

29 June - 1 July 2023 • London UK

# Long Covid Pathogen Reactivation: Testing and Therapeutic Options

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## **Agenda**

- Pathogen reactivation
  - DNA viruses
  - RNA viruses
  - Bacteria
- Testing
- Therapeutic options

# Recent study Aug. 2022 investigating the link between Long COVID and herpes viruses

Could long COVID be linked to herpes viruses? Early data offer a hint

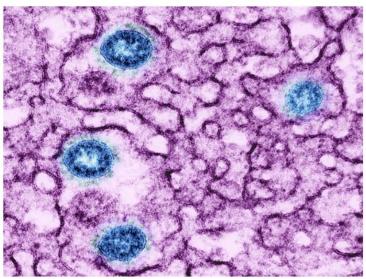
Low cortisol levels and herpes-virus reactivation are associated with prolonged COVID-19 symptoms, preliminary research suggests.

Emily Waltz





NEWS 25 August 2022



Particles of the SARS-CoV-2 virus (blue) inside an infected cell. Credit: NIH/SPL

"Most strikingly, the study found ... hints that in people with long COVID, Epstein-Barr virus, which can cause mononucleosis, and Varicella Zoster virus, which causes chickenpox and shingles, might recently have been 'reactivated'. Both of these viruses are in the herpes family, persist indefinitely in the body after infection and can start to multiply again after a period of quiescence.

 $Source: \ https://www.nature.com/articles/d41586-022-02296-5\#: ``:text=Low\%20 cortisol\%20 levels\%20 and \%20 herpes, 19\%20 symptoms\%20\%20 preliminary\%20 research\%20 suggests. \& text=Researchers\%20 looking\%20 for\%20 biological\%20 drivers, of\%20 a\%20 stress\%20 hormone 1.$ 

# "Long COVID Symptoms Likely Caused by Epstein-Barr Virus Reactivation"

> Pathogens. 2021 Jun 17;10(6):763. doi: 10.3390/pathogens10060763.

### Investigation of Long COVID Prevalence and Its Relationship to Epstein-Barr Virus Reactivation

Jeffrey E Gold <sup>1</sup>, Ramazan A Okyay <sup>2</sup>, Warren E Licht <sup>3</sup>, David J Hurley <sup>4</sup>

Affiliations + expand

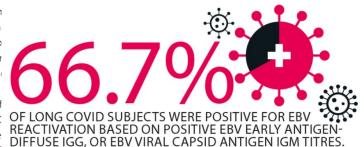
PMID: 34204243 PMCID: PMC8233978 DOI: 10.3390/pathogens10060763

Free PMC article

#### **Abstract**

Coronavirus disease 2019 (COVID-19) patients sometimes experience long-term symptoms following resolution of acute disease, including fatigue, brain fog, and rashes. Collectively these have become known as long COVID. Our aim was to first determine long COVID prevalence in 185 randomly surveyed COVID-19 patients and, subsequently, to determine if there was an association between occurrence of long COVID-19 symptoms and reactivation of Englandary virus (EDV) in 69 COVID-19

patients recruited fron 30.3% (56/185), which COVID symptoms. New control subjects in our for EBV early antigensignificant (*p* < 0.001, subjects 21-90 days af or concurrently with C may not be a direct relinduced EBV reactivation.



"We found similar rates of EBV reactivation in those who had long COVID symptoms for months, as in those with long COVID symptoms that began just weeks after testing positive for COVID-19," said coauthor David J. Hurley, PhD, a professor and

molecular microbiologist at the

to us that EBV reactivation likely

COVID-19 infection."

University of Georgia. "This indicated

occurs simultaneously or soon after

We found that 66.7% (20/30) of

long-term long COVID subjects

versus 10% (2/20) of long-term

**FBV** reactivation

control subjects were positive for

Source: <a href="https://pubmed.ncbi.nlm.nih.gov/34204243/">https://www.news-medical.net/news/20210623/Epstein-Barr-virus-reactivation-may-be-the-cause-of-long-COVID-symptoms.aspx;">https://world.org/EBV/</a>

# High EBV results post COVID, backed up by hundreds of lab tests

```
EBV EliSpot (lytic+latent)
```

```
1 EBV EliSpot (lytic) ! 657 SI
```

0-1 = negative

2-3 = weak positive

> 3 = positive

### 1 EBV EliSpot (latent) ! 65 SI

0-1 = negative

2-3 = weak positive

> 3 = positive

The result of the EliSpot test indicates current celluar activity against Epstein-Barr-Virus (EBV).

Explanation of EBV antigens:

EBV-lytic antigen: sign for replication of infectious EBV

virions

EBV-latent antigen: sign for EBV latency with no production of infectious EBV virions

# CMV reactivation and virus-induced immune dysfunction may be underestimated as a driver

**BMC** Part of Springer Nature

**Immunity & Ageing** 

Home About Articles Submission Guidelines

Commentary Open Access | Published: 12 March 2021

Does reactivation of cytomegalovirus contribute to severe COVID-19 disease?

Cecilia Söderberg-Nauclér <sup>™</sup>

Immunity & Ageing 18, Article number: 12 (2021) Cite this article

25k Accesses | 18 Citations | 29 Altmetric | Metrics

#### Abstract

The majority of people infected with SARS-CoV-2 are asymptomatic or have mild to moderate symptoms. However, for unknown reasons, about 15 % have severe pneumonia requiring hospital care and oxygen support, and about 5 % develop acute respiratory distress syndrome, septic shock, and multiorgan failure that result in a high mortality rate. The risk of severe COVID-19 is highest among those who are over 70 years of age. Why severe COVID-19 develops in some people but not others is not understood. Could some cases involve reactivation of latent cytomegalovirus (CMV)?

Source: 1. Söderberg-Nauclér, C. Does reactivation of cytomegalovirus contribute to severe COVID-19 disease?. Immun Ageing 18, 12 (2021). https://doi.org/10.1186/s12979-021-00218-z; 2. https://pubmed.ncbi.nlm.nih.gov/35101103/

"CMV reactivation and virus induced immune dysfunction may be under-estimated as a driver of immuno-pathogenesis in patients with severe COVID-19."

"... diagnosing CMV in COVID-19 patients could be well worth the effort." <sup>1</sup>

"Intriguingly, severe acute respiratory syndrome coronavirus 2 and cytomegalovirus may potentiate each other, since they share some innate immune pathways."<sup>2</sup>

# Our lab and others are seeing a definite correlation between COVID/Long COVID and CMV reactivation

CMV EliSpot

1 CMV EliSpot

! 13 SI

May 2019, before COVID diagnosis

0-1 = negative
2-3 = weak positive
> 3 = positive

The result of the EliSpot test indicates current cellular activity against Cytomegalo-Virus.

