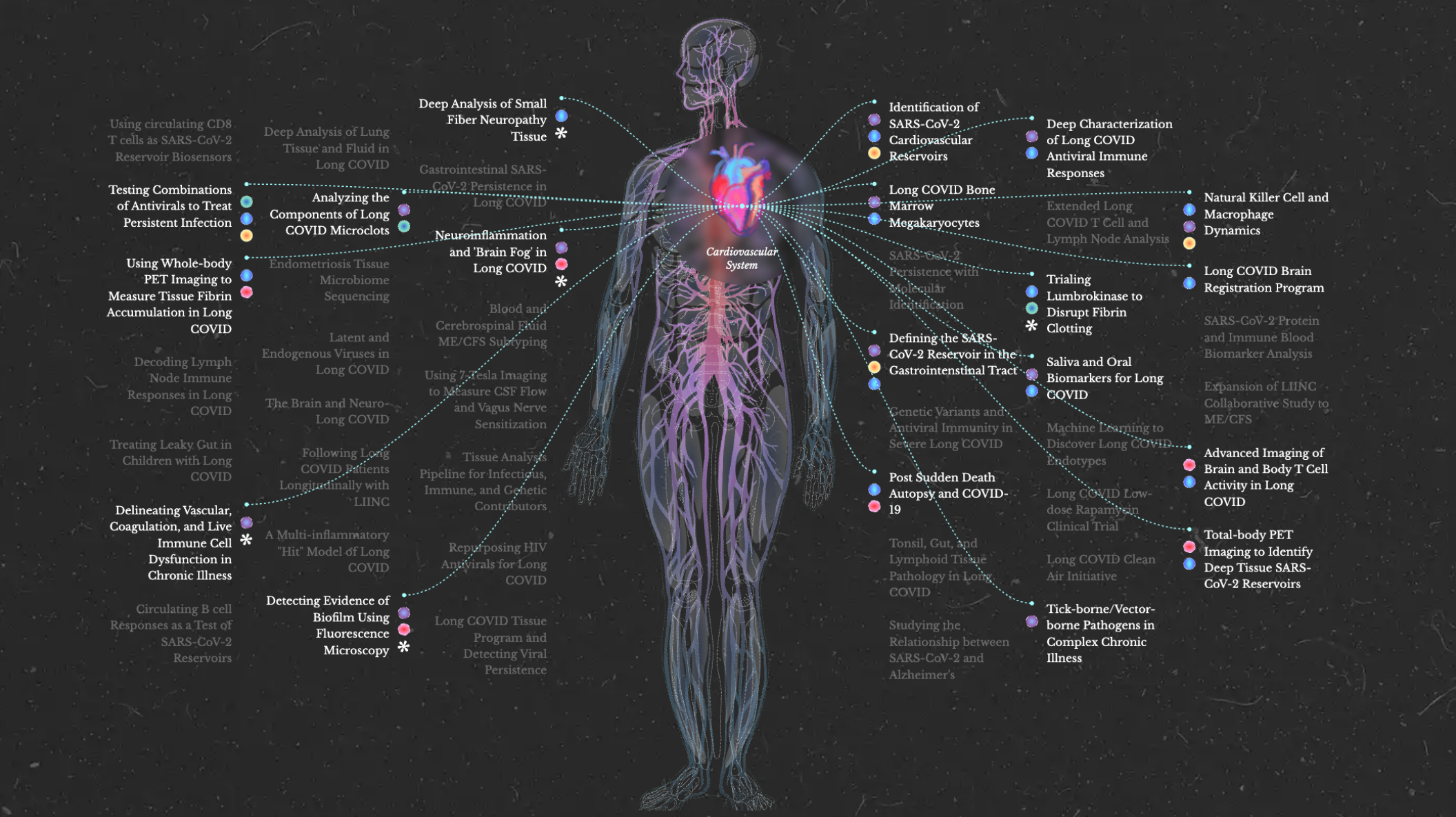

IMPACT REPORT

Science In Action.

2025

POLYBIO

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AMY PROAL, PHD
PRESIDENT/CEO POLYBIO
RESEARCH FOUNDATION

MICHAEL VANELZAKKER, PHD
CO-FOUNDER POLYBIO
RESEARCH FOUNDATION

LETTER FROM OUR FOUNDERS

Since our inception in 2018, PolyBio has transformed how science approaches infectious contributions to chronic disease. We've done this by bringing together leading experts from HIV, cancer, and other fields to collectively tackle Long COVID and related chronic conditions. These teams use the most cutting-edge virology, imaging, and diagnostic test platforms, allowing us to rapidly innovate research on Long COVID disease mechanisms.

At the heart of this effort is the Long COVID Research Consortium (LCRC), a global collaboration of scientists PolyBio created to pursue "high risk, high reward" research. LCRC documents SARS-CoV-2 tissue persistence and other drivers of Long COVID, focusing on root cause drivers of disease as opposed to symptom management and palliation.

During a period when NIH's Long COVID program stalled, LCRC innovated rapidly, leveraging more than $42 million to build and fund over 54 Long COVID research projects.

Together, we've achieved many world firsts: for example, the first Long COVID Tissue Bank, the first study of SARS-CoV-2 persistence and microbiome activity in Long COVID lung tissue, and the first imaging study measuring fibrin accumulation across the bodies and brains of Long COVID patients. Key studies are also documenting if *Borrelia* (the Lyme pathogen) or other organisms carried by ticks can reactivate in patients with Long COVID.

We have helped to conceptualize and fund six Long COVID clinical trials of immunotherapies, antivirals, and other targeted therapies. In parallel we have built strong collaborations with industry partners, including Invivyd and ImmunityBio, to set the stage for yet other important treatment trials in the space. To maximize engagement on a global stage we wrote an op-ed for LA Times emphasizing the urgent need for more Long COVID clinical trials.

The ripple effects of this work extend far beyond Long COVID. Insights from LCRC are now informing projects on chronic tick-borne/vector-borne illness, ME/CFS, and infectious drivers of endometriosis, Alzheimer's disease, neuropsychiatric illness, and even human aging. This includes support of a program innovating diagnostic methods to identify the tick-borne parasite *Babesia*, and publication of a seminal paper that identified distinct ME/CFS subgroups, marking a step toward precision medicine for patients diagnosed with the condition.

Importantly, data from our research and trials is shared directly with the community. Every six months we hold an online Symposium where our scientists give updates on their research projects - ensuring that patients impacted by Long COVID and related chronic disease can participate in the discovery process.

Now, as we approach 2026, we stand at an inflection point. Long COVID is not a mystery. Our work has uncovered key drivers of the disease, including neuroinflammation and persistence of the SARS-CoV-2 virus in tissue. However, despite this knowledge, no validated diagnostic tests exist that can measure key Long COVID biomarkers in an average medical clinic.

To fill that gap we've created the Long COVID Cure Initiative: a program to fast-track new Long COVID treatments. The first step in the Initiative is VIPER: a program designed to zero in on the top diagnostic tests to diagnose SARS-CoV-2 persistence in Long COVID. Findings will additionally set the stage for validation of diagnostic tests for blood vessel, immune, mitochondrial, and related biomarkers in patients with the disease. We will use the validated diagnostic tests to determine which therapeutics will lead to effective treatment for tens of millions of Long COVID sufferers around the globe.

Diagnostic technologies validated by the Initiative are positioned to expand beyond Long COVID into Lyme, Epstein-Barr Virus, and other infections that drive chronic disease, multiplying our impact.

As we move into 2026, our momentum has never been stronger. With your partnership, we will continue to accelerate collaboration, research, and innovation, bringing us closer to a world where Long COVID and related conditions can be successfully diagnosed and treated.

With thanks,

Amy & Mike

POLYBIO

PolyBio advances research on how viral, bacterial, and parasite infections drive chronic disease and aging. We build collaborative projects that identify, diagnose, and treat root causes of infection-associated chronic illness. Focus areas include Long COVID, chronic tick-borne illness, ME/CFS, Alzheimer's, neuropsychiatric illnesses, and endometriosis – conditions that impact the health and lives of hundreds of millions of people around the world.

