness Relationships

THE CONVERSATION

Video Ad Feedback


02:29 What do you need to know about coronavirus?


00:59 Hear Rugby coach give motivational French speech in the...


02:14 Couple's former daughter-in-law suspected in...


03:19

(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.

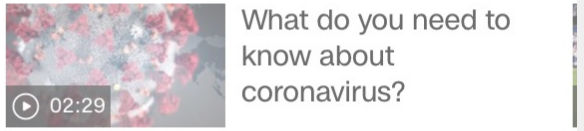
The many-banded krait (Bungarus multicinctus), also known as the Taiwanese krait or the Chinese krait, is a highly venomous species of elapid snake found in much of central and southern China and Southeast Asia.

CNN health Life, But Better Fitness Food Sleep Mindfulness Relationships

# Snakes could be the source of the Wuhan coronavirus outbreak

THE CONVERSATION

CNN health Life, But Better Fitness Food Sleep Mindfulness Relationships



What do you need to know about coronavirus?

02:29

(CNN) — Snakes – the Chinese krait and the coronavirus that has triggered an outbreak

The many-band
Chinese krait, i
southern China

SciTechDaily

BIOLOGY CHEMISTRY EARTH HEALTH PHYSICS SCIENCE SPACE TECHNOLOGY

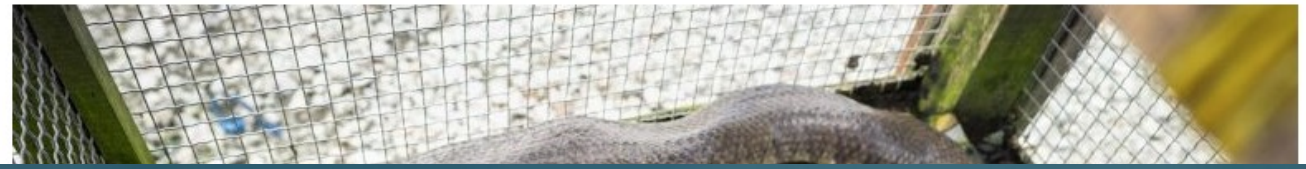
HOT TOPICS MARCH 8, 2022 | TATOOINE-LIKE EXOPLANET WITH TWO SUNS DETECTED BY GROUND-BASED TELESCOPE

HOME HEALTH NEWS

# "Snake Pneumonia" – Coronavirus Outbreak in China Traced to Snakes by Genetic Analysis

**TOPICS:** COVID-19 Genetics Popular Public Health Snake Virology Wiley

By WILEY JANUARY 22, 2020



SUBSCRIBE

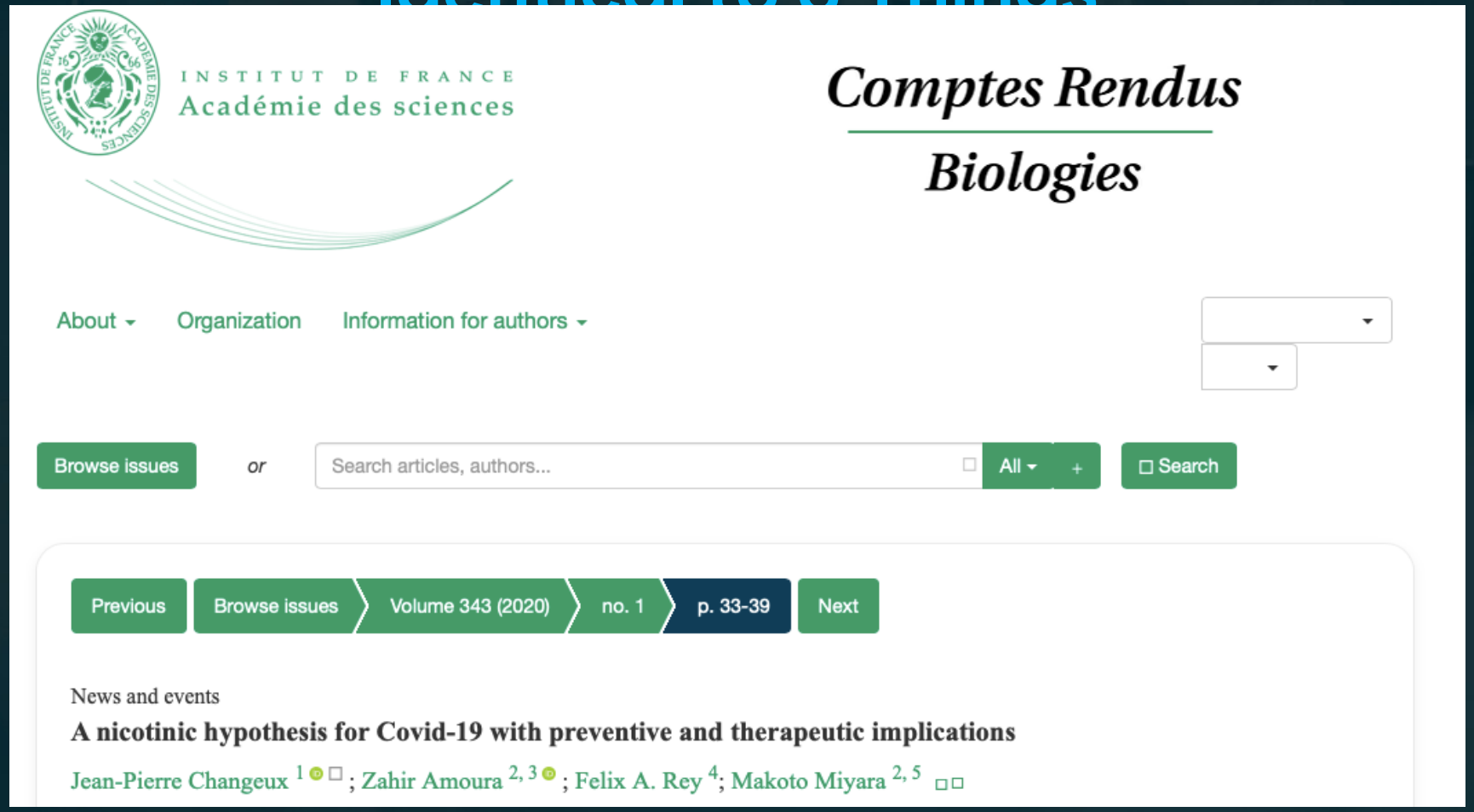
SciTechDaily: Hom
technology news s
scitech news via e

E-mail

POPULAR ARTICLES

LABS

# 4/2020: France Researchers Isolate The 'Spike Protein Gene' of COVID-19 Virus & Publish, It's Identical to 3 Things



INSTITUT DE FRANCE
Académie des sciences

*Comptes Rendus*
*Biologies*

About ▾ Organization Information for authors ▾

Browse issues or Search articles, authors... All ▾ + Search

Previous | Browse issues | Volume 343 (2020) | no. 1 | p. 33-39 | Next

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]

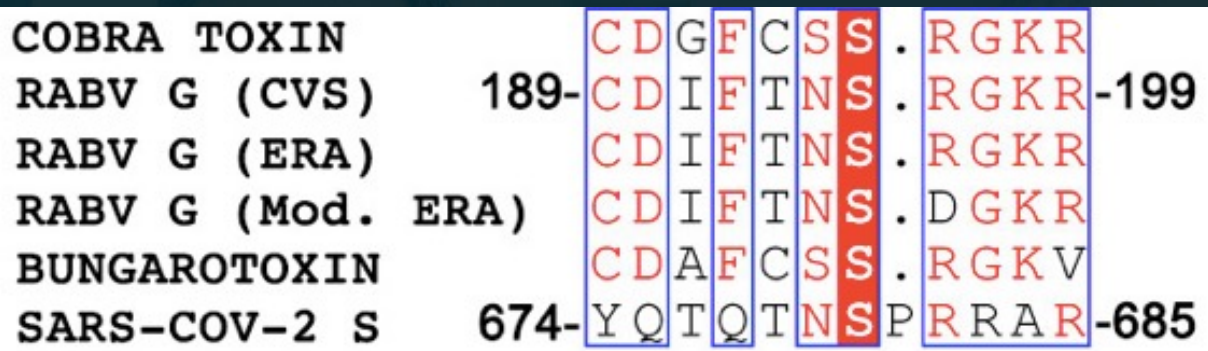



**Figure 1.**

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.