#### CMV EliSpot

1 CMV Lytisch ! 279 SI

0-1 = negative

2-3 = weak positive

> 3 = positive

1 CMV Latent ! 79 SI

0-1 = negative

2-3 = weak positive

> 3 = positive

The result of the EliSpot test indicates current cellular activity against Cytomegalo-Virus.

Explanation of CMV antigens:

 ${\tt CMV-lytic\ antigen:\ sign\ for\ replication\ of\ infectious\ {\tt CMV}}$ 

virions

June 2020, after COVID

## Herpes Simplex Virus also reactivating with COVID-19





Article

# Herpes Simplex Virus Re-Activation in Patients with SARS-CoV-2 Pneumonia: A Prospective, Observational Study

Erica Franceschini <sup>1,\*</sup>, Alessandro Cozzi-Lepri <sup>2</sup>, Antonella Santoro <sup>1</sup>, Erica Bacca <sup>3</sup>, Guido Lancellotti <sup>3</sup>, Marianna Menozzi <sup>1</sup>, William Gennari <sup>4</sup>, Marianna Meschiari <sup>1</sup>, Andrea Bedini <sup>1</sup>, Gabriella Orlando <sup>1</sup>,

Cinzia Puzzolante <sup>1</sup>, Margherita Digaetano <sup>1</sup>, Jovana Milic <sup>3</sup>, Mauro Codeluppi <sup>5</sup>, Monica Pecorari Federica Carli <sup>1</sup>, Gianluca Cuomo <sup>1</sup>, Gaetano Alfano <sup>6</sup>, Luca Corradi <sup>1</sup>, Roberto Tonelli <sup>7</sup>, Nicola Stefano Busani <sup>9</sup>, Emanuela Biagioni <sup>9</sup>, Irene Coloretti <sup>9</sup>, Giovanni Guaraldi <sup>3</sup>, Mario Sarti <sup>4</sup>, Mari Enrico Clini <sup>7</sup>, Massimo Girardis <sup>9</sup>, Inge C. Gyssens <sup>11,12</sup> and Cristina Mussini <sup>1,3</sup>,\*

Rheumatology International (2022) 42:1523–1530 https://doi.org/10.1007/s00296-022-05146-9 Rheumatology

**OBSERVATIONAL RESEARCH** 



"Conclusions: our study shows a high incidence of HSV-1 reactivation both virologically and clinically in patients with

SARS-CoV-2 severe pneumonia"<sup>1</sup>

## Herpesvirus infections and post-COVID-19 manifestations: a pilot observational study

Svitlana Zubchenko 1 · Irvna Kril · Olena Nadizhko · Oksana Matsvura · O · Valentvna Chopyak · O

Received: 17 March 2022 / Accepted: 5 May 2022 / Published online: 1 June 2022

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#### Abstract

The global spread of SARS-CoV-2 points to unrivaled mutational variation of the virus, contributing to a variety of post-COVID sequelae in immunocompromised subjects and high mortality. Numerous studies have reported the reactivation of "sluggish" herpes virus infections in COVID-19, which exaggerate the course of the disease and complicate with lasting post-COVID manifestations CMV, EBV, HHV6). This study aimed to describe clinical and laboratory features of post-COVID manifestations accompanied by the reactivation of herpes virus infections (CMV, EBV, HHV6). 88 patients were recruited for this study, including subjects with reactivation of herpes viruses, 68 (72.3%) (main group) and 20 (27.7%) subjects without detectable DNA of herpesviruses (control group): 46 (52.3%) female and 42 (47.7%) male; median age was  $41.4\pm6.7$  years. Patients with post-COVID manifestations presented with reactivation of EBV in 42.6%, HHV6 in 25.0%, and EBV plus HHV6 in 32.4%. Compared with controls, patients with herpes virus infections presented with more frequent slight fever temperature, headache, psycho-neurological disorders, pulmonary abnormalities and myalgia (p < 0.01), activation of liver enzymes, elevated CRP and D-dimer, and suppressed cellular immune response (p < 0.05). Preliminary results indicate a likely involvement of reactivated herpes virus infections, primarily EBV infections in severe COVID-19 and the formation of the post-COVID syndrome. Patients with the post-COVID syndrome and reactivation of EBV and HHV6 infections are at high risk of developing various pathologies, including rheumatologic diseases.

Keywords COVID-19 · Herpes virus · Epstein-Barr virus · Rheumatology · An autoimmune disease

## August 2022: Reactivation of HHV-6 and EBV

#### JOURNAL OF

### MEDICAL VIROLOGY

Presence and clinical impact of human herpesvirus-6 infection in patients with moderate to critical coronavirus disease-19

Katia Lino, Lilian S. Alves, Jessica V. Raposo, Thalia Medeiros, Cintia F. Souz≀ S. de Paula, Jorge R. Almeida 💌

First published: 14 October 2021 | https://doi.org/10.1002/jmv.27392

Cohort of 67: "We found that 15/67 (22.4%) patients had detectable EBV and 3/67 (4.5%) had detectable HHV-6"

> Viruses. 2022 Aug 25;14(9):1872. doi: 10.3390/v14091872.

### Epstein-Barr Virus and Human Herpesvirus-6 Reactivation in Acute COVID-19 Patients

Bailey Brooks <sup>1 2</sup>, Christina Tancredi <sup>2</sup>, Yufeng Song <sup>2</sup>, Alemu Tekewe Mogus <sup>2</sup>, Meei-Li W Huang <sup>3</sup>, Haiying Zhu <sup>3</sup>, Tuan L Phan <sup>4 5</sup>, Harrison Zhu <sup>5 6</sup>, Alexandra Kadl <sup>7 8</sup>, Judith Woodfolk <sup>7 9</sup>, Keith R Jerome <sup>3 10</sup>, Steven L Zeichner <sup>2 9</sup>