SINCE 2021, POLYBIO HAS:

RAISED $42 MILLION
from private donors and foundations

Founded the Long Covid Research Consortium, bringing together top researchers from **25+ INSTITUTIONS** to disrupt bureaucracy and speed discovery

COORDINATED 5 POLYBIO POSITION PAPERS
published in *Nature Immunology*, *Immunometabolism*, *Lancet Infectious Diseases*, *Frontiers in Microbiology*, *Ageing Research Reviews*

54+ RESEARCH PROJECTS FUNDED

31 AND COUNTING SCIENTIFIC PAPERS

>2730 CITATIONS

350 COLLABORATIVE CO-AUTHORS

HOW WE **WORK**

In a field where siloed science has stalled progress, PolyBio connects the right people and data across disciplines to fast-track diagnostics, treatments, and ultimately cures. We're not just advancing research, we're transforming it by:

DEFINING THE RESEARCH AGENDA
Our team publishes strategic papers in top journals to chart treatment and diagnostic pathways for chronic disease.

SOURCING BREAKTHROUGH SCIENTIFIC OPPORTUNITIES
We identify and support high-potential researchers advancing infection-associated chronic disease science.

ACCELERATING COLLABORATIVE RESEARCH
We conceptualize and manage cross-disciplinary partnerships with leading institutions to drive Long COVID and related research.

SHARING INSIGHTS TO SPEED DISCOVERY
We promote open data, sample sharing, freely-available and public forums to make research accessible and accelerate progress.

PIONEERING SCALABLE SCIENCE-TO-IMPACT MODELS
We develop funding models that move discoveries from the lab to the clinic for patient benefit.

FORMED STRATEGIC PARTNERSHIPS:

- Funded 6 clinical trials and/or their analysis infrastructure
- Amy joined the Invyvd SPEAR Study Group to help guide upcoming clinical trials of monoclonal antibody therapy for Long COVID

SHARING INSIGHTS:

- Held 5 public PolyBio symposia
- PolyBio's work covered in 48 articles in outlets including the *NYT*, *USA Today*, *Wall Street Journal*, etc.

13 UNIQUE TISSUE TYPES BEING COLLECTED FOR RESEARCH

- Gut wall (UCSF, Sinai, Karolinska)
- Lung and bronchial lavage fluid (JCVI, Karolinska, Cardiff)
- Lymph node (Penn, UCSF)
- Bone marrow (UCSF)
- Peripheral nerve (Harvard, JCVI)
- Female endometrium (Gladstone Institutes)
- Blood/vessels arteries (NYU)
- Heart/blood vessels (UCSF)
- Brain/nervous system (Georgetown)
- Vagus nerve (University of Washington)
- Craniocervical ligament (Sinai, JCVI)
- Endometriosis (Pittsburg, JCVI)
- Spinal cord (Brown)

PROJECTS BY CATEGORY

- TISSUE ANALYSIS: 17
- ADVANCED IMAGING: 5
- FLUID DIAGNOSTIC: 16
- ANIMAL/MODEL: 6
- LONG-TERM CONSEQUENCES: 4
- THERAPEUTIC: 6

25+ UNIVERSITIES FUNDED WORLDWIDE

Cardiff University, Georgetown University, Harvard Medical School, Icahn School of Medicine at Mount Sinai, J. Craig Venter Institute, Johns Hopkins, Karolinska Institutet, New York University, Paris Cité University, Stellenbosch University, UMass Chan Medical School, University of California San Fransico, University of Colorado Boulder, University of Pennsylvania, Yale School of Medicine, Emory University, University of Pittsburg, University of Washington, University of Arizona Banner Research Institute, Stanford University, Institut Pasteur France, Gladstone Institutes, Rega Institute Belgium, Joint Genome Institute, INSERM (France), ESPOIRS (France), Brown University

WHO WE ARE

MISSION/VISION

We are a 501(c)(3) advancing research on how viral, bacterial, and parasite infections drive chronic disease and aging. We build collaborative projects that identify, diagnose, and treat root causes of infection-associated chronic illness. Focus areas include Long COVID, chronic tick-borne illness, ME/CFS, Alzheimer's, neuropsychiatric illnesses, and endometriosis.

HOW WE WORK

DEFINING THE RESEARCH AGENDA

Our scientific team leads the writing and development of strategic review articles that outline key treatment and diagnostic pathways for chronic diseases. Published in top-tier journals, these papers consolidate the expertise of leading researchers and create a roadmap for the field, such as our influential position paper in *Lancet Infectious Diseases* on targeting the SARS-CoV-2 reservoir in Long COVID.

SOURCING BREAKTHROUGH SCIENTIFIC OPPORTUNITIES

PolyBio's founders and Scientific Advisory Board stay at the forefront of scientific discovery, networking to identify high-potential research. When we identify a team that can advance the field of infection-associated chronic disease, we engage them directly to help build out their research agenda, facilitate access to patient samples, and secure funding through grants or private donations.

ACCELERATING COLLABORATIVE RESEARCH

PolyBio built and coordinates the Long COVID Research Consortium and manages complex, cross-disciplinary research partnerships with leading institutions like Harvard Medical School, Yale, UCSF, Mount Sinai, and the J. Craig Venter Institute.

SHARING INSIGHTS TO SPEED DISCOVERY

We believe discovery should travel fast. PolyBio supports public-facing tools, sample sharing between research teams, and free biannual virtual symposia that make insights immediately accessible to researchers, patients, and clinicians - fueling faster follow-on science and broader impact.

PIONEERING SCALABLE SCIENCE-TO-IMPACT MODELS

PolyBio is developing venture philanthropy and hybrid funding models to support the diagnostics and treatments that emerge from our science. These contributions help bridge the gap between the lab and the clinic, turning discoveries into tangible advances for patients.

LONG COVID: A GLOBAL CHALLENGE

Long COVID is a complex, chronic condition that can follow even a mild SARS-CoV-2 infection. It is estimated to affect hundreds of millions of people worldwide, debilitating patients with symptoms such as crushing fatigue, brain fog, cardiovascular issues, and neurological problems. In the United States alone, the economic impact exceeds billions of dollars, with millions pushed out of the workforce.

Because Long COVID can involve multiple organ systems and ongoing viral persistence, it requires an entirely new approach to research and treatment — one that integrates virology, immunology, neuroscience, and more. PolyBio has been at the center of this shift, catalyzing groundbreaking discoveries that are transforming how science understands and addresses infection-associated chronic disease.

Since our founding, PolyBio has led at every step:

STEP 1 Creating collaborative scientific infrastructure

STEP 2 Conceptualizing and funding basic science breakthroughs

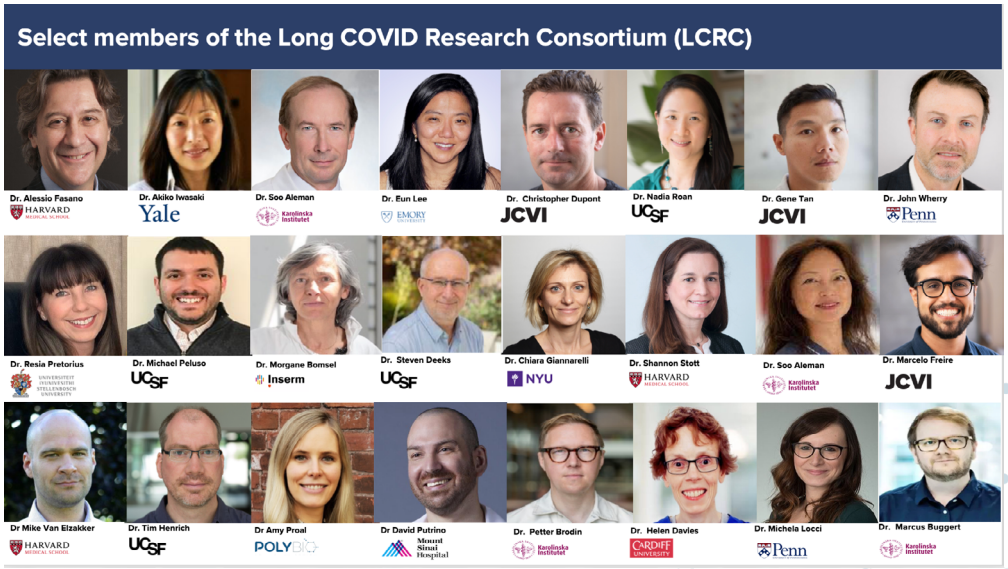
STEP 3 Driving diagnostics and treatments.