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

Caption

| | | |
|---|---|---|
| COBRA TOXIN | | C D G F C S S . R G K R |
| RABV G (CVS) | 189- | C D I F T N S . R G K R -199 |
| RABV G (ERA) | | C D I F T N S . R G K R |
| RABV G (Mod. ERA) | | C D I F T N S . D G K R |
| BUNGAROTOXIN | | C D A F C S S . R G K V |
| SARS-COV-2 S | 674- | Y Q T Q T N S P R R A R -685 |

**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.

King cobra - Wikipedia

en.wikipedia.org

474 × 354

View File

Caption

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| COBRA TOXIN | | C | D | G | F | C | S | S | . | R | G | K | R | |
| RABV G (CVS) | 189- | C | D | I | F | T | N | S | . | R | G | K | R | -199 |
| RABV G (ERA) | | C | D | I | F | T | N | S | . | R | G | K | R | |
| RABV G (Mod. ERA) | | C | D | I | F | T | N | S | . | D | G | K | R | |
| BUNGAROTOXIN | | C | D | A | F | C | S | S | . | R | G | K | V | |
| SARS-COV-2 S | 674- | Y | Q | T | Q | T | N | S | P | R | R | A | R | -685 |

**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.


Many Banded Krait - Bungarus — HongKongSnakeID.com

hongkongsnakeid.com

2500 × 1563

View File

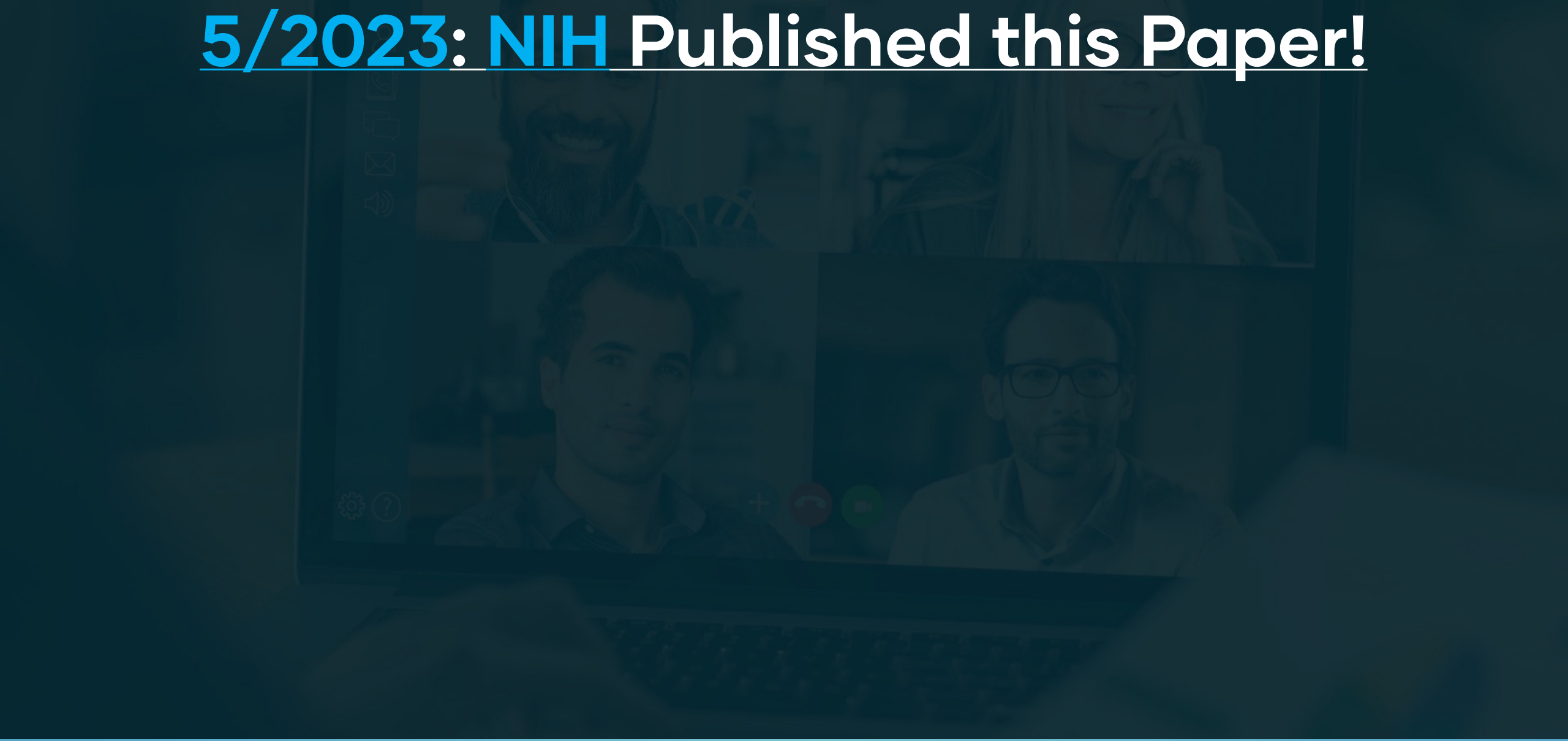
Caption

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.

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 electrophysiological recordings, high resolution EM and by animal model studies. Further work should also specify

# 5/2023: NIH Published this Paper!



# 5/2023: NIH Published this Paper!

JBC JOURNAL OF BIOLOGICAL CHEMISTRY OPEN ACCESS

## SARS-CoV-2 spike ectodomain targets α7 nicotinic acetylcholine receptors

Brittany C.V. O'Brien • Lahra Weber • Karsten Hueffer • Maegan M. Weltzin

Open Access • DOI: https://doi.org/10.1016/j.jbc.2023.104707 • Check for updates



Virus entry into animal cells is initiated by attachment to target macromolecules located on host cells. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) trimeric spike glycoprotein targets host angiotensin converting enzyme 2 to gain cellular access. The SARS-CoV-2 glycoprotein contains a neurotoxin-like region that has sequence similarities to the rabies virus and the HIV glycoproteins, as well as to snake neurotoxins, which interact with nicotinic acetylcholine receptor (nAChR) subtypes *via* this region. Using a peptide of the neurotoxin-like region of SARS-CoV-2 (SARS-CoV-2 glycoprotein peptide [SCoV2P]), we identified that this area moderately inhibits α3β2, α3β4, and α4β2 subtypes, while potentiating and inhibiting α7 nAChRs. These nAChR subtypes

# 5/2023: NIH Published this Paper!

JBC JOURNAL OF BIOLOGICAL CHEMISTRY OPEN ACCESS

## SARS-CoV-2 spike ectodomain targets α7 nicotinic acetylcholine receptors

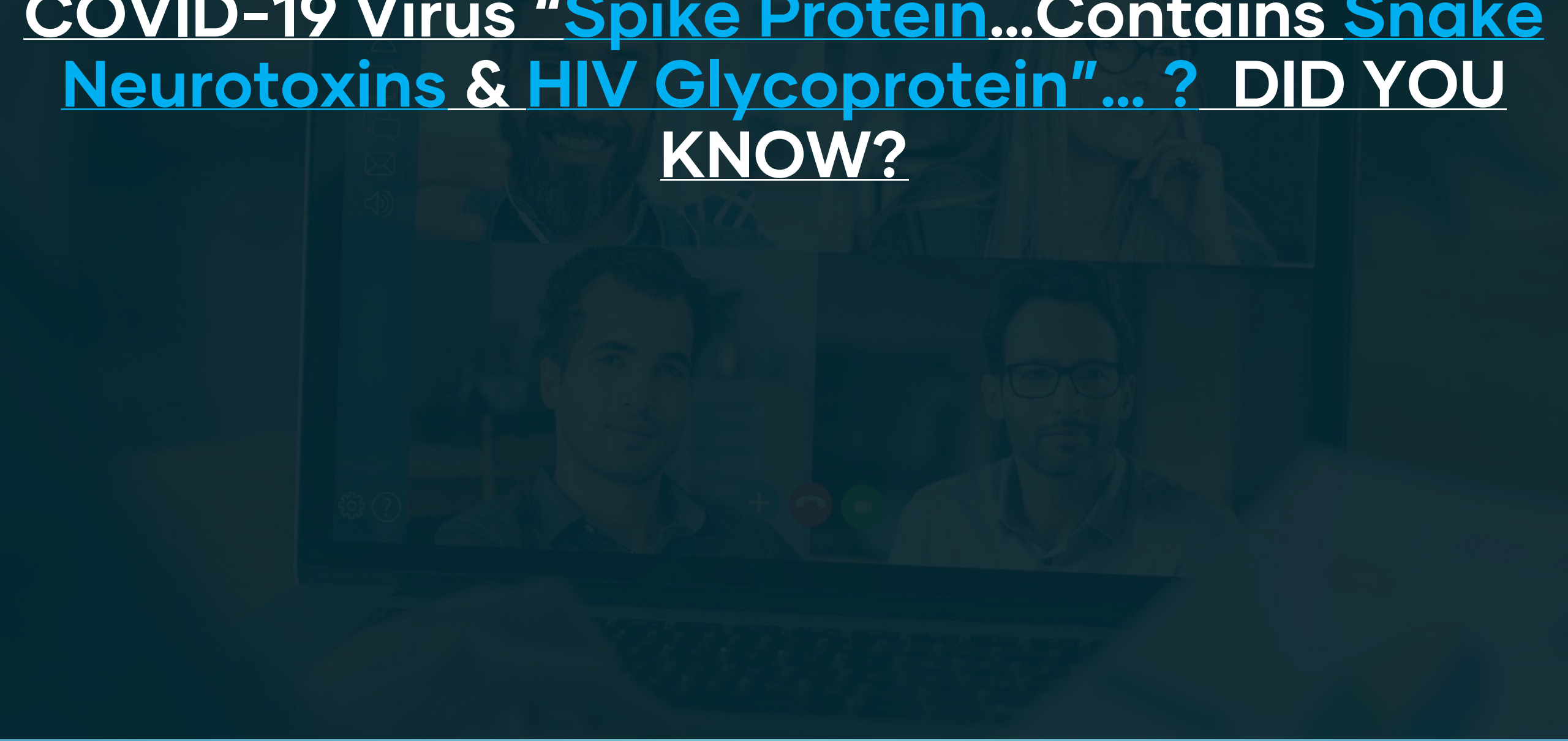
Brittany C.V. O'Brien • Lahra Weber • Karsten Hueffer • Maegan M. Weltzin