Affiliations + expand

PMID: 36146679 PMCID: PMC9504756 DOI: 10.3390/v14091872

Free PMC article

#### Abstract

Beyond their pulmonary disease, many COVID-19 patients experience a complex constellation of characteristics, including hyperinflammatory responses, autoimmune disorders, and coagulopathies. However, the pathogenesis of these aspects of COVID-19 is obscure. More than 90% of people are latently infected with the lymphotropic herpesviruses Epstein-Barr Virus (EBV) and/or Human Herpesvirus-6 (HHV-6). Some of the inflammatory features of COVID-19 resemble clinical syndromes seen during EBV and HHV-6 infection, and these latent viruses can be reactivated by inflammatory mediators. We hypothesized that EBV and HHV-6 reactivation might be a common feature of early COVID-19, particularly in patients with more inflammation. We tested for EBV and HHV-6 reactivation in 67 patients acutely hospitalized with COVID-19 using previously validated quantitative PCR assays on the plasma. In our cohort, we found that 15/67 (22.4%) patients had detectable EBV and 3/67 (4.5%) had detectable HHV-6. This frequency of activation is somewhat more than the frequency

Source: https://pubmed.ncbi.nlm.nih.gov/36146679/

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## Coxsackie virus and myocarditis/pericarditis as coinfections in COVID-19

Fulminant myocarditis as an early presentation of SARS-CoV-2

Tamara Naneishvili,<sup>™1</sup> Arsalan Khalil, <sup>1</sup> Ryan O'Leary, <sup>2</sup> and Neeraj Prasad<sup>1</sup>

► Author information ► Article notes ► Copyright and License information <u>Disclaimer</u>

This article has been <u>cited by</u> other articles in PMC.

"Myocarditis is well known to be caused by viral infections such as Coxsackie virus group B, human herpes virus 6 and parvovirus B19."1

#### Abstract

Myocarditis is well known to be caused by viral infections s

"Both types of [Coxsackie] viruses (A and B) can cause meningitis, myocarditis, and pericarditis"2

herpes virus 6 and parvovirus B19. However, during the current emerging outbreak of SARS-CoV-2, there have been few case reports describing myocarditis as a possible presentation. In our case re-

Journal List > Elsevier Public Health Emergency Collection > PMC8503119

Elsevier Public Health Emergency Collection

Chest. 2021 Oct; 160(4): A976.

Published online 2021 Oct 11. doi: 10.1016/j.chest.2021.07.909

PMCID: PMC8503119

COVID-19 AND COXSACKIE B COINFECTION: A RARE CASE OF ACUTE PERICARDITIS

AMANDA ENG, NIKISHA PANDYA, and RATTAN PATEL

... this is the first case presenting pericarditis caused by COVID 19 and Coxsackieviruses B (CV-B) coinfection.

Source: 1. https://pubmed.ncbi.nlm.nih.gov/32928810/; 2. https://www.medicinenet.com/coxsackie\_virus/article.htm; https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC8503119/; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8330013/pdf/IETT 0 1952985.pdf;

# Reactivation of Enteroviruses (Coxsackie, Echovirus) also evident in many cases

Analysis	Result U	nits Referenc	e Range	Chart
EBV-latent antigen: sign for	EBV latency with n	o production		
of infectious EBV virions				
Coxsackie IgG-/IgA-antibodies				
4 Coxsackie-IgG Typ A7 (IFT) +	1:10000	< 1:100	[	. *>
4 Coxsackie-IgG Typ B1 (IFT) +	1:10000	< 1:100	[	. *>
7 Coxsackie-Virus IgA A7 (IFT) +	1:10	< 1:10	[	. *>
7 Coxsackie-Virus IgA B1 (IFT) +	1:100	< 1:10	[	. *>
The specific positive Coxsack:	ie-Virus Type			
A7/B1-IgG-/IgA-antibodies ind:	icate current humo	ral immune		
responses against Coxsackie-V	irus Type A7 and			
Coxsackie-Virus Type B1 (rece	nt infection with			
Coxsackie-Virus Type A7/B1?).				
The test system is highly spec	cific for Coxsacki	e Virus		
antibodies. Other Enterovirus				
Echovirus IgG/IgA-antibodies)		-		
,				
(for example Echovirus IgG/Ig	A-antibodies) are	not		
detectable.	,			
validated by				
Dr.Armin Schwarzbach				
22.ALMIII DOINGLEDGOII				

Source: ArminLabs results, with permission

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## Can Covid lead to reactivation of Lyme Disease?

www.nature.com/scientificreports

## **scientific** reports



## **OPEN** Correlation between COVID-19 severity and previous exposure of patients to Borrelia spp.

Alina Szewczyk-Dąbrowska<sup>1,2</sup>, Wiktoria Budziar<sup>1</sup>, Marek Harhala<sup>1,4</sup>, Krzysztof Baniecki<sup>3</sup>, Aleksandra Pikies<sup>3</sup>, Natalia Jędruchniewicz<sup>1</sup>, Zuzanna Kaźmierczak<sup>1,4</sup>, Katarzyna Gembara<sup>1,4</sup>, Tomasz Klimek<sup>1</sup>, Wojciech Witkiewicz<sup>1</sup>, Artur Nahorecki<sup>3</sup>, Kamil Barczyk<sup>3</sup>, Marlena Kłak<sup>1</sup>, Urszula Grata-Borkowska<sup>2</sup> & Krystyna Dąbrowska<sup>1,4™</sup>

Predictors for the risk of severe COVID-19 are crucial for patient care and control of the disease. Other infectious diseases as potential comorbidities in SARS-CoV-2 infection are still poorly understood. Here we identify association between the course of COVID-19 and Lyme disease (borreliosis), caused by Borrelia burgdorferi transmitted to humans by ticks. Exposure to Borrelia was identified by multiantigenic (19 antigens) serological testing of patients: severe COVID-19 (hospitalized), asymptomatic to mild COVID-19 (home treated or not aware of being infected), and not infected with SARS-CoV-2. Increased levels of Borrelia-specific IgGs strongly correlated with COVID-19 severity and risk of hospitalization. This suggests that a history of tick bites and related infections may contribute to the risks in COVID-19. Though mechanisms of this link is not clear vet, screening for antibodies targeting Borrelia may help accurately assess the odds of hospitalization for SARS-CoV-2 infected patients, supporting efforts for efficient control of COVID-19.

"increased levels of Borrelia-specific IgGs strongly correlated with **COVID-19 severity** and with the risk of hospitalization"

Source: Szewczyk-Dąbrowska A et al. Correlation between COVID-19 severity and previous exposure of patients to Borrelia spp. Sci Rep. 2022 Sep 24;12(1):15944.