STEP 1

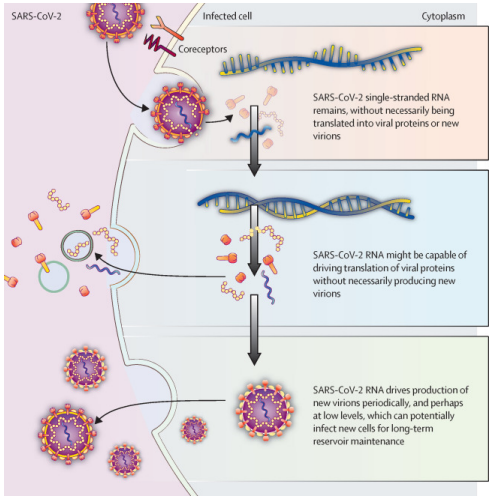
CREATING COLLABORATIVE SCIENTIFIC INFRASTRUCTURE

The Long COVID Research Consortium: Science Without Walls

At the start of the COVID-19 pandemic, PolyBio Co-founders Amy Proal, PhD and Michael VanElzakker, PhD published the world's first scientific paper outlining key potential drivers of the Long COVID disease process. A core insight of this paper is that the study of Long COVID disease mechanisms requires research that spans far beyond the analysis of blood samples alone. **To unlock root causes of Long COVID, scientists must work to study tissue, nerve, and brain-based abnormalities in patients with the disease.**



Through thousands of strategy sessions and meetings, we identified and mobilized scientific teams across continents — from biopsy specialists who could access tissue in the gut, lymph nodes, and bone marrow, to imaging experts with the tools to map abnormalities across the body and brain. Key to this effort was drawing top experts from HIV and cancer into the Long COVID space, including pivoting the world-renowned UCSF LIINC team to focus directly on the disease.



Out of this momentum, we built the Long COVID Research Consortium (LCRC): a first-of-its-kind network of world-class scientists. Designed for speed and openness, the LCRC shattered traditional silos, with researchers across the U.S., UK, France, Belgium, South Africa, and Sweden sharing data, ideas, and even patient samples in real time.

What began as a bold vision quickly grew into a global movement driving the search for the tissue-based causes — and ultimately, the cures — for Long COVID. In 2023, the Consortium's seminal paper in *Nature Immunology* further delineated a research roadmap centered on the study of SARS-CoV-2 persistence: the idea that persistent virus reservoirs in tissue may continue to drive immune dysfunction and symptoms long after initial infection.

Guided by this roadmap, PolyBio co-founder Amy Proal and the LCRC built a research agenda (see right). Through the LCRC, PolyBio has now conceptualized and funded more than 54 research projects that are redefining how Long COVID and other infection-associated chronic conditions are understood. Together, these projects are documenting viral persistence, immune activation, and neuroinflammation in Long COVID — and even linking SARS-CoV-2 reservoirs to Alzheimer's, cardiovascular disease, and aging. Findings are already informing multiple clinical trials, including by the very same teams that helped make HIV a treatable disease. Research is also determining if herpesviruses or tick-borne pathogens like *Borrelia* and *Bartonella* can reactivate and contribute to Long COVID symptoms.

We have helped to create and fund the first-ever Long COVID tissue bank at the UCSF, and the first-ever Long COVID brain registration/autopsy program at Georgetown University. We've also pioneered the first whole-body PET imaging of Long COVID, mapping viral reservoirs throughout the body, and even visualizing the vagus nerve in unprecedented detail.

Today, the LCRC stands as the only global program dedicated to uncovering root cause drivers of the Long COVID disease process. Powered by PolyBio, it has transformed visionary papers into a living, collaborative research engine — one that is pushing the boundaries of technology and opening the path to diagnostics and treatments for millions.

The LCRC model has allowed researchers to move faster than government-led initiatives. At a time when NIH's $1.3B Long COVID program stalled, **the LCRC has leveraged $42M+ to drive breakthrough science.**

LCRC SCIENCE PROGRAM

A comprehensive research agenda using multiple angles to study SARS-CoV-2 persistence and related dysfuntion.

1. Tissue Biopsy Studies

Designed to identify SARS-CoV-2, its proteins, and its effects on the immune and genetic landscape in tissue samples collected from Long COVID patients.

2. Autopsy and Imaging Studies

Designed to reveal the deep-tissue locations of SARS-CoV-2 reservoirs, T cell activity, neuroinflammation, and other abnormalities throughout the body and brain.

3. Blood-based Biomarker Studies

Designed to capture key metrics in blood such a spike protein or immune cell patterns that infer the presence of SARS-CoV-2 in tissue, setting the stage for accessible diagnostic tests.

4. Downstream Consequences of Persistence

Designed to characterize the downstream consequences of SARS-CoV-2 persistence including impacts on clotting, cerebrospinal fluid flow, and vagus nerve signaling.

5. Impact on Other Pathogens and Microbiome

Designed to determine the extent to which SARS-CoV-2's impact on the immune response facilitates the reactivation of other latent pathogens such as herpesviruses, tick-borne/vector-borne pathogens, and components of the microbiome.

DISCOVERY FUELED BY INNOVATION

MICHAEL VANELZAKKER, PHD
HARVARD MEDICAL SCHOOL

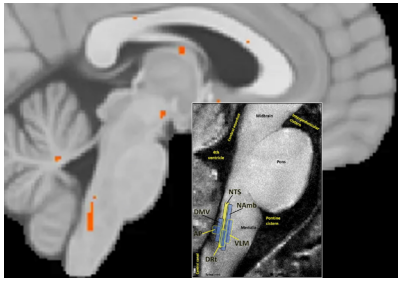
PolyBio is accelerating the translation of cutting-edge technologies into the study of Long COVID. The six projects below illustrate how PolyBio-funded scientists are using these tools to pinpoint viral reservoirs, track immune dysfunction, and identify paths to treatment.

WHOLE BODY IMAGING TO MEASURE TISSUE FIBRIN ACCUMULATION IN LONG COVID

This project is the first in the world to use **advanced positron emission tomography (PET)** imaging to determine if Long COVID symptoms are driven in part by the accumulation of fibrin, a protein involved in blood clotting that can be seeded by the SARS-CoV-2 spike protein. Early results suggest increased fibrin accumulation in the lining of the lungs in patients whose Long COVID symptoms involve breathing problems, pointing to a possible mechanism behind this lingering symptom.

USING A VAGUS NERVE STIMULATING DEVICE (TVNS) IN AN MRI TO DETECT ACTIVATION OF SMALL VAGUS NERVE BODIES IN THE BRAINSTEM

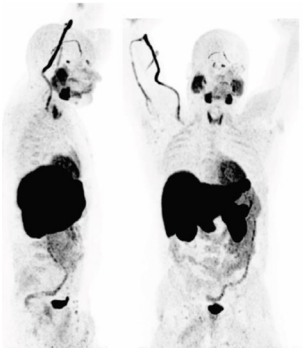
Dr. VanElzakker's team is also studying how hyperactive signaling of the vagus nerve may drive symptoms of infection-associated chronic illness, including in patients with craniocervical instability. The team is using **a vagus nerve stimulating device (tVNS) while patients are inside of an ultrahigh resolution 7T MRI scanner** to detect activation of small vagus nerve bodies in the brainstem. The inset image is from an article written by VanElzakker and Proal in 2021, showing the brainstem region they hypothesized to be involved in hyperactive vagus nerve signaling, and the background image shows the actual data from the imaging scanner aligning with this prediction.



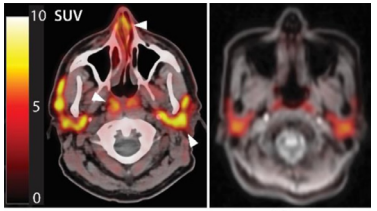
TIM HENRICH, MD
UNIVERSITY OF CALIFORNIA SAN FRANCISCO

ADVANCED IMAGING OF BRAIN AND BODY T CELL ACTIVITY IN LONG COVID

Using cutting-edge advanced imaging **whole-body positron emission tomography (PET)**, researchers are mapping activated T cells throughout the bodies and brains of Long COVID patients. The scans reveal increased T cell activation in the brain stem, bone marrow, and gut in Long COVID patients, offering critical clues to how the disease persists and affects multiple organ systems.



Pt 21: 654 Days Post-Acute COVID-19



Pt 15: 246 Days Post-Acute COVID-19

Pre-COVID-19 Control 3

MICHELA LOCCI, PHD
UNIVERSITY OF PENNSYLVANIA

DECODING LONG COVID LYMPH NODE TISSUE IMMUNE RESPONSES

The project team is the **first in the world** to collect lymph node tissue from Long COVID patients to understand how their immune systems respond to the virus. Using technologies including **high-parameter flow cytometry and combined single-cell proteomic and transcriptomic analysis,** the team has uncovered a profound disruption of B cell responses directed against SARS-CoV-2 in Long COVID lymph node tissue, suggesting the body may struggle to fully eliminate the virus.