Open Access • DOI: https://doi.org/10.1016/j.jbc.2023.104707 • Check for updates



Virus entry into animal cells is initiated by attachment to target macromolecules located on host cells. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) trimeric spike glycoprotein targets host angiotensin converting enzyme 2 to gain cellular access. The SARS-CoV-2 glycoprotein contains a neurotoxin-like region that has sequence similarities to the rabies virus and the HIV glycoproteins, as well as to snake neurotoxins, which interact with nicotinic acetylcholine receptor (nAChR) subtypes *via* this region. Using a peptide of the neurotoxin-like region of SARS-CoV-2 (SARS-CoV-2 glycoprotein peptide [SCoV2P]), we identified that this area moderately inhibits α3β2, α3β4, and α4β2 subtypes, while potentiating and inhibiting α7 nAChRs. These nAChR subtypes

# COVID-19 Virus "Spike Protein...Contains Snake Neurotoxins & HIV Glycoprotein"... ? DID YOU KNOW?



# COVID-19 Virus "Spike Protein...Contains Snake Neurotoxins & HIV Glycoprotein"... ? DID YOU KNOW?

da Mata *et al. Journal of Venomous Animals and Toxins including Tropical Diseases* (2017) 23:3
DOI 10.1186/s40409-016-0089-0

Journal of Venomous Animals and Toxins including Tropical Diseases

REVIEW Open Access

## Antiviral activity of animal venom peptides and related compounds

Élida Cleyse Gomes da Mata[1], Caroline Barbosa Farias Mourão[1], Marisa Rangel[1,2] and Elisabeth Ferroni Schwartz[1*]

**Abstract**

Viruses exhibit rapid mutational capacity to trick and infect host cells, sometimes assisted through virus-coded peptides that counteract host cellular immune defense. Although a large number of compounds have been identified as inhibiting various viral infections and disease progression, it is urgent to achieve the discovery of more effective agents. Furthermore, proportionally to the great variety of diseases caused by viruses, very few viral vaccines are available, and not all are efficient. Thus, new antiviral substances obtained from natural products have been prospected, including those derived from venomous animals. Venoms are complex mixtures of hundreds of molecules, mostly peptides, that present a large array of biological activities and evolved to putatively target the biochemical machinery of different pathogens or host cellular structures. In addition, non-venomous compounds, such as some body fluids of invertebrate organisms, exhibit antiviral activity. This review provides a panorama of peptides described from animal venoms that present antiviral activity, thereby reinforcing them as important tools for the development of new therapeutic drugs.

**Keywords:** Antiretroviral agents, Antiviral agents, HIV, Scorpion venom, Snake venom, Amphibian venom, Insect venom, Marine animal peptides

# COVID-19 Virus "Spike Protein...Contains Snake Neurotoxins & HIV Glycoprotein"... ? DID YOU KNOW?

**Snake venoms**

Snake venoms are composed of a mixture of proteins, peptides (90–95%), free amino acids, nucleotides, lipids, carbohydrates and metallic elements coupled to proteins (5%) [45]. Some studies have reported the antiviral activity of snake venoms and their components against measles virus, Sendai virus, dengue virus (DENV), yellow fever virus (YFV) and HIV [46–50]. Thus, snake venoms are sources of promising candidates for new antiviral drugs (Table 2). In relation to antiretroviral activity, the benefits of treating a patient with multidrug-resistant HIV with a snake venom preparation in addition to the antiretroviral therapy were demonstrated in clinical practice [51]. The response was a decreased viral load and elevated T $CD4^{+}$cell count. The authors suggest that this activity may be related to the presence of some snake venom molecules that are homologous to HIV-1 glycoprotein or proteases [51, 52].

# COVID-19 Virus "Spike Protein...Contains Snake Neurotoxins & HIV Glycoprotein"... ? DID YOU KNOW?

What does "Homologous" Mean?

**Snake venoms**

Snake venoms are composed of a mixture of proteins, peptides (90–95%), free amino acids, nucleotides, lipids, carbohydrates and metallic elements coupled to proteins (5%) [45]. Some studies have reported the antiviral activity of snake venoms and their components against measles virus, Sendai virus, dengue virus (DENV), yellow fever virus (YFV) and HIV [46–50]. Thus, snake venoms are sources of promising candidates for new antiviral drugs (Table 2). In relation to antiretroviral activity, the benefits of treating a patient with multidrug-resistant HIV with a snake venom preparation in addition to the antiretroviral therapy were demonstrated in clinical practice [51]. The response was a decreased viral load and elevated T $CD4^+$cell count. The authors suggest that this activity may be related to the presence of some snake venom molecules that are homologous to HIV-1 glycoprotein or proteases [51, 52].

# COVID-19 Virus "Spike Protein...Contains Snake Neurotoxins & HIV Glycoprotein"... ? DID YOU KNOW?

**What does "Homologous" Mean?**

Merriam-Webster | Dictionary | Thesaurus | homologous | Games & Quizzes | Word of the Day

Dictionary

Definition

Did you know?

Example Sentences

Word History

Entries Near

Show More

Save Word

## homologous adjective

ho·mol·o·gous hō-ˈmä-lə-gəs hə-

Synonyms of *homologous* >

1 **a** : having the same relative position, value, or structure: such as

(1) **biology** : exhibiting biological homology

(2) **biology** : having the same or allelic genes with genetic loci usually arranged in the same order

*homologous* chromosomes

**b** **chemistry** : belonging to or consisting of a chemical series (see SERIES sense 6) whose successive members have a regular difference in composition especially of one methylene group

2 **biology** : derived from or developed in response to organisms of the same species

# COVID-19 Virus "Spike Protein...Contains Snake Neurotoxins & HIV Glycoprotein"... ? DID YOU KNOW?

What does "Homologous" Mean?

"DERIVED FROM"

**Snake venoms**

Snake venoms are composed of a mixture of proteins, peptides (90–95%), free amino acids, nucleotides, lipids, carbohydrates and metallic elements coupled to proteins (5%) [45]. Some studies have reported the antiviral activity of snake venoms and their components against measles virus, Sendai virus, dengue virus (DENV), yellow fever virus (YFV) and HIV [46–50]. Thus, snake venoms are sources of promising candidates for new antiviral drugs (Table 2). In relation to antiretroviral activity, the benefits of treating a patient with multidrug-resistant HIV with a snake venom preparation in addition to the antiretroviral therapy were demonstrated in clinical practice [51]. The response was a decreased viral load and elevated T $CD4^{+}$cell count. The authors suggest that this activity may be related to the presence of some snake venom molecules that are homologous to HIV-1 glycoprotein or proteases [51, 52].

# COVID-19 Virus "Spike Protein…Contains Snake Neurotoxins & HIV Glycoprotein"… ? DID YOU KNOW?

**What does "Homologous" Mean?**

**"DERIVED FROM"**

**Snake venoms**

Snake venoms are composed of a mixture of proteins, peptides (90–95%), free amino acids, nucleotides, lipids, carbohydrates and metallic elements coupled to proteins (5%) [45]. Some studies have reported the antiviral activity of snake venoms and their components against measles virus, Sendai virus, dengue virus (DENV), yellow fever virus (YFV) and HIV [46–50]. Thus, snake venoms are sources of promising candidates for new antiviral drugs (Table 2). In relation to antiretroviral activity, the benefits of treating a patient with multidrug-resistant HIV with a snake venom preparation in addition to the antiretroviral therapy were demonstrated in clinical practice [51]. The response was a decreased viral load and elevated T $CD4^{+}$cell count. The authors suggest that this activity may be related to the presence of some snake venom molecules that are homologous to HIV-1 glycoprotein or proteases [51, 52].