# Many luminaries in the field have seen clinical indications

Dr. Richard Horowitz: Has been alluding to this since the start of the Pandemic, many presentations and podcasts

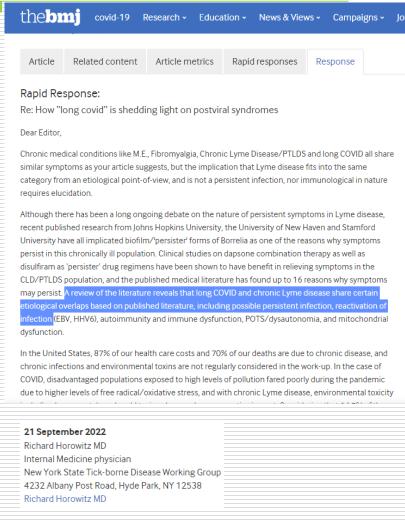
Dr. Joe Burrascano: Yes (numerous statements in interviews)

Dr. Robert Bransfield: A Tale of Two Pandemics <a href="https://aonm.org/webinars/">https://aonm.org/webinars/</a>

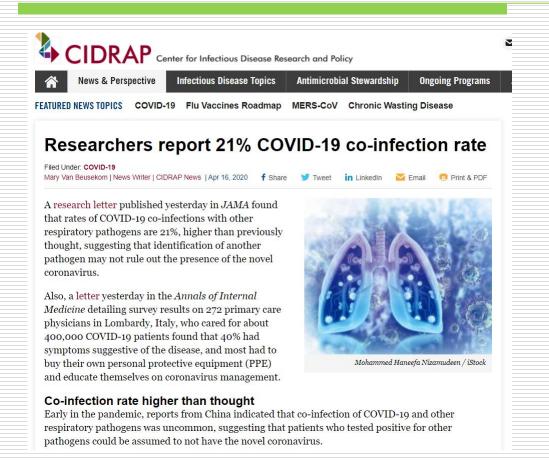
Dr. Joseph Jemsek: Lyme Borreliosis Complex and COVID-19

https://aonm.org/view-past-webinars/

Dr. Daniel Kinderlehrer: has heard of this "most often in association with Bartonella and Mycoplasma, both capable of causing serious autoimmune problems"



## Considerable % of respiratory pathogens in CV-19: Chlamydia/Mycoplasma pneumoniae and others



Some sites tested the specimens for COVID-19 as well as influenza A and B, respiratory syncytial virus (RSV), non-COVID-19 coronaviruses, adenovirus, parainfluenza 1 through 4, human metapneumovirus, rhinovirus/enterovirus, Chlamydia pneumoniae, and Myco plasma pneumoniae.

*Source:* https://www.cidrap.umn.edu/news-perspective/2020/04/researchers-report-21-covid-19-co-infection-rate; https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30494-8/fulltext

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# **NEW: ArminLabs Post-COVID Viral Reactivation Panels: Basic and Advanced**

## arminiabs

PATIENT INFORMATION



ORDERING DR/PRACT

### **Post-COVID Reactivated Infection Panels**

Patient FIRST NAME:		BARCODE		Dr. / Practitioner name:	
Patient SURNAME:		(Lab ı	(Lab use only)		
DATE OF	BIRTH (DD/MM/Y	YYY):			Street Address:
SEX (plea	se circle): nonbina	ry male female	Time of Blood Draw:		Postcode:
Street Ac	ldress:		Date (DD/MM):		County:
Postcode	::	City:	Material/Quantity	☐ CPDA (yellow)	Tel no:
County:		Country:		☐ Serum (orange)	Email:
Tel no:			AONM	HELPLINE:	
Email:			+44 (0) 3	331 210 305	
		Basic	:: Post-COVID V	'iral Reactivatio	n Panel
	EBV EliSpot, t	-cell test, lytic only			CPDA
	CMV EliSpot, t-cell test, lytic only		CPDA		
	VZV IgG/IgM/IgA antibodies		Serum		
	Coxsackie A7	& B1 IgG/IgA antibodi	es		Serum

# Advanced reactivated infection panel includes further viruses, and bacteria

	Advanced: Post-COVID Reactivated Infe	ction Panel
	EBV EliSpot, t-cell test, lytic only	CPDA
	CMV EliSpot, t-cell test, lytic only	CPDA
	VZV IgG/IgM/IgA antibodies	Serum
	Coxsackie A7 & B1 IgG/IgA antibodies	Serum
	HSV 1 & 2 IgG/IgM/IgA antibodies	Serum
	HHV6 EliSpot, t-cell test	CPDA
	Chlamydia pneumoniae IgG/IgA antibodies	Serum
	Mycoplasma pneumoniae IgG/IgA antibodies	Serum

# Electronic checklist helps decide which coinfections to test for in Post-COVID; fills automatically



	Your current and former symptoms Please click on the boxes next to the symptoms that you suffer from	X
1	Stomach ache, gut problems	
2	Anaemia	
3	Diarhoea intermittent, intestinal crampings/pain	
4	Fever or feverish feeling	
5	Lack of concentration, memory loss, forgetfulness	×
6	Encephalitis/Inflammation of the brain	
7	Yellowish colour of the skin/eyes	
8	Painful joints or swollen joints	$\overline{\times}$
9	General aches and pains, tendon problems	
10	Flu-like symptoms	$\overline{\times}$
11	Rash(es), striae, exanthema	
12	Small red/purple spots of the skin	
13	Heart problems, disturbed cardiac rhythm	
14	Cough, expectoration, "air-hunger"	
15	Headache, dizziness	
16	Impaired liver function/ liver laboratory values	
17	Pneumonia, bronchitis	
18	Swollen lymph nodes	$\boxtimes$
19	Enlargement of the spleen	
20	Fatigue / exhaustion, intermittent or chronic CFS	$\times$
21	Muscle pain, muscle weakness	
22	Shivering, chill	
23	Blurred, foggy, cloudy, flickering, double vision	
24	Nausea, vomiting	
25	Dark urine	
26	Itching or pain when urinating	
27	Tingling, numbness, "burning" sensations	
28	Neck pain, neck stiffness	
29	Shoulder pain	

Ranked in order of priority:
CPn, Mycoplasma and the Herpesviruses draw for first place here ↓

Below you'll find the number of the symptoms for each of the infections that we test for and the ranking, in which order you should test for them