MARCELO FREIRE, PHD
J. CRAIG VENTER INSTITUTE

IDENTIFICATION OF LONG COVID NEUROPATHY TISSUE BIOMARKERS

Researchers are applying advanced **metatranscriptomic sequencing and spatial transcriptomics** to skin tissue from Long COVID patients with small fiber neuropathy. These innovative tools characterize the infectious, genetic, and immune landscape of the tissue and nerves in unprecedented detail. The team is finding SARS-CoV-2, spike protein, and immune dysregulation in some Long COVID samples, deepening understanding of how infection may persist in tissue and drive chronic symptoms.

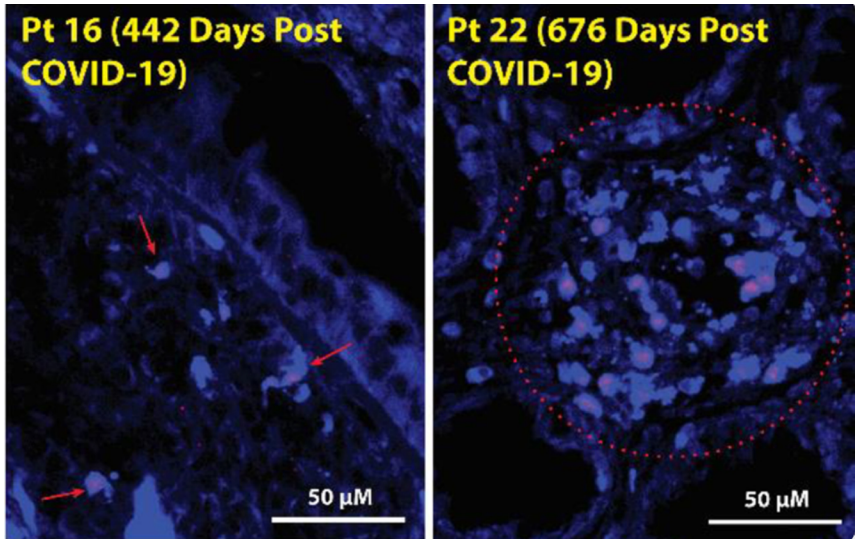
JOHN WHERRY, PHD
UNIVERSITY OF PENNSYLVANIA

USING CIRCULATING CD8+ T CELLS AS VIRAL PERSISTENCE BIOSENSORS

Using tetramers assays, flow cytometry, and single-cell sequencing the team is determining the activation state of Long COVID T cells. These methods reveal whether T cells are responding to SARS-CoV-2 and herpesvirus proteins, serving as **blood-based biosensors of viral persistence.** Thus far, up to 60% of Long COVID patients have T cells that are recognizing persistent viruses - indicating that the immune system is still fighting lingering infection.

CONCEPTUALIZING AND FUNDING BASIC SCIENCE BREAKTHROUGHS

BREAKTHROUGH SCIENCE IN ACTION



The research we've funded has resulted in some of the top papers in the world delineating Long COVID disease mechanisms. Here are some examples.

1. SARS-CoV-2 Persistence in Long COVID

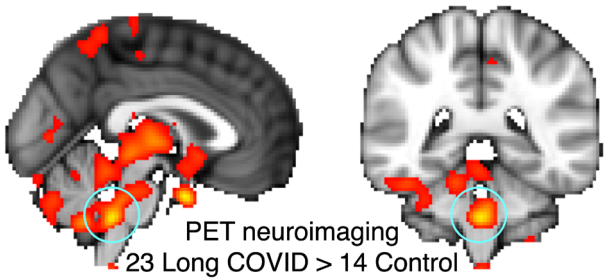
A landmark UCSF study published in *Science Translational Medicine* provided early evidence that the SARS-CoV-2 virus can persist in Long COVID gut tissue for almost two years. Led by a UCSF team with deep expertise in HIV research, the study also revealed widespread T cell immune activation across the body and brain — with particularly elevated activity in the spinal cord and gut wall of Long COVID participants.

These findings confirm viral persistence and immune activation as central drivers of disease and highlight immune pathways that can be targeted for diagnostics and treatments.

"Long COVID is not a mystery" says Michael Peluso MD, an infectious disease researcher in the UCSF School of Medicine who co-led the study. "Our findings provide clear evidence of virus persistence and sustained immune activation after COVID-19. We will use this information to test treatments that might get people better."

2. Neuroinflammation in the Long COVID Brain

A Harvard Medical School/MGH study published in *Brain, Behavior & Immunity* delivered the first evidence of neuroinflammation in the Long COVID brain accompanied by evidence of vascular problems. Using advanced imaging at the Harvard Medical School/MIT Martinos Center for Biomedical Imaging, the team, led by PolyBio co-founder Michael VanElzakker, PhD., pinpointed inflammation in brain regions exposed to circulating blood factors through gaps in the blood–brain barrier.



The team also measured blood factors tied to vascular health and damage, identifying six markers — including fibrinogen (a clotting protein) and sL-selectin (an immune adhesion molecule) — that correlated with the neuroinflammation signal. Together, these findings establish a link between vascular damage, immune activity, and brain inflammation in Long COVID, providing critical targets for future diagnostics and treatments.

3. Autoantibodies and Long COVID Symptoms

Using a human protein array of more than 21,000 proteins, researchers at Yale University identified diverse autoantibodies (AABs) in Long COVID patients that correlate with symptoms. Some patients with neurocognitive or neurological symptoms showed elevated AABs against nervous system proteins, and purified IgG from these patients were transferred into mice. They reacted with brain and nerve tissue, producing pain, dizziness, and coordination problems mirroring patient experiences. These findings suggest that targeting autoantibodies could be a therapeutic strategy for certain Long COVID patients.

4. Biomarkers of Breathlessness in Long COVID

A *Nature Immunology* study from Karolinska Institut in Sweden used advanced technologies to identify a plasma biomarker signature in Long COVID patients with breathlessness, pointing to pathways of lung injury, platelet activation, and vascular remodeling that may impair oxygen exchange. The team also found higher frequencies of T cells targeting SARS-CoV-2 and herpesviruses in affected patients, suggesting roles for viral persistence or reactivation.

The group is now collaborating with other LCRC teams to extend this work by analyzing lung, gut, and lymph node tissue from Long COVID patients, comparing immune responses in blood versus tissues to deepen understanding of immune responses and disease mechanisms.

5. Viral Persistence and Immune Dysfunction in Long COVID

A *Lancet Infectious Diseases* study from UCSF showed that viral proteins can remain in the bloodstream for up to 14 months after infection in a significant subset of people, providing strong evidence that SARS-CoV-2 persistence is a key driver of chronic disease after COVID.

In a companion paper in *The Journal of Clinical Investigation*, the team reported the first evidence of dysfunctional natural killer cells in Long COVID blood. Patients showed reduced levels of cytotoxic natural killer cells — immune cells that normally help clear viral reservoirs — suggesting impaired antiviral defense that could enable persistence.

These findings are already shaping clinical research. UCSF and collaborators are moving forward with an immunotherapy trial (ImmunityBio) aimed at boosting natural killer cell activity to help patients clear lingering virus and improve outcomes.

"The results suggest that natural killer cells may struggle to effectively clear persistent virus reservoirs in individuals with Long COVID," said PolyBio's President Dr. Amy Proal. "The findings set the stage for immunotherapy trials of drugs that activate NK activity."

LONG COVID IN CHILDREN

Early in the pandemic, many believed that children were largely spared from COVID's long-term impacts, but that narrative has proven untrue. A September 2025 study found that children and teens were twice as likely to develop Long COVID after a second infection compared with a first, highlighting the serious impact COVID can have on young people.

We are supporting research and treatment on children with Long COVID: studying immune cell activity, spike protein levels, and blood microclotting levels in pediatric patients. One study by our team at Harvard Medical School found that neutrophil immune cells from Long COVID children were hyperactive and associated with pro-inflammatory pathway signaling. Circulating spike protein, potentially leaking from SARS-CoV-2 tissue reservoirs, was detected in blood from a subset of children. We are supporting a clinical trial in Long COVID children, to test if the drug Larazotide can reduce gut barrier permeability, thereby stopping spike leakage into blood.

DRIVING DIAGNOSTICS AND TREATMENT

Despite the immense burden of Long COVID, there are still no FDA-approved treatments and no validated diagnostic tests to guide care. We stand at an inflection point: will this remain a mass disabling condition, or will we summon the resources and resolve to solve it?

