



The Solve CHRONICLE

Research 1st Roundup

SUMMER 2025

From Biomarkers to Breakthroughs: This Quarter’s Top Research on ME/CFS, Long Covid, and More

In our comeback edition of the Research 1st Roundup (now part of *The Chronicle*), we highlight noteworthy research studies from the last quarter.

These studies include ones from the most prestigious journals in the world (*JAMA*, *Science*). Important themes from this quarter include new biomarkers for diseases like Long Covid, fibromyalgia, and ME/CFS; new ideas for treatments; and how these diseases damage lung tissues (and drugs to reverse this

damage). For more easy-to-read summaries of recent significant studies related to ME/CFS, Long Covid, and other associated conditions, visit the [Solve Science Spotlight](#) page on our website.

Identifying Soluble Biomarkers That Associate with Distinct Manifestations of Long Covid

Immunologists [Dr. David Price](#) (Cardiff University School of Medicine, United Kingdom) and [Dr. Marcus Buggert](#) (Karolinska Institute, Sweden) recently reported new biomarkers that correlate with for Long Covid symptoms. Their team compared immune cells and blood-plasma proteins from people with Long Covid with those from people recovering from SARS-CoV-2 infection with no ongoing symptoms (healthy participants). In general, the immune cells from people with Long Covid behaved like those from healthy people. However, immune cells from people with Long Covid seemed to have been more exposed to SARS-CoV-2 antigens over time than were cells from healthy people. And antibodies from people with Long Covid were less effective at neutralizing SARS-CoV-2 virus.

Importantly, the team found a unique protein signature in people with Long Covid who experienced breathlessness, one of the most prominent symptoms in the cohort. Further analyses of this protein signature (which included proteins regulating cell death, inflammation, and platelet activation) suggested people with Long Covid can lose breath because their lungs get damaged by inflamed blood vessels and too much blood clotting. Overall, this study is important because it reveals biomarkers of Long Covid-associated breathlessness and suggests that reducing damage to lung tissue can improve breathing for these people. This [study appears in the journal *Nature Immunology*](#).

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How COVID and Long Covid Damage Lung Tissues, and a Drug to Reverse This Damage

[Dr. Jie Sun](#) is the associate director of the University of Virginia Carter Center for Immunology Research. His team recently discovered a key mechanism by which COVID and Long Covid damage lung tissues. The team compared lung tissues of healthy participants, people with severe COVID, and people with Long Covid (as well as lung tissues from mice infected with SARS-CoV-2 or influenza).

They found that high interferon levels in people with COVID or Long Covid (as part of their bodies' inflammatory response) impaired peroxisomes in lung-tissue macrophages. Macrophages are important for resolving lung inflammation and repairing lung tissues; and peroxisomes are organelles that metabolize lipids, neutralize dangerous oxidants, and support mitochondrial health. With impaired peroxisomes, the lung macrophages became dysregulated. They couldn't

properly resolve inflammation nor adequately repair virus-damaged lung tissues. They also became hyperactive and released too much interleukin-1 β , which stunted development of epithelial cells (also needed to repair lung tissues).

Because SARS-CoV-2 can disrupt brain-cell peroxisomes too, this mechanism may also account for neurological symptoms of COVID and Long Covid. And peroxisome dysfunction in macrophages may also drive acute and chronic respiratory symptoms induced by other viruses, like flaviviruses, HIV, and influenza. Performing experiments with mice, the team found that sodium 4-phenylbutyrate (an [FDA-approved drug](#) that boosts peroxisome functions) reversed problems with lung macrophage and epithelial cells; helped repair lung tissues; and reduced symptoms of both COVID and Long Covid. This [study appears in the journal Science](#).

A Genetic Risk Score for ME/CFS

Dr. [Michael Snyder](#), a renowned professor of genetics at Stanford University, has posted a [preprint](#) of what promises to be an important study on genetic factors important for ME/CFS. Sequencing the genomes of over 1,000 people (about half with ME/CFS and half without), his team found 115 genes for which mutations predict ME/CFS risk. A significant fraction of these genes produce proteins important for regulating brain signals or for degrading unwanted proteins. Many of these genes are also important for serious neurological disorders—depression, attention deficit hyperactivity disorder, and autistic spectrum disorder. And many of these genes also predict risk for COVID-19 and relate

to Long Covid symptoms, consistent with the fact that symptoms of ME/CFS are like symptoms of Long Covid.

This work is important because it describes a risk score for diagnosing people with ME/CFS. Also, the identified genetic factors show which cellular and physiological mechanisms are dysregulated by ME/CFS, suggesting targets for future treatments. For example, proteasome modulators (drugs that regulate how cells degrade unwanted proteins) and drugs for treating people with certain neurological conditions may be especially effective for reducing ME/CFS symptoms.