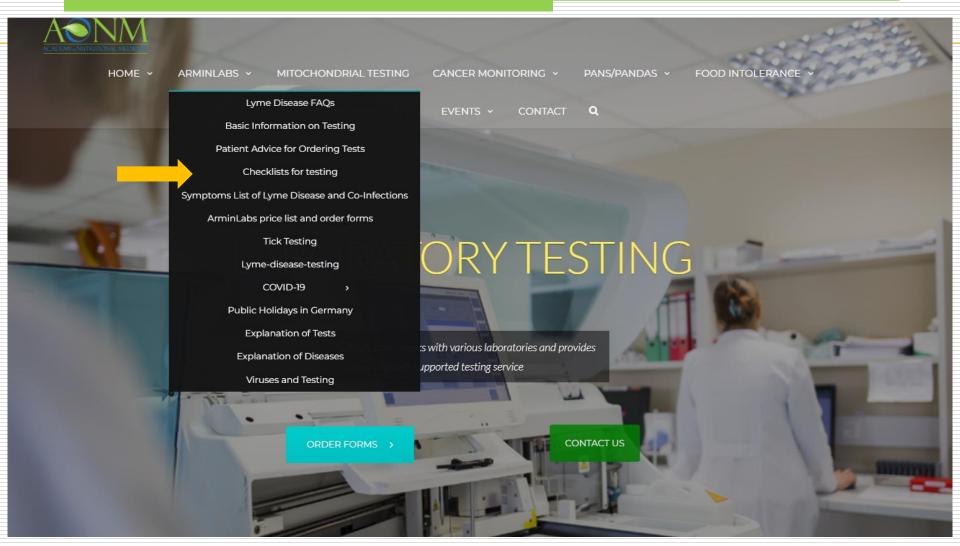
Ranking of the infections	No. of symptoms	Rank
Chlamydia pneumoniae	4	1
Mycoplasma pneumoniae	4	1
Yersinia	2	3
Campylobacter	2	3
HSV 1/2	4	1
EBV	4	1
CMV	4	1
VZV	3	2
HHV 6	4	1
Parvovirus	3	2
Coxsackie-Virus	3	2
Echovirus	2	3

# Visit our stand B3 for the chance to win a voucher on ArminLabs testing



## Where to find the checklists:

## www.aonm.org - ArminLabs tab



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## Seminal "Frontiers" article: S1 protein in Post-COVID patients up to 15 months post infection ...



ORIGINAL RESEARCH published: 10 January 2022 doi: 10.3389/fimmu.2021.746021



## Persistence of SARS CoV-2 S1 Protein in CD16+ Monocytes in Post-Acute Sequelae of COVID-19 (PASC) up to 15 Months Post-Infection

OPEN ACCESS

Bruce K. Patterson 1\*, Edgar B. Francisco 1, Ram Yogendra 2, Emily Long 1, Amruta Pise 1, Hallison Rodrigues<sup>1</sup>, Eric Hall<sup>3</sup>, Monica Herrera<sup>3</sup>, Purvi Parikh<sup>4</sup>, Jose Guevara-Coto<sup>5,6</sup>, Timothy J. Triche<sup>7</sup>, Paul Scott<sup>7</sup>, Saboor Hekmati<sup>7</sup>, Dennis Maglinte<sup>7</sup>, Xaiolan Chang<sup>8</sup>,

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National Institute of Health (ISS), Italy

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#### Specialty section:

This article was submitted to Viral Immunology, a section of the journal Frontiers in Immunology

Rodrigo A. Mora-Rodríguez<sup>5</sup> and Javier Mora<sup>5</sup> <sup>1</sup> Department of Research and Development, IncelIDx Inc, San Carlos, CA, United States, <sup>2</sup> Department of Anesthesia, Lawrence General Hospital, Lawrence, MA, United States, 3 Department of Molecular Diagnostics, Bio-Rad Laboratories, Hercules, CA, United States, 4 Department of Allergy and Immunology, New York University (NYU) Langone Health, New

York, NY, United States, 5 Lab of Tumor Chemosensitivity, Research Center on Tropical Diseases (CIET)/Research Center on Surggery and Cancer (DC) Lab, Faculty of Microbiology, Universidad de Costa Rica, San Jose, Costa Rica, <sup>6</sup> Department of Computer Science and Informatics (ECCI), Universidad de Costa Rica, San Jose, Costa Rica, 7 Department of Molecular Biology, Avrok Laboratories, Inc., Azusa, CA, United States, 8 Vaccine & Gene Therapy Institute and Oregon National Primate Research Center, Oregon Health & Science University, Portland, OR, United States

The recent COVID-19 pandemic is a treatment challenge in the acute infection stage but the recognition of chronic COVID-19 symptoms termed post-acute seguelae SARS-CoV-2 infection (PASC) may affect up to 30% of all infected individuals. The underlying mechanism and source of this distinct immunologic condition three months or more after initial infection remains elusive. Here, we investigated the presence of SARS-CoV-2 S1 protein in 46 individuals. We analyzed T-cell, B-cell, and monocytic subsets in both severe COVID-19 patients and in patients with post-acute sequelae of COVID-19 (PASC). The ferrile of high interest little (OD44) OD40 (Variety or street extension to (OD44)

"This means the body has literally been sprayed with the virus and it spends 15 months, in a sense, trying to clean out the spike protein from our tissues. No wonder people have Long-COVID syndrome."

Board-certified internist and cardiologist Dr. Peter McCullough, https://www.facebook.com/watch/ ?v=1149250505479349, minute 6.18

> Clin Infect Dis. 2023 Feb 8;76(3):e487-e490. doi: 10.1093/cid/ciac722.

Persistent Circulating Severe Acute Respiratory Syndrome Coronavirus 2 Spike Is Associated With Post-acute Coronavirus Disease 2019 Sequelae

Zoe Swank 1 2 3, Yasmeen Senussi 1 2 3, Zachary Manickas-Hill 4, Xu G Yu 1 4 5, Jonathan Z Li 1 5, Galit Alter 4 6, David R Walt 1 2 3

Confirmed a year later, in Feb. 2023 1

Source: Patterson BK et al. Persistence of SARS CoV-2 S1 Protein in CD16+ Monocytes in Post-Acute Sequelae of COVID-19 (PASC) up to 15 Months Post-Infection, Front Immunol, 2022 Jan 10:12:746021.

# ... so it's likely important to counter the spike protein in those suffering Long Covid/post-Covid reinfection

### **Nattokinase**

> Molecules. 2022 Aug 24;27(17):5405. doi: 10.3390/molecules27175405.