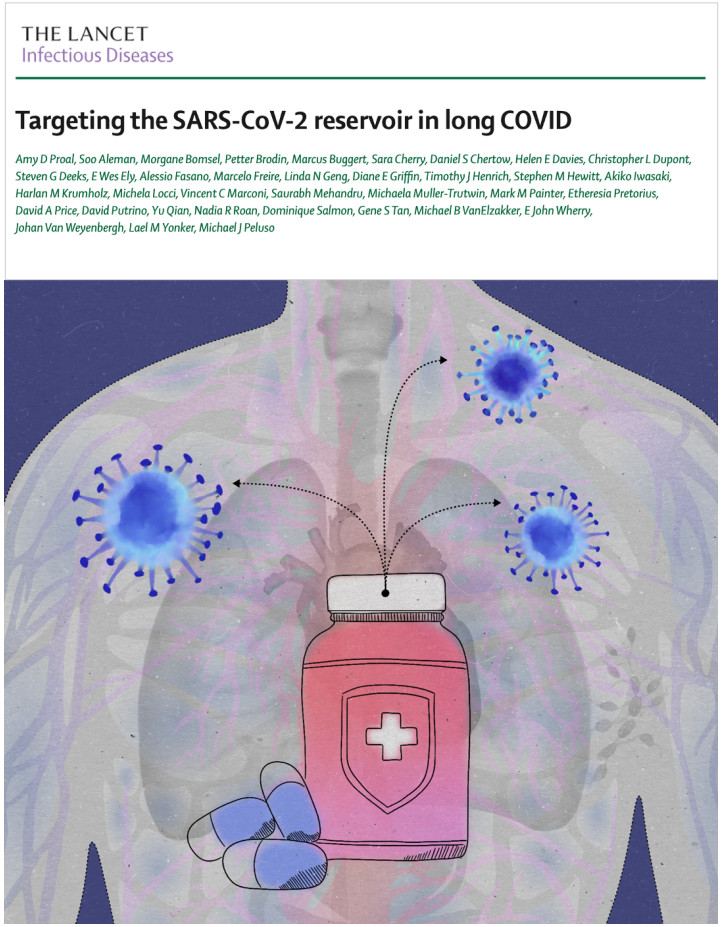
AN URGENT MOMENT FOR LONG COVID

At PolyBio, our motto — *Science in Action* — drives us to move fast. The LCRC's *Lancet Infectious Diseases Viewpoint* has provided the world's first roadmap for testing interventions to clear SARS-CoV-2 reservoirs — outlining trial design principles, promising drug candidates, and the urgent need for validated biomarkers.

Together with the LCRC, we are collaborating directly with leading companies such as Invivyd and ImmunityBio to accelerate the development of monoclonal antibodies, immunotherapies, and antivirals designed to target persistent virus.

In 2025, PolyBio President Dr. Amy Proal and LCRC colleagues joined SPEAR (Spike Protein Elimination and Recovery), an initiative convened by Invivyd, to work directly with the U.S. Food and Drug Administration (FDA) on the design of monoclonal antibody trials for Long COVID.

Together, these efforts demonstrate how PolyBio is turning urgency into action — creating the partnerships, roadmaps, and trials that will bring the first effective diagnostics and treatments to patients.



TARGETED TRIAL RESPONDER ANALYSIS TO BEST TAILOR TREATMENT

We have specifically designed several of our Long COVID trials to identify which patients are most likely to respond to specific treatments by measuring targeted immune, hormonal, and other parameters in participants over time. For example, we are supporting a Mount Sinai/Yale University clinical trial of low-dose rapamycin in Long COVID. Taken in a once-weekly low dose, rapamycin has been shown capable of boosting components of the immune response to better control persistent infection. We designed our trial so that Akiko Iwasaki's lab at Yale University measures immune parameters including T cell exhaustion and interferon signaling in trial participant blood before and after rapamycin intervention. These analyses will clarify if Long COVID trial participants with certain immune system characteristics optimally respond to rapamycin, allowing us to eventually tailor treatment of the drug most effectively.

LONG COVID TRIAL PIPELINE

To date, PolyBio has funded 4 clinical trials and counting, creating a direct pipeline from scientific discovery to patient care:

1 Lumbrokinase microclot disruption (Mt. Sinai):

A trial funded in collaboration with the Steven & Alexandra Cohen Foundation, testing whether **lumbrokinase**, a fibrinolytic enzyme, can safely break down or disrupt the formation of microclots seeded by persistent spike protein or bacteria, reduce clotting burden, and improve symptoms in Long COVID, ME/CFS, and Chronic Lyme participants.

2 Repurposed HIV antivirals (Mt. Sinai):

A trial of Truvada and Maraviroc to see if targeting reactivated Epstein-Barr virus or SARS-CoV-2 tissue reservoirs can reduce symptom burden in Long COVID, with biomarker analyses guiding antiviral impact.

3 Larazotide/gut barrier in children (Harvard Medical School):

A pediatric trial testing whether improving gut permeability with **Larazotide** can reduce leakage of spike protein from the gut into blood and alleviate post-COVID inflammation in children with Long COVID.

4 Low-dose rapamycin (Mt. Sinai & Yale):

A trial at Mt. Sinai testing whether **low-dose rapamycin** can improve Long COVID symptoms, with Yale researchers tracking immune and infectious changes to understand its therapeutic mechanism.

PolyBio has also funded the incorporation of gut biopsies and other advanced biological measurements into two clinical trials, expanding the depth and precision of patient analysis.

5 Monoclonal antibodies / AER002 (UCSF):

A trial that evaluated whether a **monoclonal antibody infusion** can safely clear persistent SARS-CoV-2 viral remnants in Long COVID patients, with one-year follow-up on safety and symptoms.

6 N-803 / ANKTIVA® immunotherapy (UCSF):

A Phase 2 trial of **ANKTIVA® (N-803)** designed to boost natural killer and CD8+ T cell activity, enhance clearance of viral reservoirs, and improve clinical outcomes in Long COVID. PolyBio is supporting sample analysis around the trial.

"PolyBio and Amy Proal represent the apex of virology and infectious disease science acumen, knowledge, and clarity of purpose. In complex medicine dealing with human response to acute and chronic viral infections, there are many groups who believe they know what they are talking about, but very few truly do. PolyBio and Amy are the absolute top of the list. **When we went looking for intellectual partnership in developing monoclonal antibody therapies for Long COVID, we sought out Amy and PolyBio because we cannot afford less than the best knowledge and information to help guide our work.** We are proud to consider her a trusted advisor."

MARC ELIA, CHAIRMAN OF INVIVYD

INTRODUCING THE LONG COVID CURE INITIATIVE

After years of breakthrough research uncovering the root causes of Long COVID, **PolyBio is proud to launch the Long COVID Cure Initiative (LCCI)**—a bold new effort to turn discovery into action. LCCI will accelerate the development of validated diagnostics and targeted treatments, moving the field from understanding the disease to curing it. To power this transition, we will:

- Develop diagnostic tools that identify the root causes of Long COVID and related infection-associated conditions with precision.
- Work with industry to deliver personalized treatments by linking each patient's biology to the therapies most likely to help.

- Accelerate cures by mobilizing transformative collaborations across science, industry, and philanthropy.
- Build validated diagnostic tests and treatments into our Mount Sinai Long COVID medical education program

VIPER: THE FIRST STEP TOWARD CURES

To unlock treatments, we must first have the right tools to measure the disease. That is where VIPER — "Viral Immunopathogenesis Repeat Donor Cohort"— comes in. VIPER is a pioneering initiative that will validate the first diagnostic tests for persistent SARS-CoV-2 and other key drivers of Long COVID.

How VIPER Works

1. **Recruitment of Participants** – 150 individuals with and without Long COVID are enrolled in UCSF's Long-Term Infection with Novel Coronavirus (LIINC) Study.
2. **Collection of Samples** – A carefully curated set of blood, saliva, stool, and tissue samples is collected and stored in a professional biobank.
3. **Cross-Lab Testing** – Multiple top laboratories receive identical, de-identified samples and apply their most promising diagnostic platforms.
4. **Head-to-Head Evaluation** – VIPER's data team compares results to identify the most accurate, scalable tests.
5. **Path to Patients** – The strongest diagnostics are fast-tracked into clinical trials at UCSF, Mount Sinai, and with pharma partners. This collaborative, comparative design ensures transparency, rigor, and speed — producing results that regulators, industry, and clinicians can trust.

