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*Breakthrough* magazine is published by **ME RESEARCH UK**, a Scottish Charitable Incorporated Organisation with the principal aim of commissioning and funding high-quality scientific (biomedical) investigation into the causes, consequences and treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). We **INFLUENCE**, **INFORM** and **INVEST** in ME research globally by identifying potentially important areas for future biomedical research, and by producing high quality professional reviews and reports. *Breakthrough* is an open-access publication and, apart from images and illustrations, the content may be reproduced free of charge, subject to the terms and conditions found at meres.uk/bt-terms. **© ME Research UK, 2026 – SCIO Charity No. SC036942, The Gateway, North Methven Street, Perth, PH1 5PP, UK, Tel: 01738 451234, Email: contact@meresearch.org.uk, Web: www.meresearch.org.uk.**

# EDITORIAL

Jonathan Davies
Chair, Board of Trustees

Welcome to the Spring 2026 issue of *Breakthrough* magazine. Our work on your behalf continues…

We hope you will find plenty to keep you interested and encouraged by the scale and spread (both geographically and by subject area) of high-quality research that your continued support has allowed us to fund.

The projects featured in this issue come from Latvia, Spain, Belgium and the UK, and cover a range of research areas including the immune system, biomarkers and diagnosis, retroviruses, and chronic pain.

All of us at ME Research UK remain completely committed to our mission of informing, influencing and investing in biomedical research that we hope and believe will ultimately provide answers for everyone whose lives are affected by ME.

It won't come as a surprise that we want to do more, and as a charity we are entirely reliant on the generosity of all those who raise funds or donate money to allow us to invest in high-quality biomedical research.

We include some of your recent and wonderful fundraising stories on page 30. With this issue, you will also find a leaflet detailing some of the ways you can support our work through fundraising and donations.

Thank you all for your continued support – we can't do it without you!

# SPRING BOOST

**Our portfolio of innovative ME/CFS research continues to grow with three new projects announced in the last few months, all of which build on previous work. You can read about all our projects at meresearch.org.uk/research**

## Understanding the role of autoimmunity in ME/CFS

*Lead researcher: Prof. Bhupesh Prusty, Riga Stradins University*

**Background**

Our immune system is responsible for protecting our body from infections such as viruses and bacteria, destroying harmful substances from the environment, and combating changes in the body that can cause disease.

Immunoglobulins (also known as antibodies) play a key role in the immune system. They are proteins produced by the white blood cells which recognise and attack harmful invaders such as bacteria and viruses.

Some immunoglobulins (autoantibodies) are directed against the body's own proteins, cells or tissues. While these may have useful functions (such as destroying cancer cells or removing waste), they can lead to the development of an autoimmune disease such as multiple sclerosis or lupus.

Autoimmune mechanisms may be involved in ME/CFS, but the findings to date have been inconclusive due partly to the complexity of the disease and differences between individuals.

Prof. Bhupesh Prusty's previous research found that immunoglobulins taken from people with ME/CFS caused dysfunction of the mitochondria when mixed with cells taken from healthy individuals (read more on page 27 of this issue).

The mitochondria are responsible for generating energy in the body, so these findings could have important implications in ME/CFS.

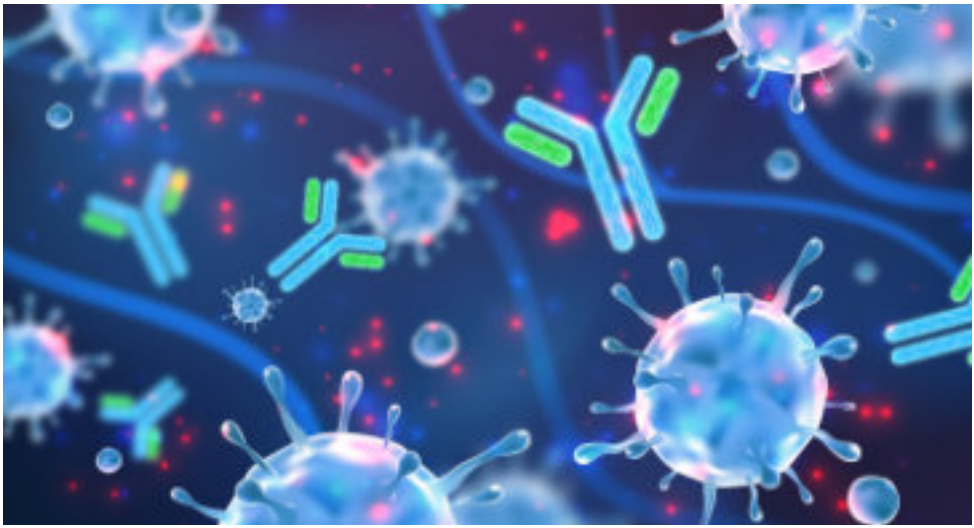
**Name**
Prof. Bhupesh Prusty

**Position**
Professor of Science

**Institution**
Institute of Microbiology and Virology, Rīga Stradiņš University

**Main research interests**
Understanding virus infection; herpesvirus reactivation and the development of post-viral chronic illnesses; host–pathogen interaction; linking autoimmunity to ME/CFS and long COVID.