Degradative Effect of Nattokinase on Spike Protein of SARS-CoV-2

Takashi Tanikawa <sup>1</sup>, Yuka Kiba <sup>2</sup>, James Yu <sup>3</sup>, Kate Hsu <sup>3</sup>, Shinder Chen <sup>3</sup>, Ayako Ishii <sup>4</sup>, Takami Yokogawa <sup>2</sup>, Ryuichiro Suzuki <sup>5</sup>, Yutaka Inoue <sup>1</sup>, Masashi Kitamura <sup>2</sup>

### **Dandelion extract**

New Results

A Follow this preprint

Common dandelion (*Taraxacum officinale*) efficiently blocks the interaction between ACE2 cell surface receptor and SARS-CoV-2 spike protein D614, mutants D614G, N501Y, K417N and E484K *in vitro* 

Hoai Thi Thu Tran, Nguyen Phan Khoi Le, Michael Gigl, O Corinna Dawid, Evelyn Lamy doi: https://doi.org/10.1101/2021.03.19.435959

### Nigella sativa

See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/341537951

Thymoquinone: shield and sword against SARS-CoV-2

Article in Precision Nanomedicine · May 2020

### Autophagy/Mitophagy

ARTICLE

https://doi.org/10.1038/s41467-021-24007-w

OPEN

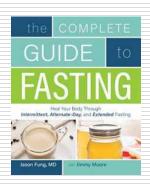
SARS-CoV-2-mediated dysregulation of metabolism and autophagy uncovers host-targeting antivirals

Source: Further sources available

# Supporting autophagy particularly vital because SARS-CoV-2 and reactivated pathogens disable it\*

### **Interventions**

Dietary
Calorie restriction/intermittent fasting



Complete Guide To Fasting: Heal Your Body Through Intermittent, Alternate-Day, and Extended Fasting

**Exercise** 

> Front Physiol. 2019 Aug 22;10:1088. doi: 10.3389/fphys.2019.01088. eCollection 2019.

Regular Endurance Exercise Promotes Fission, Mitophagy, and Oxidative Phosphorylation in Human Skeletal Muscle Independently of Age

Curcumin, Berberine, Quercetin, Sulphurophane

Estelle Balan <sup>1</sup>, Céline Schwalm <sup>1</sup>, Damien Naslain <sup>1</sup>, Henri Nielens <sup>2</sup>, Marc Francaux <sup>1</sup>, Louise Deldicque <sup>1</sup>

### Herbal/nutraceutical













E.g. Urolithin A, Spermidine, Resveratrol (Japanese knotweed),



<sup>\*</sup> References on this and presentation available from info@aonm.org

# Monolaurin and Baicalein with evidenced antibacterial efficacy

## **Monolaurin**

An organic compound derived from lauric acid.

Found in coconut oil (highest natural source), and breast milk.

A bioactive lipid with proven antimicrobial properties.

"Monolaurin is a bioactive lipid from medium-chain fatty acids that have been proven safe for consumption, has a broad spectrum as an antibacterial, boosts the immune system, and acts as an antiviral."

"The most effective antimicrobial compounds against all morphological forms of the two tested Borrelia sp. were baicalein and **monolaurin**. This might indicate that the presence of fatty acid and phenyl groups is important for comprehensive antibacterial activity."<sup>2</sup>

Food Research 4 (6): 2355 - 2365 (December 2020)

Journal homepage: http://www.myfoodresearch.com



## Bioactive monolaurin as an antimicrobial and its potential to improve the immune system and against COVID-19: a review

\*Subroto, E. and Indiarto, R.

Department of Food Industrial Technology, Faculty of Agro-Industrial Technology, Universitas Padjadjaran, Jl.Raya Bandung-Sumedang Km. 21, Jatinangor, Sumedang 40600, Indonesia

#### Article history:

Received: 3 July 2020 Received in revised form: 2 August 2020 Accepted: 2 September 2020 Available Online: 8 November 2020

#### Keywords:

Monolaurin, Antimicrobial, Immune system, Antiviral, COVID-19

#### DOI:

https://doi.org/10.26656/fr.2017.4(6).324

#### Abstract

Monolaurin is monoacylglycerol which is a bioactive lipid since it can affect the human biological systems. This review discusses the bioactive properties of monolaurin, especially its role as an antibacterial, immune system enhancement, and its ability as an antiviral so that it has the potential to fight against various viral attacks. Monolaurin can act as an antibacterial in inhibiting the growth of several pathogenic bacteria, especially gram-positive bacteria. Monolaurin is known to be able to enhance the immune system through modulation of various immune systems, controlling pro-inflammatory cytokines, activating and attracting leukocytes to the site of infection. Monolaurin can also act as an antiviral, especially against enveloped viruses, such as Maedi-visna virus, vesicular stomatitis, herpes simplex-1, measles, HIV, cytomegalovirus, influenza, and corona. Monolaurin inhibits the virus through the mechanism of the disintegration of the viral membrane, prevents binding of the viral protein to the host-cell membrane, inhibits the process of assembling the viral RNA, and the process of virus maturation in the replication cycle. Therefore monolaurin has the potential for human consumption to boost the immune system and ward off various virus attacks, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the cause of COVID-19 which became a pandemic in the world.



Sources: 1. Subroto, Edy & Indiarto, Rossi. (2020). Bioactive monolaurin as an antimicrobial and its potential to improve the immune system and against COVID-19: a review. Food Research. 4. 2355-2365. 10.26656/fr.2017.4(6).324;; 2. Goc, A., Niedzwiecki, A. and Rath, M. (2015), In vitro evaluation of antibacterial activity of phytochemicals and micronutrients against Borrelia burgdorferi and Borrelia garinii. J Appl Microbiol, 119: 1561–1572. doi:10.1111/jam.12970

# Many phytonutrients with action against the pleomorphic form of Borrelia, the "round body" or cyst form

Chlorella pyrenoidosa, Stinging Nettle extract, Bilberry extract, Cranberry extract, Lingonberry fruit powder, Artichoke extract, Sage leaf extract, Wild garlic, Cistus incanus



















A review of the literature reveals that long COVID and chronic Lyme disease share certain etiological overlaps based on published literature, including possible persistent infection, reactivation of infection









www.elsevier.com/locate/micir

Original article

Pleomorphic forms of *Borrelia burgdorferi* induce distinct immune responses

Leena Meriläinen a,\*, Heini Brander a, Anni Herranen a, Armin Schwarzbach b, Leona Gilbert a

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Received 12 July 2015; accepted 8 April 2016 Available online 30 April 2016