Help Launch VIPER

We've raised over $1M to make VIPER a reality and are **actively fundraising to reach our total $8 million program goal.** Donate today to help make VIPER happen.

NEW UCSF VIDEO

When COVID-19 struck, UCSF's LIINC team swiftly pivoted decades of HIV research expertise to uncover the root causes of Long COVID. By studying patients in extraordinary depth—including rare tissue biopsies—the team discovered that Long COVID is a tissue-based disease, marked by viral persistence and chronic immune activation.

Check out our new video featuring leading UCSF scientists and PolyBio partners Dr. Steven Deeks, Dr. Michael Peluso, and Dr. Tim Henrich as they share their groundbreaking work to uncover— and ultimately cure— Long COVID.

EXPANDING THE HORIZON OF INFECTION-ASSOCIATED CHRONIC DISEASE RESEARCH

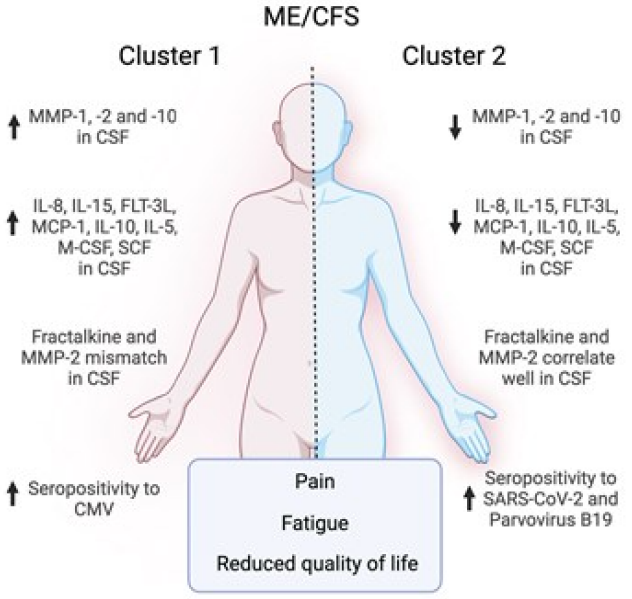
Discoveries from PolyBio's Long COVID Research Consortium are already reshaping how science approaches chronic tick-and vector-borne illness, women's health, ME/CFS, and infection-linked drivers of Alzheimer's, neuropsychiatric disorders, and aging. These initiatives are generating foundational data and partnerships that will inform a strategic expansion of our infection-associated chronic disease portfolio in the years ahead.

ADVANCING ME/CFS RESEARCH

PolyBio is driving new discoveries in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) — a debilitating, infection-associated chronic condition affecting up to 24 million people worldwide. Despite its severity and prevalence, ME/CFS remains under-researched and without approved diagnostics or treatments — making new scientific advances especially urgent.

In collaboration with Dr. Akiko Iwasaki's team at Yale, PolyBio's co-founders helped identify biomarkers that divide ME/CFS patients into two subgroups. One group showed elevated matrix metalloproteinases and cytokines consistent with central nervous system inflammation; the other showed unique immune correlations linked to joint hypermobility. Researchers also found altered cytokine interactions, including disrupted fractalkine and eotaxin pathways, which may drive neuroinflammation and cognitive symptoms.

PolyBio also awarded $1M to UCSF to expand the LIINC program into ME/CFS, using tissue biopsy and advanced ImmunoPET-CT imaging to study viral persistence and immune activation in the brain, spinal cord, and bone marrow. Despite the condition's name — which means "painful inflammation of the brain and spinal cord" — no studies have previously used such technology in ME/CFS.



"These findings mark a significant step toward precision medicine for ME/CFS."

DR. IWASAKI

The UCSF-led project called CHIIME (Chronic Infection and Inflammation in ME/CFS) is building a longitudinal biobank of well-characterized patients, with samples shared across PolyBio networks for infectious, immune, and genetic analyses. Gut tissue and blood are being tested for viral persistence, while concurrent imaging maps immune activity across organ systems.

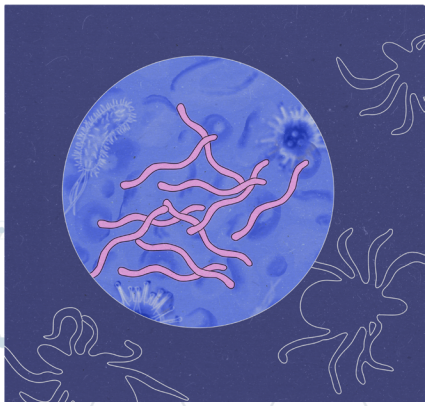
PolyBio is additionally funding a Harvard Medical School study using cutting-edge dual PET-MRI neuroimaging to quantify neuroinflammation in ME/CFS patients. To identify if inflammation is tied to other symptoms or biomarkers, patients also undergo other forms of detailed data collection, including a wearable sleep recording device the night before scanning, dynamic pupillometry as a measure of intracranial pressure and neuroautonomic function, and live (never frozen) neutrophil immune cell testing.

Together, these projects mark a transformative advance: bringing the study of persistent infection and neuroinflammation - the most understudied but important topics in ME/CFS - to the forefront, thus opening pathways to new diagnostics and treatments.

FURTHER EXPANSION INTO CHRONIC LYME AND OTHER TICK-BORNE/ VECTOR-BORNE ILLNESES (LYME+)

Many patients infected with the Lyme bacterium *Borrelia*—and other pathogens transmitted by ticks, spiders, and similar vectors—do not fully recover and go on to experience debilitating chronic symptoms. PolyBio is supporting several projects aimed at uncovering why these infections persist by determining whether these organisms "hide" within patient tissues and how emerging technologies can best detect them.

One such project is a multi-site collaboration based at the J. Craig Venter Institute, which is using advanced molecular and imaging methods to identify *Borrelia*, *Bartonella*, and related bacteria in peripheral nerve, spinal cord, and other key tissue types. Another is led by scientists at North Carolina State University, who are developing innovative approaches to visualize the tick-borne parasite *Babesia* in the tissues of people with chronic symptoms.



These efforts represent just the beginning of our broader commitment to advancing research and treatment innovation for chronic tick- and vector-borne infections. In 2026, PolyBio will expand its Long COVID Cure Initiative (LCCI) into the development of next-generation Lyme+ diagnostic tests and therapies—mobilizing many of the world's leading scientists and clinicians to bring precision diagnostics and targeted treatments to this long-overlooked field.

FROM RESEARCH TO IMPLEMENTATION: PARTNERSHIP WITH THE CORE CLINIC AT MT. SINAI

Data and insight from PolyBio projects does not sit in academic journals. Rather it is directly communicated to physicians, including those at the Cohen Center for Recovery from Complex Chronic Illness (CoRE) Clinic, where PolyBio's Dr. Amy Proal serves as Scientific Director in concert with Nash Family Director Dr. David Putrino. CoRE serves as a beta-testing site for novel Long COVID or chronic tick-borne/vector-borne infection diagnostic tests and treatment protocols informed by key LCRC findings. CoRE also powers a free medical education program, which recently released the first-ever Infection-Associated Chronic Disease Provider Manual. This landmark resource equips clinicians with practical guidance on diagnosis, multidisciplinary care models, and targeted treatments for patients with Long COVID and other complex chronic conditions.

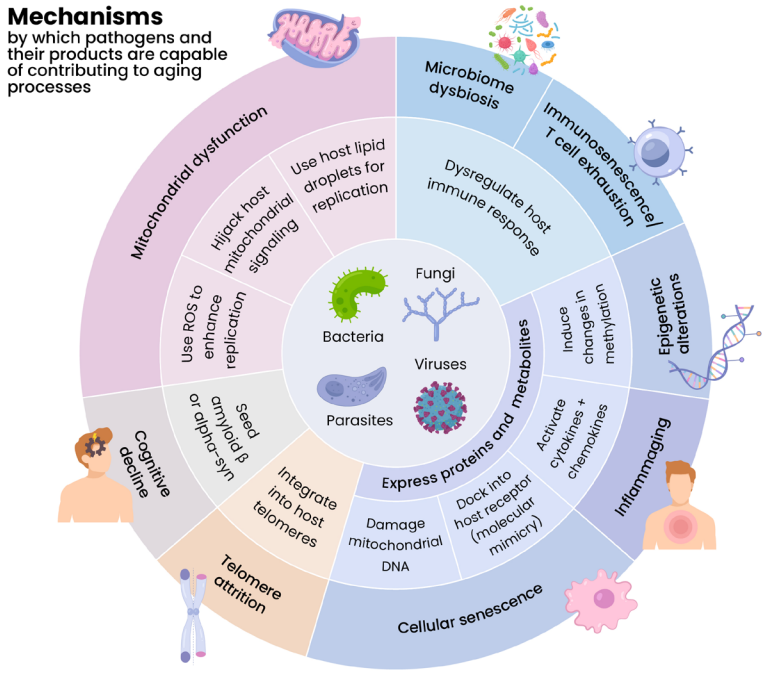
EXPANDING INTO AGING AND ALZHEIMER'S

In 2025, PolyBio's co-founders published a landmark position paper in *Ageing Research Reviews* challenging the long-held belief that human aging unfolds in a sterile environment. The paper details how lifelong exposure to viruses, bacteria, fungi, and parasites — many of which persist in tissues and nerves — can directly accelerate aging and drive age-related diseases such as Alzheimer's, where amyloid plaques may form as part of an antimicrobial response.