**Thus: HIV-1 Glycoprotein is**

**"DERIVED FROM"**

**SNAKE VENOM!**

# NIH Published this Paper, 5/2023!

JBC JOURNAL OF BIOLOGICAL CHEMISTRY OPEN ACCESS

## SARS-CoV-2 spike ectodomain targets α7 nicotinic acetylcholine receptors

Brittany C.V. O'Brien • Lahra Weber • Karsten Hueffer • Maegan M. Weltzin

Open Access • DOI: https://doi.org/10.1016/j.jbc.2023.104707 • Check for updates



Virus entry into animal cells is initiated by attachment to target macromolecules located on host cells. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) trimeric spike glycoprotein targets host angiotensin converting enzyme 2 to gain cellular access. The SARS-CoV-2 glycoprotein contains a neurotoxin-like region that has sequence similarities to the rabies virus and the HIV glycoproteins, as well as to snake neurotoxins, which interact with nicotinic acetylcholine receptor (nAChR) subtypes *via* this region. Using a peptide of the neurotoxin-like region of SARS-CoV-2 (SARS-CoV-2 glycoprotein peptide [SCoV2P]), we identified that this area moderately inhibits α3β2, α3β4, and α4β2 subtypes, while potentiating and inhibiting α7 nAChRs. These nAChR subtypes

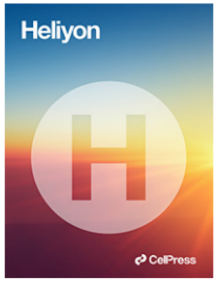
# NIH Published this Paper, 5/2023!

CellPress

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon




Review article

## Interactions between the rabies virus and nicotinic acetylcholine receptors: A potential role in rabies virus induced behavior modifications

Marianne Lian [a,b,1], Karsten Hueffer [a], Maegan M. Weltzin [c,*]

[a] University of Alaska Fairbanks, Department of Veterinary Medicine, 2141 Koyukuk Drive, Fairbanks, AK, 99775, USA
[b] Inland Norway University of Applied Sciences, Department of Forestry and Wildlife Management, Koppang, NO-2480, Norway
[c] University of Alaska Fairbanks, Department of Chemistry and Biochemistry, 1930 Yukon Dr. Fairbanks, AK, 99775, USA

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# NIH Published this Paper, 5/2023!

## Highlights

- Rabies virus glycoprotein ectodomain binds to nAChRs.
- Glycoprotein and nAChR-selective α-neurotoxins share regions of sequence homology.
- Peptide of the rabies virus glycoprotein modifies behavior in mice.
- Nicotine and genetic deletion of α7 nAChRs modulates pathological aggression.
- We hypothesize rabies virus glycoprotein-nAChR interactions modulate behavior.

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# NIH Published this Paper, 5/2023!

## Highlights

- Rabies virus glycoprotein ectodomain binds to nAChRs.
- Glycoprotein and nAChR-selective α-neurotoxins share regions of sequence homology.
- Peptide of the rabies virus glycoprotein modifies behavior in mice.
- Nicotine and genetic deletion of α7 nAChRs modulates pathological aggression.
- We hypothesize rabies virus glycoprotein-nAChR interactions modulate behavior.

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# NIH Published this Paper, 5/2023!

## 5. RGP binds to nAChRs via a neurotoxin-like domain

The RGP contains a neurotoxin-like region which shows a significant sequence homology with snake α-neurotoxins that function as potent nAChR subtype selective antagonists [62, 63]. Several lines of evidence have identified the α1 nAChR subunit to contain the RGP binding site, which overlaps with the α-bungarotoxin site. nAChR α1 subunit mono-

cultured muscles cells with a high density of nAChRs [38]. RABV binding to the muscle-type nAChR was inhibited by nAChR antagonists, up to 50% by α-bungarotoxin and up to 30% by (+)-tubocurarine, but binding was not affected by the muscarinic acetylcholine receptor antagonist atropine [64]. Later, the RABV was confirmed to bind to the *Torpedo*

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# NIH Published this Paper, 5/2023!

## 5. RGP binds to nAChRs via a neurotoxin-like domain

The RGP contains a neurotoxin-like region which shows a significant sequence homology with snake α-neurotoxins that function as potent nAChR subtype selective antagonists [62, 63]. Several lines of evidence have identified the α1 nAChR subunit to contain the RGP binding site, which overlaps with the α-bungarotoxin site. nAChR α1 subunit mono-

cultured muscles cells with a high density of nAChRs [38]. RABV binding to the muscle-type nAChR was inhibited by nAChR antagonists, up to 50% by α-bungarotoxin and up to 30% by (+)-tubocurarine, but binding was not affected by the muscarinic acetylcholine receptor antagonist atropine [64]. Later, the RABV was confirmed to bind to the *Torpedo*

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# NIH Published this Paper, 5/2023!

## 5. RGP binds to nAChRs via a neurotoxin-like domain

The RGP contains a neurotoxin-like region which shows a significant sequence homology with snake α-neurotoxins that function as potent nAChR subtype selective antagonists [62, 63]. Several lines of evidence have identified the α1 nAChR subunit to contain the RGP binding site, which overlaps with the α-bungarotoxin site. nAChR α1 subunit mono-

cultured muscles cells with a high density of nAChRs [38]. RABV binding to the muscle-type nAChR was inhibited by nAChR antagonists, up to 50% by α-bungarotoxin and up to 30% by (+)-tubocurarine, but binding was not affected by the muscarinic acetylcholine receptor antagonist atropine [64]. Later, the RABV was confirmed to bind to the *Torpedo*

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# NIH Published this Paper, 5/2023!

Loop II of α-bungarotoxin and α-cobratoxin have approximately 50% sequence homology to the RGP neurotoxin-like domain (Table 1). Cir-

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# NIH Published this Paper, 5/2023!

Loop II of α-bungarotoxin and α-cobratoxin have approximately 50% sequence homology to the RGP neurotoxin-like domain (Table 1). Cir-

mostly of beta sheet structure [70]. This study showed that a peptide of the RGP neurotoxin domain is structurally similar to loop II of α-neurotoxins. Using a Asn194-Ser195-Arg196-Gly197 tetrapeptide, early mo-

https://www.cell.com/heliyon/fulltext/S2405-8440(22)01722-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2405844022017224%3Fshowall%3Dtrue

# HIV Spike Protein Targets a-7 nAChR, Exactly Like Snake Venoms

## Nicotinic Acetylcholine Receptors in HIV: Possible Roles During HAND and Inflammation

Coral M. Capó-Vélez[1,2] · Manuel Delgado-Vélez[1,2] · Carlos A. Báez-Pagán[1,3] · José A. Lasalde-Dominicci[1,2]

Received: 31 January 2018 / Accepted: 9 July 2018 / Published online: 14 July 2018


**Abstract**

Infection with the human immunodeficiency virus (HIV) remains a threat to global health. Since its discovery, many efforts have been directed at understanding the mechanisms and consequences of infection. Although there have been substantial advances since the advent of antiretroviral therapy, there are still complications that significantly compromise the health of infected patients, particularly, chronic inflammation and HIV-associated neurocognitive disorders (HAND). In this review, a new perspective is addressed in the field of HIV, where the alpha7 nicotinic acetylcholine receptor (α7-nAChR) is the protagonist. We comprehensively discuss the available evidence implicating α7-nAChRs in the context of HIV and provide possible explanations about its role in HAND and inflammation in both the central nervous system and the periphery.

**Keywords** Nicotinic acetylcholine receptor · HIV · Gp120 · Inflammation · HAND

https://link.springer.com/article/10.1007/s10571-018-0603-8

# HIV Spike Protein Targets a-7 nAChR, Exactly Like Snake Venoms

Besides AIDS, HIV infection results in a series of systematic physiological complications such as chronic inflammation and HIV-associated neurocognitive disorders (HAND),

https://link.springer.com/article/10.1007/s10571-018-0603-8

# HIV Spike Protein Targets a-7 nAChR, Exactly Like Snake Venoms

particular, the α7-nAChR is emerging as an important player in the HIV field, since it is expressed not only in the brain, but also in a wide variety of immune cells that are targeted during HIV infection, such as macrophages, monocytes, B-lymphocytes, and T-lymphocytes ($CD4^+$) (Wang et al. 2003; van der Zanden et al. 2012; Kawashima et al. 2015), making it a suitable target for treatment development.

https://link.springer.com/article/10.1007/s10571-018-0603-8

# HIV Spike Protein Targets a-7 nAChR, Exactly Like Snake Venoms

Studies performed by Bracci et al. demonstrated a significant homology between a specific sequence of gp120, the coat protein of HIV, and the putative active sites of snake curare-mimetic neurotoxins, which have the ability to bind irreversibly to nAChRs. Furthermore, the authors demonstrated that recombinant gp120 inhibits the binding of the nAChR antagonist, α-bgtx, suggesting that other type of receptors (such as nAChRs) can function as HIV receptors, and supports the notion that ion channels may have a role during HIV infection. Even though this study

https://link.springer.com/article/10.1007/s10571-018-0603-8

# HIV Spike Protein Targets a-7 nAChR, Exactly Like Snake Venoms

Studies performed by Bracci et al. demonstrated a significant homology between a specific sequence of gp120, the coat protein of HIV, and the putative active sites of snake curare-mimetic neurotoxins, which have the ability to bind irreversibly to nAChRs. Furthermore, the authors demonstrated that recombinant gp120 inhibits the binding of the nAChR antagonist, α-bgtx, suggesting that other type of receptors (such as nAChRs) can function as HIV receptors, and supports the notion that ion channels may have a role during HIV infection. Even though this study

https://link.springer.com/article/10.1007/s10571-018-0603-8

Leitzke *Bioelectronic Medicine* (2023) 9:2
https://doi.org/10.1186/s42234-023-00104-7

Bioelectronic Medicine

**HYPOTHESIS** **Open Access**

# Is the post-COVID-19 syndrome a severe impairment of acetylcholine-orchestrated neuromodulation that responds to nicotine administration?