# For reactivated viral infections (1/2)

Herpes, especially Epstein Barr, Cytomegalovirus, Varicella Zoster virus

**Liquorice:** Its component glycyrrhizin is particularly responsible for its antiviral activity; "novel way to interrupt latency" of EBV<sup>1</sup>

Andrographis paniculata: Andrographolide, the active extract from plants of the Andrographis genus, has broad-spectrum antiviral properties: "miraculous compound to restrain virus replication and virus-induced pathogenesis ... shown to inhibit transcription of EBV IE genes and the production of EBV virions"<sup>2</sup>

Scullcap/Baicalein: Noted antiviral properties, also against Coxsackie<sup>3</sup>



Dandelion: Blocks the interaction between ACE2 cell surface receptor and SARS-CoV-2 spike protein4

Artemisia annua: "Artemisia annua L. extracts inhibit the *in vitro* replication of SARS-CoV-2 and two of its variants." "... the bioactivity of artemisinin and its semisynthetic derivative artesunate is even broader and includes the inhibition of certain viruses, such as human cytomegalovirus and other members of the *Herpesviridae* family (e.g., herpes simplex virus type 1 and Epstein-Barr virus)" 6



Artemisia annua

Sources: 1. https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC1052015/; 2. Gupta S et al. Broad-spectrum antiviral properties of andrographolide.

Arch Virol. 2017 Mar;162(3):611-623; 2. Andrei G et al. Novel Therapeutics for Epstein Barr Virus. Molecules. 2019 Mar 12;24(5):997; Lin, TP et al. Inhibition of the Epstein Barr virus lytic cycle by andrographolide. Biol. Pharm. Bull. 2008, 31, 2018–2023; 3. Fu Q, Gao L, Fu X, Meng Q, Lu Z. Scutellaria baicalensis Inhibits Coxsackievirus B3-Induced Myocarditis Via AKT and p38 Pathways. J Microbiol Biotechnol. 2019 Aug 28; 4. https://www.biorxiv.org/content/10.1101/2021.03.19.435959v1.article-info;
5. https://www.sciencedirect.com/science/article/pii/S0378874121002439; 6. https://academic.oup.com/cid/article/47/6/804/325924.

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# For the reactivated infections (2/2)

Herbal and nutraceutical remedies contd.

Nigella sativa (Black Seed oil): Black Seed oil from Nigella sativa seeds has been found to act against seasonal allergic rhinitis, avian influenza and cytomegalovirus.<sup>1, 2</sup>. It has virucidal activity against herpes simplex<sup>3</sup>



Quercetin and zinc: Quercetin acts as an ionophore and carries the zinc deep into the cell<sup>4</sup>

**Curcumin:** Antiviral and immunomodulatory<sup>5,</sup> "improves mitochondrial dynamics

regarding mitochondrial biogenesis and mitophagy"6



Cistus incanus tea – demonstrated antiviral action on several viruses, including SARS-CoV-27



The amino acid L-Lysine appears to apply universally across the entire family of herpes viruses<sup>8</sup>

### Support for immunity/natural killer cell activity:

Glutathione – liposomal; N-Acetyl Cysteine: precursor to GSH, mucolytic and perturbs SARS-CoV-2 spike protein conformation<sup>9</sup>; releases histamine however<sup>10</sup>, beware with MCAS

### **Enzymatically modified rice bran**

Sources: 1, https://pubmed.ncbi.nlm.nih.gov/23855426/; 2, https://pharmacologyonline.silae.it/files/newsletter/2019/vol2/ PhOL 2019 2 NL007 Molla.pdf; 3, https://www.sciencedirect.com/science/article/abs/pii/S0192056100000369?via%3Dihub; 4. https://journals.plos.org/ plospathogens/article?id=10.1371/journal.ppat.1001176; 5. https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7899028/; 6. de Oliveira MR et al. Curcumin, mitochondrial biogenesis, and mitophagy: Exploring recent data and indicating future needs. Biotechnol Adv. 2016;34(5):813-826; Ungvari, Z et al. (2011). 7. https://www.sciencepublishinggroup.com/journal/paperinfo?journalid =320&doi=10.11648/ i.jdmp.20210703.13; 8. https://www.research.gate.net/publication/344210822 Lysine Therapy for SARS-CoV-2; 9 https://chemrxiv.org/engage/apigateway/chemrxiv/assets/ orp/resource/item/60c753ec4c89190f3bad43ca/original/n-acetyl-cysteine-a-tool-to-perturb-sars-co-y-2-spike-protein-conformation.pdf; 10. https://pubmed.ncbi.nlm.nih.gov/ 2409763/; All images from Wikipedia, free to use on Commons License
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# Many of these ingredients available in the PhytoBox range





#### PhytoBox NO. 01

Support for Borrelia and intracellular infective pathogens

INGREDIENTS (4 CAPSULES):	DAILY DOSAGE	%RQ*
Monolaurine	900 mg	
Baikal skullcap extract	1000 mg	

#### PHYTOBOX NO. 02

Support for neuroborreliosis and neuropathic dysfunctions

INGREDIENTS (2 CAPSULES):	DAILY DOSAGE	%RQ
Andro graphis panicula ta extract	4:1 400 mg	
Uncaria rhyunchophylla	320 mg	
Thereof Ginsenosides	256 mg	
	168,4 mg	
Thereof trans-Resveratrol	159,8 mg	
Grape fruit seed extract	60 mg	
Thereof Bioflavonoids		

#### PHYTOBOX NO. 03

Breakdown of pleomorphic forms and support of detoxification & purification

INGREDIENTS (4 CAPSULES):	DAILY DOSAGE	%RQ*
Chlore La pyrenoidosa	800 mg	
Stinging Nettle extract 10:1	160 mg	
Bilberry extract	160 mg	
Thereof Anthocyanidins	40 mg	
Cranberry extract	160 mg	
Thereof Polyphenols	40 mg	
Lingonberry fruit powder	160 mg	
Artichoke extract 121	160 mg	
Thereof Cynarin	4 mg	
Sage leaf extract 4:1	100 mg	
Wild garlic herb extract 4:1	50 mg	
Cistus incanus	50 mg	

\*RQ = Reference quantity for daily intake

#### PHYTOBOX NO. 04

	am ma	

INGREDIENTS (4 CAPSULES):	DAILY DOSAGE	%R0
OPC Grape seed extract	200 mg	
Thereof Polyphenols	190 mg	
Thereof OPC	100 mg	
Curcuma Extract	200 mg	
Thereof Curcuminoids		
Thereof Curcumin	140 mg	
Rutin Powder	189,4 mg	
Thereof Rutin		
Polygonum cuspidatum	147,4 mg	
Thereof trans-Decuerated	160 mg	