The review also highlights how persistent infections disrupt key metabolic pathways, including mTOR and AMPK, suggesting that popular anti-aging interventions like low-dose rapamycin or metformin may partly work by suppressing microbial activity.

PolyBio-supported projects are already underway linking chronic infection to Alzheimer's disease. This includes research working to develop a new diagnostic blood test to identify Alzheimer's patients with active Cytomegalovirus infection. The test is positioned to measure viral activity in an important clinical trial we are working to support: a trial to determine if the widely available antiviral medication valacyclovir could help treat or prevent Alzheimer's disease.

PolyBio is now creating a dedicated program to develop next-generation diagnostics to detect persistent pathogens in aging populations.



"We need an entirely new generation of diagnostic tests to identify pathogens in people as they age," says PolyBio President Dr. Amy Proal. "These tools will revolutionize the longevity space."

By integrating infection biology into models of aging, PolyBio is pioneering a new frontier — linking pathogen activity to neurodegeneration, immune decline, and chronic inflammation — with the goal of extending not just lifespan, but healthspan.

WOMEN'S HEALTH AND INFECTION-ASSOCIATED CHRONIC DISEASE

Women disproportionately suffer from infection-associated chronic conditions, yet their unique biology remains understudied. PolyBio is addressing this gap by developing a dedicated program on women's health, with a focus on debilitating conditions such as endometriosis and interstitial cystitis.

We are leading the first study to comprehensively map the infectious, immune, and genetic landscape of endometriosis tissue, while a parallel study is collecting biopsy samples from the female reproductive tract. Using advanced methods, our researchers are investigating whether this tissue serves as a reservoir for SARS-CoV-2 or a site of immune dysregulation in women with Long COVID—factors that may help explain why women experience Long COVID at higher rates than men.

SHARING INSIGHTS TO SPEED DISCOVERY

We believe discovery should travel fast. PolyBio supports public-facing tools, open-data platforms, sample sharing between research teams, and biannual virtual symposia that make insights immediately accessible to researchers, patients, and clinicians—fueling faster follow-on science and broader impact.

SYMPOSIA

Since 2023, PolyBio has hosted five global online Symposia, bringing together leading researchers from our Long COVID Research Consortium and other projects. These public events share the latest scientific findings, highlight clinical trial progress, and connect scientists, clinicians, and patients worldwide. All presentations are freely-available, underscoring PolyBio's commitment to transparency and accelerating discovery.

TEDX TALK ON INFECTION AND AGING

In an October 2025 TEDx Boston talk, Dr. Amy Proal applied the science of persistent infection to innovations in human aging. She explained how persistent infections hijack the body's natural defenses and energy, accelerating every hallmark of human aging — from mitochondrial breakdown to immune dysfunction. She showed how pathogens act like hackers, embedding in our tissues and reprogramming our cells for their own survival, often for life. Amy argues that new diagnostics and treatments targeting these hidden infections are essential if we want to truly extend human healthspan.

MEDIA COVERAGE

PolyBio's work has been covered in 48 articles in outlets including the NYT, Forbes, Bloomberg, USA Today, Wall Street Journal, Atlantic, NPR, Science, Scientific American, and an op-ed in the LA Times by PolyBio co-Founder and President Amy Proal, calling for more Long COVID clinical trials.

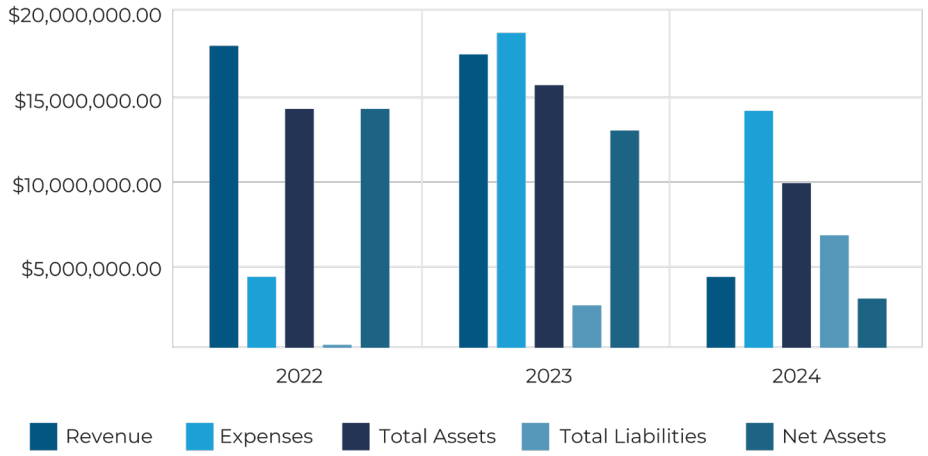
FINANCIAL OVERVIEW

PolyBio is financially sound, balancing revenue and expenses while ensuring that resources are deployed rapidly to advance groundbreaking science. We do not sit on a large endowment; instead, donor funds flow directly into research programs where they can have the greatest impact.

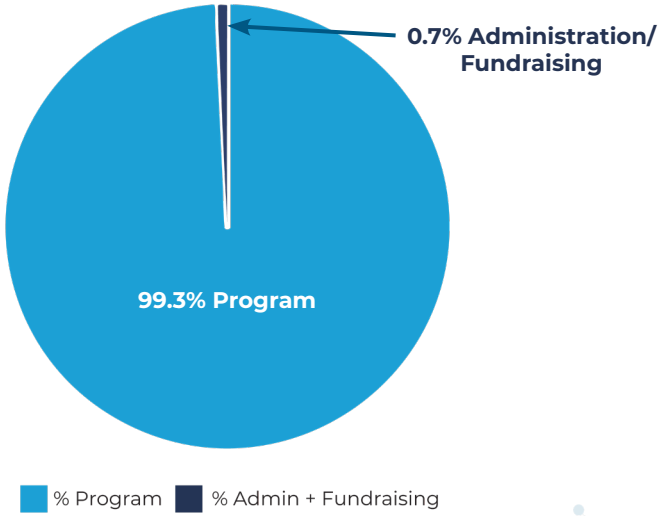
Our financials reflect this commitment: over 98% of expenditures are directed to program work, with less than 2% supporting administration and fundraising. This lean structure underscores our focus on funding discovery, collaboration, and clinical progress.

The charts below provide a clear snapshot of our revenue, expenses, and net assets, as well as the breakdown of program versus administrative costs. IRS Form 990s are publicly available on our Candid/GuideStar profile.

REVENUE/EXPENSES/NET ASSETS 2022-2024



PROGRAM COSTS VS. ADMINISTRATIVE AND FUNDRAISING COSTS 2022-2024



YOUR GENEROSITY DRIVES DISCOVERY

Every breakthrough PolyBio achieves is powered by our supporters. From major gifts to grassroots fundraisers, your contributions fuel cutting-edge research on Long COVID, ME/CFS, and other infection-associated chronic diseases. Thanks to you, world-class scientists are developing the diagnostics and treatments that patients urgently need. Together, we're turning science into hope for millions living with infection-associated chronic diseases.