Marco Leitzke*

**Abstract**

https://bioelecmed.biomedcentral.com/articles/10.1186/s42234-023-00104-7

## Abstract

Following a SARS-CoV-2 infection, many individuals suffer from post-COVID-19 syndrome. It makes them unable to proceed with common everyday activities due to weakness, memory lapses, pain, dyspnea and other unspecific physical complaints. Several investigators could demonstrate that the SARS-CoV-2 related spike glycoprotein (SGP) attaches not only to ACE-2 receptors but also shows DNA sections highly affine to nicotinic acetylcholine receptors (nAChRs). The nAChR is the principal structure of cholinergic neuromodulation and is responsible for coordinated neuronal network interaction. Non-intrinsic viral nAChR attachment compromises integrative interneuronal communication substantially. This explains the cognitive, neuromuscular and mood impairment, as well as the vegetative symptoms, characterizing post-COVID-19 syndrome. The agonist ligand nicotine shows an up to 30-fold higher affinity to nACHRs than acetylcholine (ACh). We therefore hypothesize that this molecule could displace the virus from nAChR attachment and pave the way for unimpaired cholinergic signal transmission. Treating several individuals suffering from post-COVID-19 syndrome with a nicotine patch application, we witnessed improvements ranging from immediate and substantial to complete remission in a matter of days.


**Keywords** Post COVID 19 syndrome, Cholinergic neuromodulation, Nicotine, Nicotinic acetylcholine receptors, Vagus nerve signaling

## Introduction

### Post-COVID-19-syndrome

which ultimately helped to create sufficiently protective vaccines. The pathogen, however, always seems to be one

## Abstract

Following a SARS-CoV-2 infection, many individuals suffer from post-COVID-19 syndrome. It makes them unable to proceed with common everyday activities due to weakness, memory lapses, pain, dyspnea and other unspecific physical complaints. Several investigators could demonstrate that the SARS-CoV-2 related spike glycoprotein (SGP) attaches not only to ACE-2 receptors but also shows DNA sections highly affine to nicotinic acetylcholine receptors (nAChRs). The nAChR is the principal structure of cholinergic neuromodulation and is responsible for coordinated neuronal network interaction. Non-intrinsic viral nAChR attachment compromises integrative interneuronal communication substantially. This explains the cognitive, neuromuscular and mood impairment, as well as the vegetative symptoms, characterizing post-COVID-19 syndrome. The agonist ligand nicotine shows an up to 30-fold higher affinity to nACHRs than acetylcholine (ACh). We therefore hypothesize that this molecule could displace the virus from nAChR attachment and pave the way for unimpaired cholinergic signal transmission. Treating several individuals suffering from post-COVID-19 syndrome with a nicotine patch application, we witnessed improvements ranging from immediate and substantial to complete remission in a matter of days.


**Keywords** Post COVID 19 syndrome, Cholinergic neuromodulation, Nicotine, Nicotinic acetylcholine receptors, Vagus nerve signaling

## Abstract

Following a SARS-CoV-2 infection, many individuals suffer from post-COVID-19 syndrome. It makes them unable to proceed with common everyday activities due to weakness, memory lapses, pain, dyspnea and other unspecific physical complaints. Several investigators could demonstrate that the SARS-CoV-2 related spike glycoprotein (SGP) attaches not only to ACE-2 receptors but also shows DNA sections highly affine to nicotinic acetylcholine receptors (nAChRs). The nAChR is the principal structure of cholinergic neuromodulation and is responsible for coordinated neuronal network interaction. Non-intrinsic viral nAChR attachment compromises integrative interneuronal communication substantially. This explains the cognitive, neuromuscular and mood impairment, as well as the vegetative symptoms, characterizing post-COVID-19 syndrome. The agonist ligand nicotine shows an up to 30-fold higher affinity to nACHRs than acetylcholine (ACh). We therefore hypothesize that this molecule could displace the virus from nAChR attachment and pave the way for unimpaired cholinergic signal transmission. Treating several individuals suffering from post-COVID-19 syndrome with a nicotine patch application, we witnessed improvements ranging from immediate and substantial to complete remission in a matter of days.


**Keywords** Post COVID 19 syndrome, Cholinergic neuromodulation, Nicotine, Nicotinic acetylcholine receptors, Vagus nerve signaling

## Abstract

Following a SARS-CoV-2 infection, many individuals suffer from post-COVID-19 syndrome. It makes them unable to proceed with common everyday activities due to weakness, memory lapses, pain, dyspnea and other unspecific physical complaints. Several investigators could demonstrate that the SARS-CoV-2 related spike glycoprotein (SGP) attaches not only to ACE-2 receptors but also shows DNA sections highly affine to nicotinic acetylcholine receptors (nAChRs). The nAChR is the principal structure of cholinergic neuromodulation and is responsible for coordinated neuronal network interaction. Non-intrinsic viral nAChR attachment compromises integrative interneuronal communication substantially. This explains the cognitive, neuromuscular and mood impairment, as well as the vegetative symptoms, characterizing post-COVID-19 syndrome. The agonist ligand nicotine shows an up to 30-fold higher affinity to nACHRs than acetylcholine (ACh). We therefore hypothesize that this molecule could displace the virus from nAChR attachment and pave the way for unimpaired cholinergic signal transmission. Treating several individuals suffering from post-COVID-19 syndrome with a nicotine patch application, we witnessed improvements ranging from immediate and substantial to complete remission in a matter of days.


**Keywords** Post COVID 19 syndrome, Cholinergic neuromodulation, Nicotine, Nicotinic acetylcholine receptors, Vagus nerve signaling

## Abstract

Following a SARS-CoV-2 infection, many individuals suffer from post-COVID-19 syndrome. It makes them unable to proceed with common everyday activities due to weakness, memory lapses, pain, dyspnea and other unspecific physical complaints. Several investigators could demonstrate that the SARS-CoV-2 related spike glycoprotein (SGP) attaches not only to ACE-2 receptors but also shows DNA sections highly affine to nicotinic acetylcholine receptors (nAChRs). The nAChR is the principal structure of cholinergic neuromodulation and is responsible for coordinated neuronal network interaction. Non-intrinsic viral nAChR attachment compromises integrative interneuronal communication substantially. This explains the cognitive, neuromuscular and mood impairment, as well as the vegetative symptoms, characterizing post-COVID-19 syndrome. The agonist ligand nicotine shows an up to 30-fold higher affinity to nACHRs than acetylcholine (ACh). We therefore hypothesize that this molecule could displace the virus from nAChR attachment and pave the way for unimpaired cholinergic signal transmission. Treating several individuals suffering from post-COVID-19 syndrome with a nicotine patch application, we witnessed improvements ranging from immediate and substantial to complete remission in a matter of days.


**Keywords** Post COVID 19 syndrome, Cholinergic neuromodulation, Nicotine, Nicotinic acetylcholine receptors, Vagus nerve signaling

more infected patients recovering from the acute phase of COVID-19 along with a large population needing therapy and rehab capacity (Stam et al. 2020; Barker-Davies et al. 2020; Klitzman 2020) to cure the symptoms of the chronic phase (Barker-Davies et al. 2020), better known as post-COVID-19-syndrome (Nath 2020).

## Is it just the ACE2 receptor?

For the acute infection phase, physicians are lacking a causal therapeutic strategy to challenge the viral assault on human organ systems and must confine themselves to symptomatic therapeutic approaches for their patients. In severe cases of SARS-CoV-2 infections, these options prove rather underwhelming (Iyer et al. 2020; Jeong et al. 2020), while the therapeutic situation remains vague regarding post-COVID-19 syndrome (Rimmer, 2020; particles competing with acetylcholine for nAChR binding in order to enter the human body may lead to primary neuro infection (Changeux et al. 2020; Steardo et al. 2020). Furthermore, among the severe and fatal cases of COVID-19, the proportion of nicotine consumers was significantly lower than non-consumers of nicotine (Miyara, et al. 2020). Since nicotine may protect nAChRs from viral attachment, therapeutic nicotine application was proposed in the management of acute COVID-19 infections (Changeux et al. 2020). This argument is convincingly supported by the cohort study of Hippisley-Cox et al. (2020), with a total of 8.28 million participants (including 19,486 confirmed COVID-19 cases), showing lower odds for COVID-19 infection and COVID-19-related ICU stay in association with smoking (Hippisley-Cox et al. 2020).

more infected patients recovering from the acute phase of COVID-19 along with a large population needing therapy and rehab capacity (Stam et al. 2020; Barker-Davies et al. 2020; Klitzman 2020) to cure the symptoms of the chronic phase (Barker-Davies et al. 2020), better known as post-COVID-19-syndrome (Nath 2020).