New! Solve M.E.'s Guide to Current Clinical Trials

Are you interested in learning more about current clinical trials for ME/CFS, Long Covid, and associated conditions? We've launched a new webpage listing US-based clinical trials that are recruiting or soon-to-be recruiting for the following diseases and conditions:

- Dysautonomia
- Ehlers-Danlos syndrome
- Fibromyalgia
- Gulf War Illness
- Guillain-Barré syndrome
- Long Covid
- Long Lyme
- ME/CFS
- Mitochondrial disease
- PANS: Pediatric Acute-onset Neuropsychiatric Syndrome
- PANDAS: Pediatric Autoimmune Neuropsychiatric Disorder

Click [here](#) or use the QR code to visit our new guide to clinical trials.





Endogenous Retrovirus Activation in ME/CFS, Fibromyalgia, and a Newly Discovered, Related Disease

[Dr. Elisa Oltra](#), professor at the Catholic University of Valencia San Vicente Mártir (Spain), published a study comparing how human endogenous retroviruses are activated in blood cells of healthy people or people diagnosed with ME/CFS, fibromyalgia, or both ME/CFS and fibromyalgia. Endogenous retroviruses descend from viruses that entered the genomes of human ancestors (usually millions of years ago). These endogenous retroviruses now make up ~8% of the human genome. Most endogenous retroviruses have mutated such that they can no longer replicate; however, over time they became critical for regulating other genes. Endogenous retroviruses are improperly activated in many diseases, including ME/CFS, fibromyalgia, Long Covid, and COVID.

To compare endogenous retroviruses activation among the study groups, the research team examined and diagnosed participants as having ME/CFS, having fibromyalgia, having both diseases, or having neither. Remarkably, they found endogenous retrovirus expression in participants' blood cells perfectly correlated with diagnoses and significantly correlated with severity of ME/CFS symptoms (especially fatigue and motivation). The dysregulated endogenous retroviruses may promote these diseases by affecting inflammation- and immune response-related genes. Astonishingly, patterns of endogenous retrovirus activation suggested that women diagnosed with both ME/CFS and fibromyalgia may in fact have neither disease, but a different disease altogether (distinct from both ME/CFS and fibromyalgia). This study appears in [eLife](#).

Updating the Long Covid Research Index – Results from the RECOVER-Adult Study

[Dr. Leora Horwitz](#), professor of population health and medicine at New York University Langone Health, recently led a RECOVER-Adult effort to update the Long Covid research index, which is used to classify Long Covid symptoms and subtypes. This index must be continually updated because we learn more about Long Covid each year; because symptoms of the disease can change over time; because new strains in the virus and new treatment options can affect symptoms; and because patient communities continually provide valuable feedback.

The 2024 index includes data from another ~4,000 adults (on top of the ~10,000 in the 2023 index). Unlike the 2023 index, the 2024 index does not consider broad categories of gastrointestinal symptoms or abnormal movements to be Long Covid symptoms; but it does include the more specific symptoms

of shortness of breath and snoring (or sleep apnea). Other symptoms in the new index are brain fog, changes in smell or taste, chest pain, chronic cough, dizziness, fatigue, palpitations, post-exertional malaise, and thirst. Also, the 2024 index distinguishes five main subtypes of Long Covid symptoms: subtype 1 (in which symptoms of fatigue and post-exertional malaise were prominent); subtype 2 (chronic cough); subtype 3 (brain fog); subtype 4 (palpitations); and subtype 5 (dizziness, gastrointestinal symptoms, and post-exertional soreness). People with Long Covid subtype 5 have the highest burden of symptoms, the worst health, and the worst qualities of life. This subtype has higher proportions of Hispanics, multiracial participants, unvaccinated participants, and people infected by SARS-CoV-2 before the Omicron variant. The study appears in the [Journal of the American Medical Association](#).



A Simple Hearing Test to Measure Cognitive Decline in People with Long Covid

A research team led by [Dr. Christopher Niemczak](#), professor of medicine at the Dartmouth School of Medicine, published a study to determine whether Long Covid-related cognitive fatigue relates to the auditory brainstem response, as measured by the [auditory brainstem response test](#). For this test, participants wear sensors on different parts of their heads while listening to sounds through headphones. The sensors record how their brains respond to the sounds, revealing problems in distinct brain regions or in the inner ear. The researchers found that people with Long Covid not only had more anxiety, cognitive fatigue, and depression, but also more hearing problems (abnormal auditory brainstem responses,

more perceived hearing loss, and more common tinnitus). In particular, younger adults with Long Covid had significant problems with central auditory processing, suggesting their central auditory-related brain functions had rapidly aged to the point that their auditory test results and cognitive fatigue levels were like those of older adults. People with Long Covid often have cognitive fatigue, and cognitive fatigue is difficult to objectively measure; thus, this study is important by showing how we can use this auditory test to measure cognitive fatigue-related neurological problems among people with Long Covid. This study appears in [Scientific Reports](#).