MAXIMIZING IMPACT THROUGH STRATEGIC PRO-BONO PARTNERSHIPS

To stretch every philanthropic dollar, PolyBio actively offsets operational and innovation costs through high-value, pro-bono support from mission-aligned experts. These contributions allow us to direct more resources toward scientific discovery. Our pro-bono partners include:

- JPMorgan's Atwood Group, which provides banking, investment, and complex stock donation infrastructure
- Public Purpose Strategies, led by Michael Brown, City Year co-founder, who serves as a Senior Advisor on nonprofit strategy and organizational growth
- John Galvin, Gordon Brothers executive, who advises on legal frameworks and strategic agreements

YOUR MONEY AT WORK

PolyBio is proud to uphold the highest standards of transparency and accountability. We have earned the Candid/GuideStar Platinum Seal of Transparency and a 4-Star rating from Charity Navigator — the highest recognition for financial health, accountability, and impact.

Independent audits, board oversight, and annual IRS Form 990s ensure that every dollar is stewarded responsibly. Our 990s can be accessed anytime through our Candid/GuideStar profile.

These independent ratings reflect PolyBio's commitment to stewarding every gift with integrity and ensuring that resources flow where they matter most — fueling scientific breakthroughs that lead to diagnostics and treatments.

Charity Navigator ✦ FOUR-STAR ✦ 2025

Platinum Transparency 2025 Candid.

HOW TO SUPPORT POLYBIO

PolyBio's work is powered by philanthropy. You can support our mission in many ways:

- Donate Online – Make a one-time or monthly gift at polybio.org/donate.
- Peer-to-Peer Fundraising – Launch a no-fee fundraiser through Zeffy, GoFundMe, or Facebook.
- Stock, Wire, or Crypto Gifts – Contact skalloch@polybio.org for transfer instructions.
- Donor-Advised Funds – Recommend a grant through your DAF.
- Legacy Gifts – Create a lasting impact by including PolyBio in your estate plans.

Considering a gift? The PolyBio team would be glad to discuss how your support can make the greatest impact. Please contact Sarah Kalloch at skalloch@polybio.org to schedule a conversation.

DONOR SPOTLIGHT: VITALIK BUTERIN

Vitalik, the founder of Ethereum, began his involvement in public health in 2021 with major philanthropic gifts both to alleviate the burden of COVID-19 and in airborne pandemic prevention. His funding concentrated on high risk bets that were too early or too uncertain for established funding sources, whether commercial, philanthropic, or government research budgets. Grants were made across the spectrum of interventions from early detection, clear air, therapeutics and basic scientific research towards a cure.

While working in this space, Vitalik quickly, and correctly, realized that the ability of SARS-CoV-2 to drive debilitating chronic disease - Long COVID - was one of the most detrimental aspects of the pandemic. Noting PolyBio's presence on X and in academic citations, and the Foundation's deep focus on documenting root cause drivers of chronic disease, Vitalik provided key support for PolyBio's Long COVID Research Consortium. This helped to create the infrastructure for tissue biopsy studies and imaging programs critical for identifying SARS-CoV-2 reservoirs in Long COVID patients. His philanthropic funds provided resources for Long COVID clinical trials of generic drugs like Truvada, Maraviroc, and low-dose rapamycin that would likely never have happened otherwise.

Vitalik also facilitated a collaboration between the OSLUV project and the Mount Sinai CoRE clinic to install state of the art far-UVC germicidal lights - setting a precedent for clear indoor air in medical settings.

Vitalik Buterin and PolyBio's Dr. Amy Proal during a San Francisco d/acc Discovery Day panel discussion.

Vitalik's support for PolyBio has been monumental, says PolyBio-cofounder Michael VanElzakker, PhD. "He has been an incredibly thoughtful, principled, and generous donor and we're really proud of our relationship and all we've accomplished together."

BOARD AND LEADERSHIP

FOUNDERS / LEADERSHIP

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PolyBio Co-Founder, President/CEO and Scientific Director, Mt. Sinai CORE Clinic

MICHAEL VANELZAKKER, PHD

PolyBio Co-Founder, Assistant Professor in the Division of Neurotherapeutics at Harvard Medical School

SARAH KALLOCH

PolyBio Chief Operating and Innovation Officer

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CHARLOTTE MAO, MD

Pediatric infectious disease physician

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Founder and CEO of TLDM Technologies

AMY PROAL, PHD

PolyBio Co-Founder, President/CEO and Scientific Director, Mt. Sinai CORE Clinic

MICHAEL VANELZAKKER, PHD

PolyBio Co-Founder, Assistant Professor in the Division of Neurotherapeutics at Harvard Medical School

SENIOR ADVISOR

MICHAEL BROWN

Co-Founder and Former CEO of City Year; Principal at Public Purpose Strategies

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Instructor in the Neurology Department of Massachusetts General Hospital & Harvard Medical School

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Pediatric infectious disease physician

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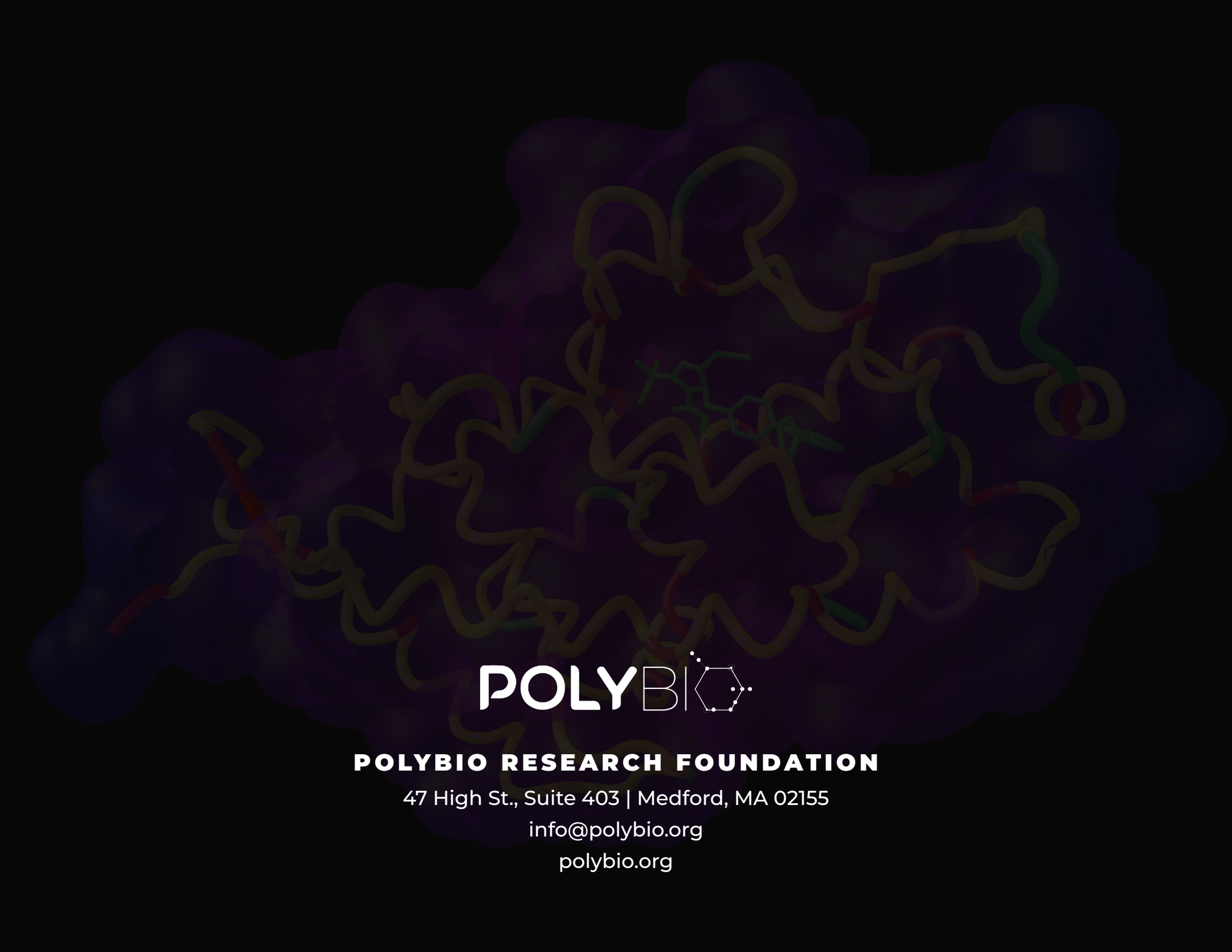
Professor of Genomic Medicine, and member of the J. Craig Venter Institute infectious disease department; Oral surgeon

DAVID PAEZ-ESPINO, PHD

Co-founder & Head of Bioinformatics at Ancilia Therapeutics

LENA PERNAS, PHD

Scientist at the Max-Planck-Institute for Biology of Ageing



POLYBIO

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