**Is it just the ACE2 receptor?**

For the acute infection phase, physicians are lacking a causal therapeutic strategy to challenge the viral assault on human organ systems and must confine themselves to symptomatic therapeutic approaches for their patients. In severe cases of SARS-CoV-2 infections, these options prove rather underwhelming (Iyer et al. 2020; Jeong et al. 2020), while the therapeutic situation remains vague regarding post-COVID-19 syndrome (Rimmer, 2020; particles competing with acetylcholine for nAChR binding in order to enter the human body may lead to primary neuro infection (Changeux et al. 2020; Steardo et al. 2020). Furthermore, among the severe and fatal cases of COVID-19, the proportion of nicotine consumers was significantly lower than non-consumers of nicotine (Miyara, et al. 2020). Since nicotine may protect nAChRs from viral attachment, therapeutic nicotine application was proposed in the management of acute COVID-19 infections (Changeux et al. 2020). This argument is convincingly supported by the cohort study of Hippisley-Cox et al. (2020), with a total of 8.28 million participants (including 19,486 confirmed COVID-19 cases), showing lower odds for COVID-19 infection and COVID-19-related ICU stay in association with smoking (Hippisley-Cox et al. 2020).

Farsalinos et al. (2020) examined and identified a "toxin-like" aa sequence in the receptor binding domain of the SARS-CoV-2 spike glycoprotein (SGP) (*aa 375–390*) which shows significant sequence homology with the neurotoxin homolog NL1, one of the many snake venom toxins interacting with nAChRs (Farsalinos, et al. 2020). Additionally, they performed computa-

Farsalinos et al. (2020) examined and identified a "toxin-like" aa sequence in the receptor binding domain of the SARS-CoV-2 spike glycoprotein (SGP) (*aa 375–390*) which shows significant sequence homology with the neurotoxin homolog NL1, one of the many snake venom toxins interacting with nAChRs (Farsalinos, et al. 2020). Additionally, they performed computa-

Farsalinos et al. (2020) examined and identified a "toxin-like" aa sequence in the receptor binding domain of the SARS-CoV-2 spike glycoprotein (SGP) (*aa 375–390*) which shows significant sequence homology with the neurotoxin homolog NL1, one of the many snake venom toxins interacting with nAChRs (Farsalinos, et al. 2020). Additionally, they performed computa-

# "Profound similarities between…toxins (*found in the venom of*)…snakes of the *Ophiophagus* (king cobra) and *Bungarus* (krait snake)…and SARS-CoV-2 (spike) proteins…were found… (Farsalinos et al. 2020; Changeux et al. 2020)."



Our group recently described the crucial relevance of autonomic balance for the severity of COVID-19 disease courses (Leitzke et al. 2020; Leitzke and Schönknecht 2021) and highlighted the significance of nicotinic acetylcholine receptors (nAChRs) for the limiting regulation of cytokine liberation and virus replication on the transcriptional level, restricting NF-KB action along the cholinergic anti-inflammatory pathway (CAP) (Leitzke et al. 2020; Leitzke and Schönknecht 2021). Profound similarities between highly nAChR affine toxins (i.e., from snakes of the *Ophiophagus* (cobra) and *Bungarus* genera, the G-ectodomains of three *Rabies lyssavirus* (formerly Rabies virus) (RABV) strains (Changeux et al. 2020) or muscarinic toxin-like protein and Cobratoxin (naja siamensis) (Farsalinos et al. 2020)) and SARS-CoV-2 specific proteins (Farsalinos et al. 2020; Changeux et al. 2020) were found by analyzing the toxin's amino-acid (aa) sequence alignment and comparing it to the motifs in spike glycoprotein (SGP) from SARS-CoV-2 (Farsalinos et al. 2020; Changeux et al. 2020).

of the extracellular domain of the nAChR α9 subunit (Farsalinos, et al. 2020), the core of the "toxin-binding site" of nAChRs (Farsalinos, et al. 2020). Likewise, a similar interaction could be demonstrated between the ligand binding domain of the pentameric α7 nicotinic acetylcholine receptor (α7nAChR) chimera and the SARS-CoV-2 SGP (Farsalinos, et al. 2020). The authors concluded that their findings strongly support the hypothesis of a dysregulation in the nicotinic cholinergic system being a considerable part of COVID-19's pathophysiology (Farsalinos, et al. 2020).

### The pivotal neuromodulation role of nicotinic acetylcholine receptors

Within the central nervous system (CNS), acetylcholine (ACh) is released mainly from projection neurons (PN), which innervate distal areas, and local interneurons interspersing their cellular targets. PNs are found in several nuclei, including the medial habenula, pedunculopontine and laterodorsal tegmental areas, as well