Chronic Inflammation Raises IL-6 to Drive Neurobehavioral Symptoms via Dopamine Disruption

Dr. [Adam Kepecs](#) and Dr. [Marco Pignatelli](#), professors of neuroscience at the Washington University of St. Louis School of Medicine, recently discovered a mechanism by which chronic inflammation causes [cachexia](#)—a wasting syndrome characterized by severe weight loss, apathy, depression, chronic fatigue, energy imbalance, and poor motivation.

Studying cancer (a chronic inflammation-associated disease), the researchers found that implanted cancer cells significantly increased IL-6 cytokine levels in mice. The inflammatory cytokine crossed the blood-brain barrier and activated a brain signaling pathway to lower dopamine production by the nucleus accumbens (important for feeling motivation and pleasure). As IL-6 levels rose and dopamine levels dropped, the cachexia symptoms worsened. The researchers could alleviate cachexia symptoms by blocking IL-6 (with anti-IL-6 antibodies), by boosting dopamine (with a dopamine stimulant), or by modulating the affected brain signaling pathway.

Although the team studied these effects in cancer, this mechanism may also happen in other chronic inflammation-related diseases, like ME/CFS, which share symptoms of apathy, depression, fatigue, and poor motivation. Thus, drugs that reduce IL-6 or boost dopamine may reduce neurobehavioral symptoms for people with other IL-6-associated inflammatory conditions. The FDA has approved anti-IL-6 and anti-IL-6 receptor antibodies (e.g., tocilizumab) for treating people with rheumatoid arthritis, cytokine release syndrome, and COVID-19; these therapies could be tested for reducing cachexia-related symptoms in people with ME/CFS, many of whom have high levels of IL-6. This study appears in [Science](#).



Clinical Trial Spotlight: The ADDRESS-LC Trial

The [NE3107 in Adults With Neurological Symptoms of Long COVID trial \(ADDRESS-LC, headed by BioVie, LLC\)](#) will assess the potential impact of bezis-
terim on cognitive impairment/brain fog and fatigue in individuals with Long
Covid. BioVie is recruiting people aged 18–64 diagnosed with Long Covid.

In an upcoming webinar hosted by Solve M.E. President and CEO Emily Tay-
lor, panelists Michael Peluso, MD (Assistant Professor of Medicine, University
of California, San Francisco), Ezra Spier (Creator, Long Covid Studies), and
Penelope Markham, PhD (Senior Vice President, BioVie) will share how the lived
experience of patients has guided the development and conduct of the trial and
the importance of patient-researcher collaboration. Attendees will learn more
about the requirements for participation and how to join the trial.



For more info on the
ADDRESS-LC trial, scan the
QR code or click [this link](#).

Register for Solve's ADDRESS-LC Trial Webinar

Webinar Date: Tuesday, July 22, 2025 | Webinar Time: 3 pm PT / 6 pm ET
Register for the ADDRESS-LC webinar [here](#).



Support Solve’s Groundbreaking Research Projects

From our [Ramsay Research Grant Program](#) to our new [ME/CFS Catalyst Awards](#), Solve has a long history of funding innovative research projects in pursuit of treatments and cures for ME/CFS and associated conditions.



Solve ME/CFS Catalyst Awards: The Catalyst Award program delivers rapid-response funding to protect and accelerate critical scientific projects. By providing targeted support, it ensures high-impact studies reach completion, publication, or the next phase faster – sustaining momentum and advancing discovery even in challenging times.



Ramsay Research Grants: Solve’s signature research grant program awards seed funding to key early career researchers and successfully demonstrates a 34x ROI.



Solve Together: Our real-world data platform gives users the tools to create reports for their doctors, sync health-tracking wearables, and discern their own distinct symptoms and health trends while also connecting researchers with people who want to participate in clinical research studies.

unhide®/Solve Together: We’re excited to announce a partnership with the Brain Inflammation Collaborative. Patients can still enroll in Solve Together and can download the MyDataHelps app to enter and view their data. The Solve Together functionality that you know and love will remain – and no further action will be needed for current participants.



unhide® and Solve Together as a unified platform will launch later this year. This will allow us to build upon and enhance our platform to include Spanish, children and teens, mental health symptom tracking, and an expanded list of diagnoses. Sign up for our newsletter to be notified when open enrollment begins for new participants looking to be included in the enhanced platform. Existing participants will automatically see the enhanced options and features and will not need to enroll again.

If you’d like to support our research efforts, consider making a gift to Solve today.



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