#### PHYTOBOX NO. 05

Synbiotic with prebiotic

INGREDIENTS (4 CAPSULES):	DAILY DOSAGE	%RQ*
Acacia fibre	1.400 mg	
thereof dietary fibre	1260 mg	
Bacterial cultures	ca. 1,2* 10^10 CFUs**	
Biotin	50 µg	100
Nia cin	16 mg	100
Riboflavin	1,4 mg	100

#### \*\*CFUs = colony forming units

PHYTOBOX NO. 06

DAILY DOSAGE	%R0
10 mg	100
240 mg	
120 mg	
17 mg	
100 mg	
3 mg	
100 mg	
40 mg	
80 mg	
1,6 mg	
	DAILY DOSAGE 10 mg

For chronic opportunistic virus infections, especially the herpes viruses

#### PHYTOBOX NO. 07

Support in cytokine storms

INGREDIENTS (4 CAPSULES):	DAILY DOSAGE	%RQ*	
Licorice root extract	880mg		
thereof glycyrrhizin	26mg		
Shiitake extract	650mg		
Black cumin extract	600mg		
Astaxanthin	4mg		

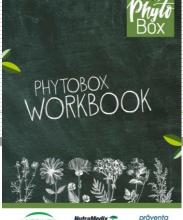
#### PHYTOBOX NO. 08

Support in Bartonella infection

INGREDIENTS (2 CAPSULES):	DAILY DOSAGE	%
Houttuynia cordata extract 4:1	150 mg	
Oregano extract		
thereof rosmatinic acid	1,8 mg	
Fenugreek seed 8:1 extract	75 mg	
thereof sa ponins	15 mg	
Cinnamon extract 10:1	50 mg	
Liquorice root		
Willow bark dry extract	25 mg	
thereof Salicin		
Cistus incanus extract		
thereof polyphenols		
Grapefruit seed extract	25 mg	
thereof flavonoids		
Cloves 4:1 extract		
thereof flavonoids		
Uncaria rhyncho phylla 10:1 extract		
thereof indole alkaloids		
Garlic 15:1 extract		
thereof alliin	0,9 mg	

\*RQ = Reference quantity for daily intake





prāventa

### PHYTOBOX NO. 09

Support in Chlamydia Pneumoniae infection

INGREDIENTS (3 CAPSULES):	DAILY DOSAGE	%RQ*
Vitamin C	200 mg	250
Nasturtium extract	500 mg	
Horsera dish root extract	500 mg	
Chinese Lime Tree Extract	300 mg	
White mustard extract	120 mg	
of which Sinalbin	7,2 mg	
Barberry extract	85 mg	

#### PHYTOBOX NO. 10

NK Cell support

INGREDIENTS (4 CAPSULES):	DAILY DOSAGE	%RQ
Vitamin C	40 mg	50
Reishi Extract	600 mg	
Shiitake extract	600 mg	
Spirulina Powder	350 mg	
Cordyceps Extract	300 mg	
Maitake extract	300 mg	
Ginseng root extract	35 mg	
thereof ainsenosides	2.8 ma	

#### PHYTOBOX NO. 11

Support in Coxsackie and Echoviruses infections

INGREDIENTS (3 CAPSULES):	DAILY DOSAGE	%RQ*
Elderflower extract	500 mg	
thereof Rutin		
Rho diola rosea extract		
thereof Salidrosides	7,5 mg	
Astragalus membranaceus root extract	250 mg	
Oregano extract	180 mg	
thereof Rosmarinic acid	3,6 mg	
Barberry extract		
Mint, Tibetan		
Ginkgo biloba	80 mg	
thereof Flavone glycosides		
thereof ginkgolides	4,8 mg	
St. John's Wort extract	50 mg	
thereof Hypericin	0,15 mg	

Source: https://shop.aonm.org/

# Discounts off the PhytoBox range with Code IPM20 – go to <a href="https://shop.aonm.org/">https://shop.aonm.org/</a>, or ask at Stand B3



## Webinars with further information available at https://aonm.org/view-past-webinars/

## Scientific evidence to support the use of phytochemicals for Lyme Borreliosis

Dr. Leona Gilbert, PhD, **Docent of Cell and Molecular** Biology CEO Te?ted Ov leona.gilbert@tezted.com copyright protected

@tez\_ted #notjustlyme

**Prepared for AONM** 16 May 2023



AONM Webinar with Prof. Leona Gilbert and Markus Berger (ArminLabs)

Academy of Nutritional Medicine -... 2.33K subscribers









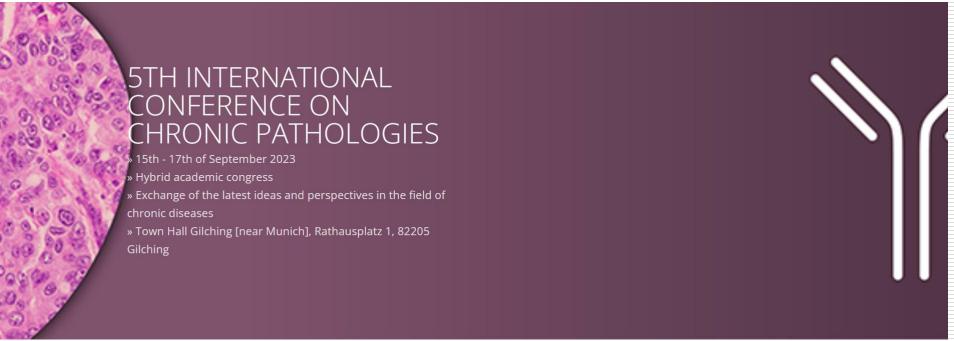




https://www.youtube.com/watch?v=cpDIq9eu5mI

# 5TH INTERNATIONAL CONFERENCE ON CHRONIC PATHOLOGIES: <a href="www.chronic-pathologies.com">www.chronic-pathologies.com</a>

- » 15th 17th of September 2023
- » Hybrid academic congress
- » Exchange of the latest ideas and perspectives in the field of chronic diseases
- » Town Hall Gilching [near Munich], Rathausplatz 1, 82205 Gilching



# Thank you very much! Q&A/Discussion

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Medical Doctor and Specialist for Laboratory Medicine

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