ardis LABS

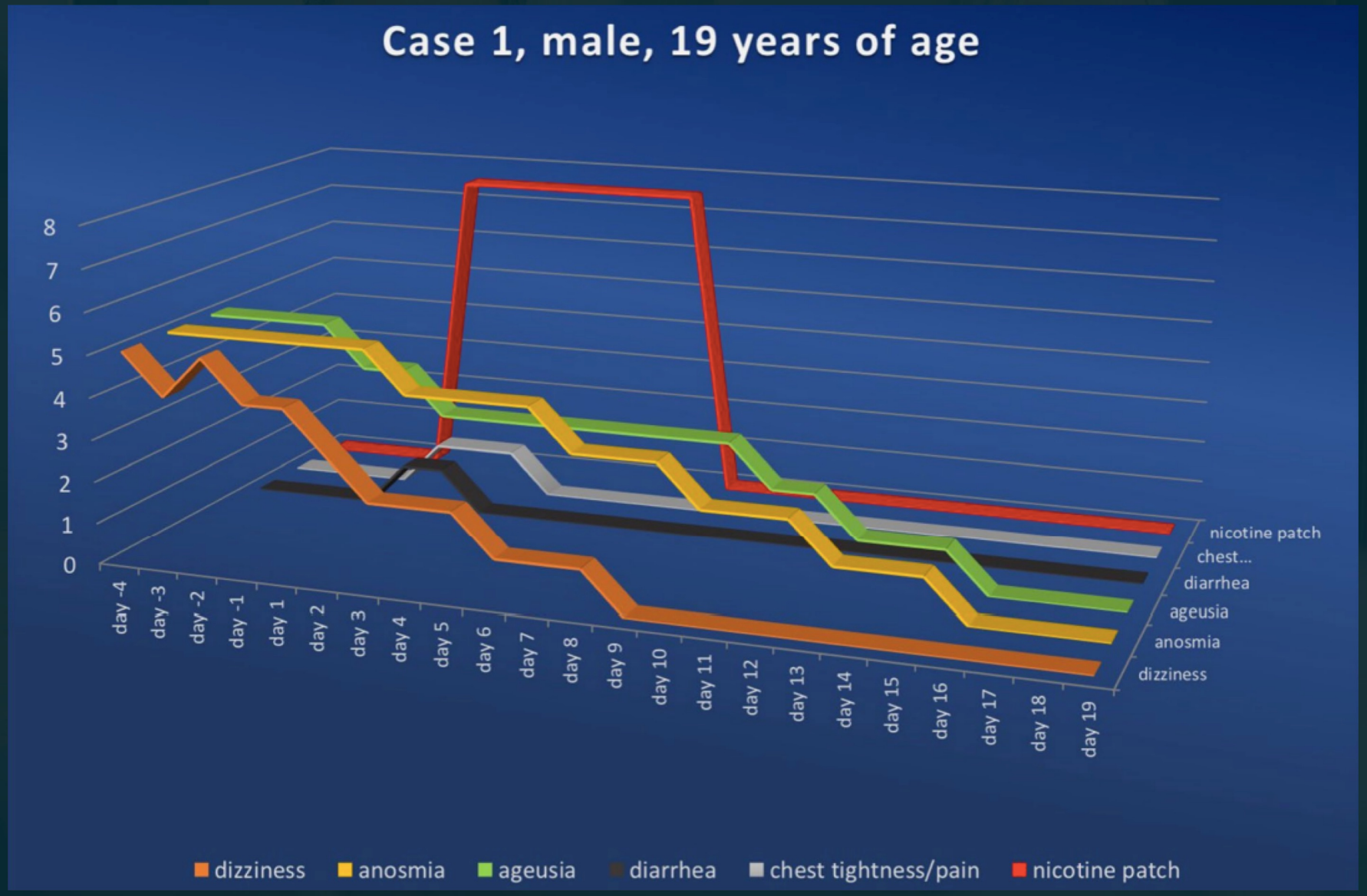
ardis SHOW

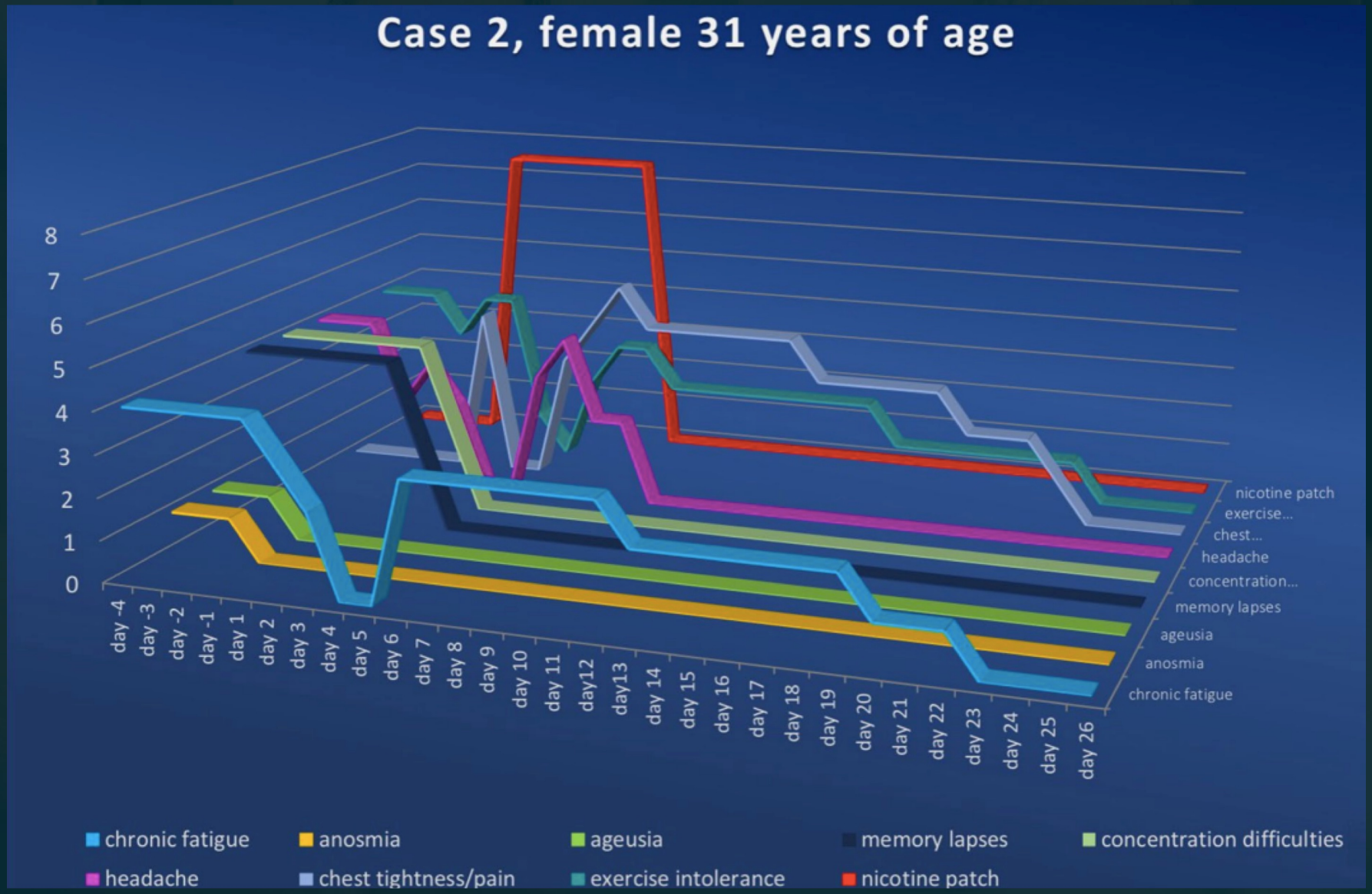
## Material

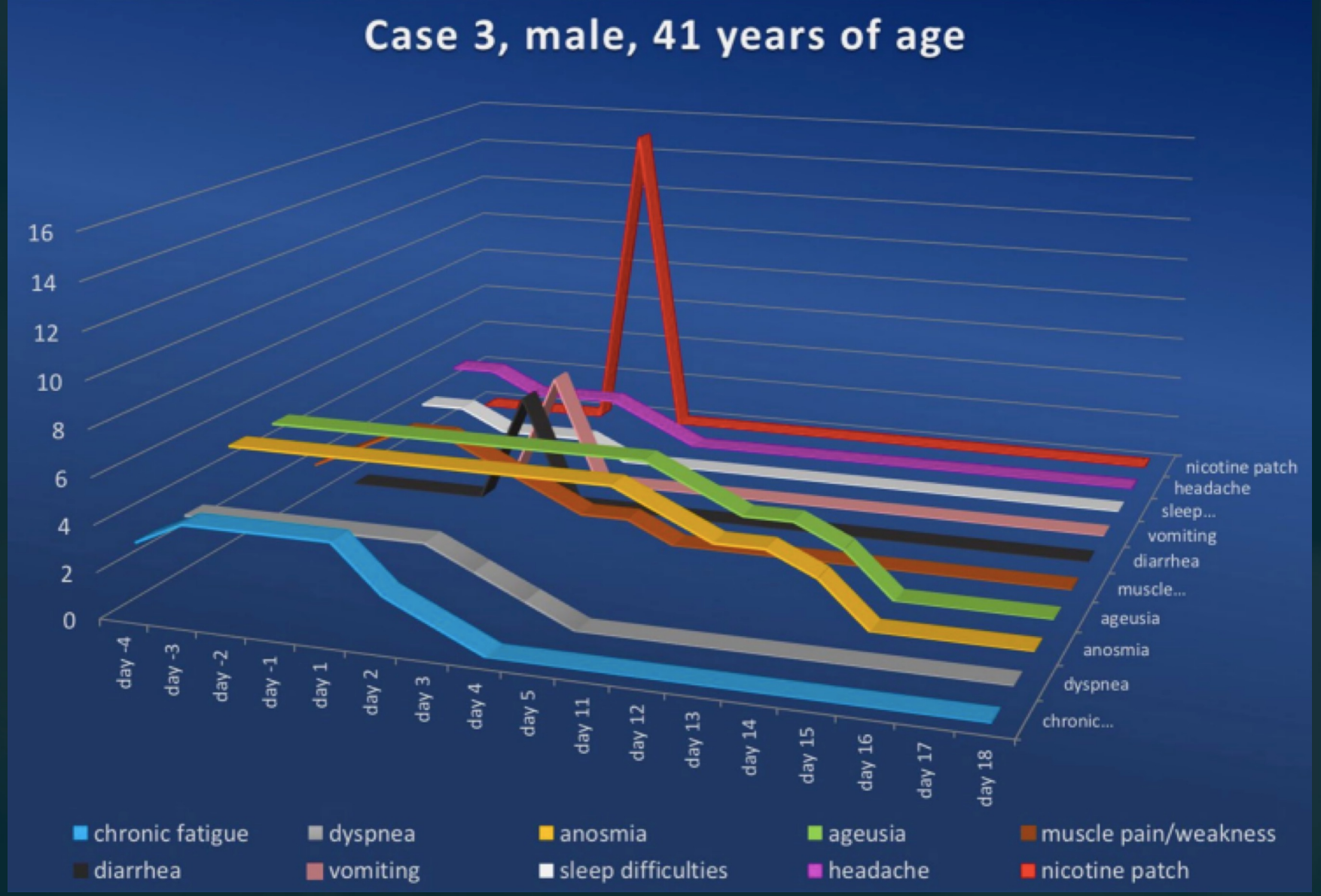
We investigated one female (32 years old) and 3 males (19, 41 and 52 years old, respectively) who suffered from numerous symptoms indicative of post-COVID-19 syndrome following a PCR-confirmed SARS-CoV-2 infection with a subsequent mild course of disease. The patients described weakness, dyspnea, sleep disturbances, dizziness, complete ageusia and anosmia, along with a variety of other symptoms. Except for the youngest, the patients

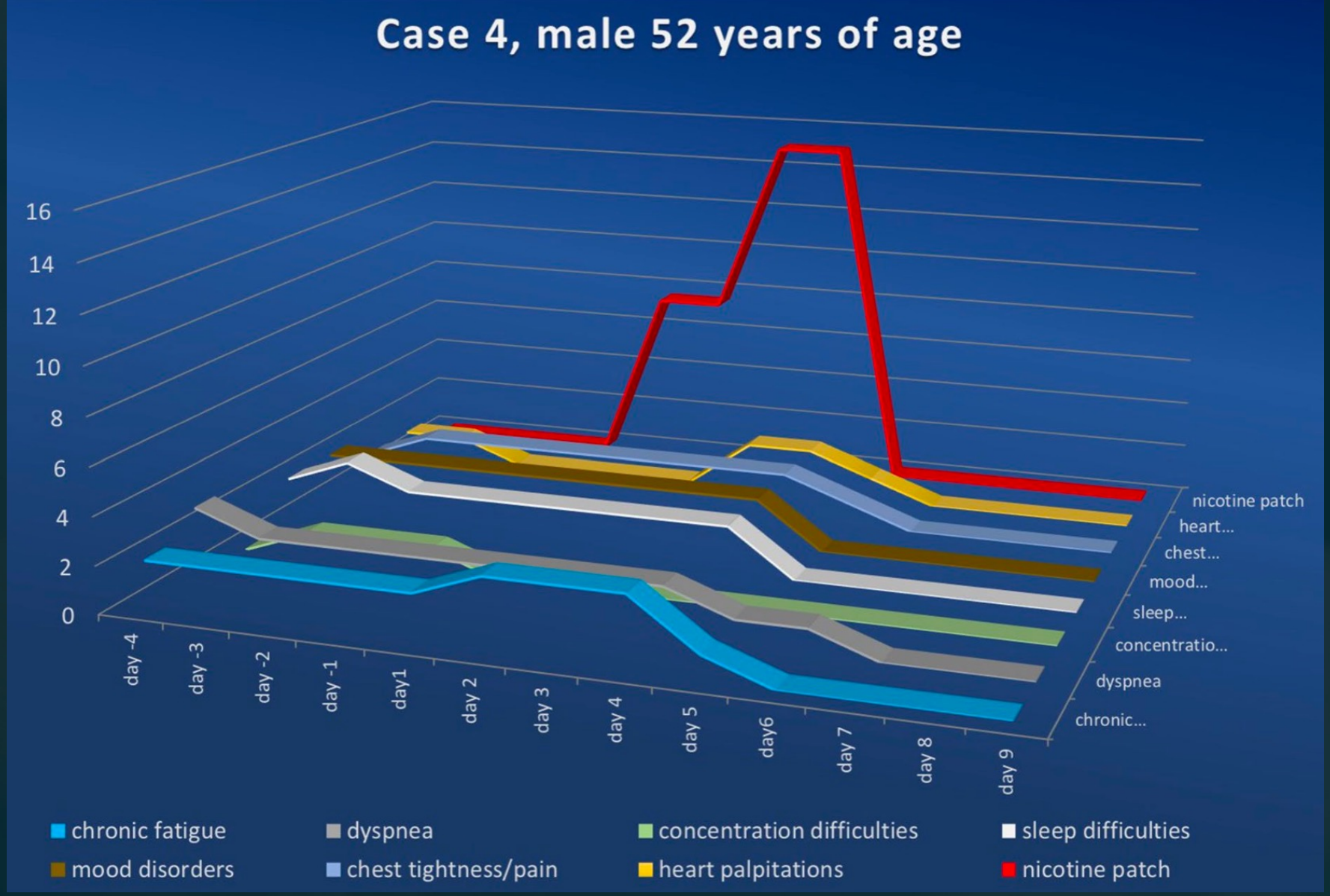
## Methods

After meticulously explaining the hypothesis described above, as well as the expected effects of nicotine and possible side effects, the patients were advised to apply a standard nicotine patch. Since all included individuals were nicotine-naïve persons, they were instructed to use the lowest available dosage (7.5 mg/24 h) and to administer the patch once daily (in the morning). All patients


Case 1, male, 19 years of age
8
7
6
5
4
3
2
1
0
day -4
day -3
day -2
day -1
day 1
day 2
day 3
day 4
day 5
day 6
day 7
day 8
day 9
day 10
day 11
day 12
day 13
day 14
day 15
day 16
day 17
day 18
day 19
nicotine patch
chest...
diarrhea
ageusia
anosmia
dizziness
dizziness
anosmia
ageusia
diarrhea
chest tightness/pain
nicotine patch


Case 2, female 31 years of age
8
7
6
5
4
3
2
1
0
day -4
day -3
day -2
day -1
day 1
day 2
day 3
day 4
day 5
day 6
day 7
day 8
day 9
day 10
day 11
day12
day13
day 14
day 15
day 16
day 17
day 18
day 19
day 20
day 21
day 22
day 23
day 24
day 25
day 26
nicotine patch
exercise...
chest...
headache
concentration...
memory lapses
ageusia
anosmia
chronic fatigue
chronic fatigue
anosmia
ageusia
memory lapses
concentration difficulties
headache
chest tightness/pain
exercise intolerance
nicotine patch


Case 3, male, 41 years of age
16
14
12
10
8
6
4
2
0
day -4
day -3
day -2
day -1
day 1
day 2
day 3
day 4
day 5
day 11
day 12
day 13
day 14
day 15
day 16
day 17
day 18
nicotine patch
headache
sleep...
vomiting
diarrhea
muscle...
ageusia
anosmia
dyspnea
chronic...
chronic fatigue
dyspnea
anosmia
ageusia
muscle pain/weakness
diarrhea
vomiting
sleep difficulties
headache
nicotine patch


Case 4, male 52 years of age
16
14
12
10
8
6
4
2
0
day -4
day -3
day -2
day -1
day1
day 2
day 3
day 4
day 5
day6
day 7
day 8
day 9
nicotine patch
heart...
chest...
mood...
sleep...
concentratio...
dyspnea
chronic...
chronic fatigue
dyspnea
concentration difficulties
sleep difficulties
mood disorders
chest tightness/pain
heart palpitations
nicotine patch

## Discussion

Each of the four presented cases showed significant alleviation of their persistent symptoms; improvement was reached either immediately following nicotine patch application or in rapid succession after treatment began. There were clear differences in the patterns and the time spans for symptom relief among the four cases. It is also worth noting that the course of symptom improvement in each of the presented cases was independent of their drastically different lengths and progression prior to nicotine therapy.

In each case, signs of exhaustion such as fatigue, weakness, breathlessness and exercise intolerance improved rapidly and across the board following nicotine exposure (at the very latest by day six). In cases with impairment or loss of the senses of taste and smell, improvement was observed over a longer period, with complete restoration of these senses over anywhere from thirteen to sixteen days.

The release of the SARS-CoV-2 virus from nAChR receptors can lead to short-term viremia with signs of acute SARS-CoV-2 infection when starting nicotine therapy; however, this viral load should be neutralized within a short period of time by the humoral component of the immune system due to SARS-CoV-2 antibodies formed during the acute phase of infection (Fig. 2C,D).

# The Published Conclusion of this Study!

option more closely seem feasible. Based on the results of this case study, this treatment option—using nicotine patches to combat long-haul COVID—seems far superior to the time-consuming, often underwhelming or disappointing, costly and complex rehabilitation measures currently available to these patients.

# Will I Become Addicted To Nicotine Patches?

Transcutaneous administration of nicotine ensures constant serum levels without relevant peak levels. Thus, we did not see any development of nicotine dependence in the context of nicotine patch therapy. From the author's point of view, this is not to be expected.

https://bioelecmed.biomedcentral.com/articles/10.1186/s42234-023-00104-7

# "Ask Your Doctor if 7mg NICOTINE PATCHES Are Right For You?"


THE dr.ardis SHOW

# FREE RESOURCES

SCAN ME

## SCAN TO SIGNUP & ACCESS DR ARDIS FREE DOCUMENTS, RESOURCES, & RESEARCH

ardis LABS

www.thedrardisshow.com

THE dr.ardis SHOW

# NEW LIQUID FORMULATION


# EDTA

## NOW EVEN BETTER!

- Calcium Disodium EDTA
- Better Absorption
- More Bioavailable
- Advanced Glycerosomal Technology
- Organic EDTA Source / USP Grade
- Powerful Protection

## 20% OFF SALE!

**Use code REAWAKEN at checkout.**

Offer applies to EDTA, Foregin Protein Cleanse, Cardio Flow, Docs Viral Defense and Propolis Throat Sprays. Offer ends at midnight 10/18/23


**Scan QR and watch Dr Ardis video on EDTA to learn more!**

# NEW PRODUCT


# FOREIGN
## PROTEIN CLEANSE

- Detox Spike Proteins
- Rapid Delivery Liquid Formulation
- Enhanced Bioavailability
- Cold-Processed Acoustic BioSomal Technology™
- Potent Cleansing Formula
- Enhance Immunity

**GET 20% OFF! Use code REAWAKEN at checkout. Scan QR to watch video!**

Offer applies to EDTA, Foregin Protein Cleanse, Cardio Flow, Doc'S Viral Defense and Propolis Throat Sprays. Offer ends at midnight 10/18/23

# HEALING FOR THE A.G.E.S.

ARDIS | GROUP | EALY | SCHMIDT

## GET DIGITAL ACCESS NOW

**$50 OFF**

You'll get access to all the session recordings, Q&A's & downloadable supporting assets.

SCAN ME

**AT CHECKOUT USE PROMOCODE: ARDIS**

**https://www.healingfortheages.com**