**More information**
prustylab.org



Prof. Prusty wants to explore this further, and his new study will investigate the mechanisms through which immunoglobulins from ME/CFS patients can cause this mitochondrial dysfunction in cells.

**Objectives**

The researchers will first take immunoglobulin samples from people with ME/CFS and from healthy volunteers, and then culture them for 12 hours with healthy muscle and nerve cells, both of which are known to be affected in the disease.

The human brain is particularly complicated and experiments using single cells do not always reflect this. So immunoglobulins will also be cultured with three-dimensional brain tissue to fully understand the pathogenic processes.

Sequencing methods will be used to assess how the genes of these cells and tissues change their activity level in response to being exposed to the immunoglobulins, which will help to identify which cellular pathways are involved.

Immunoglobulins can have specific protein targets on the cells with which they interact, and a second part of the study is to investigate the mechanism by which this interaction occurs.

Proteins will be extracted from a number of different cell types and exposed to the immunoglobulins, to identify which proteins are potential targets.

**Potential benefits**

The researchers anticipate that their findings will provide a better understanding of the role of autoimmunity in ME/CFS, and specifically the molecular mechanism by which immunoglobulins can cause mitochondrial dysfunction. This could help in the design or selection of suitable treatments to target this pathway.

## A diagnostic test for ME/CFS based on cell electrophysiology

*Lead researchers: Dr Fatima Labeed and Dr Jackie Cliff, Brunel University of London*

**Background**

There is currently no widely available, accurate diagnostic marker for ME/CFS. However, growing evidence suggests that the electrical characteristics of white blood cells could form the basis of a low-cost, reliable diagnostic test for the disease.

In 2019, Prof. Ron Davis and his team developed a nanoelectronics test that found a difference in the impedance of white blood cells taken from people with ME/CFS compared with those from control subjects.

In 2023, this work was continued by Prof. Robert Dorey, Dr Fatima Labeed, Krista Clarke and colleagues at the University of Surrey, in a study jointly funded by ME Research UK and the ME Association.

White blood cells from people with ME/CFS, people with multiple sclerosis and healthy volunteers were put into a salty solution for one-and-a-half hours. The change in the electrical properties of these cells after the salt treatment was significantly different in the ME/CFS samples compared with the other groups, supporting their potential as a diagnostic tool.

Two biomarkers showed particular potential for distinguishing ME/CFS patients from other groups: cytoplasm conductivity and zeta potential. Very simply put, cytoplasm conductivity is an indicator of how easily electrical current can flow within a cell, while zeta potential is related to the elec-

**Name**
Dr Jacqueline Cliff

**Position**
Senior Lecturer

**Institution**
Department of Life Sciences, Brunel University of London

**Main research interests**
Infectious diseases; how chronic conditions affect immune responses to pathogens; immunological changes in ME/CFS and tuberculosis.

**More information**
brunel.ac.uk/people/jacqeline-cliff

trical force needed to move a charge across the cell membrane.

**Objectives**

This new study (also jointly funded by ME Research UK and the ME Association) moves the research to Brunel University London, but still involves some core members of the original team. The researchers plan to refine and expand the initial work, to give deeper insights into the biology of ME/CFS, and to move us closer to a reliable and low-cost diagnostic test.

They aim to:

- test a larger, more diverse group of patients;
- improve how samples are prepared and tested to make the results more accurate and easier to obtain;
- compare blood cells from people with ME/CFS, those with long COVID, those with multiple sclerosis and healthy volunteers; and
- explore how ion channels and plasma ions affect these differences, and test the effects of low-dose naltrexone treatment.

The researchers will use frozen blood samples from the UK ME/CFS Biobank at the London School of Hygiene and Tropical Medicine, collected from people with ME/CFS (including some with long COVID), people with multiple sclerosis and healthy controls. Fresh samples will also be collected from people with ME/CFS. Additional analyses will compare samples from people with ME/CFS post-COVID collected at baseline and after treatment with low-dose naltrexone, to assess any impact of this treatment.

**Potential benefits**

The team hopes this work will bring us closer to a diagnostic biomarker for ME/CFS, 'allowing reliable identification of the disease at an early stage'.

Optimising the methodology will mean testing more samples more efficiently, allowing even larger trials in the future to assess sensitivity and specificity, and bringing us closer to a low-cost, reliable diagnostic test.

The research will also look at the reasons behind the electrical changes seen, advancing our understanding of the underlying biology of ME/CFS.

## Blood-based biomarkers to aid ME/CFS diagnosis

*Lead researcher: Prof. Chris Ponting, University of Edinburgh*

**Background**

Developing an accurate and reliable diagnostic test for ME/CFS is one of the holy grails of research into this disease, and was identified as a priority by the ME/CFS Priority Setting Partnership in 2022.

An interdisciplinary team of researchers led by Prof. Chris Ponting at the University of Edinburgh believe a promising diagnostic approach may be to measure the levels of different proteins in the blood, which can be done accurately and cheaply.

The team includes Audrey Ryback, Ava Khamseh and Sjoerd Beentjes from the University of Edinburgh, and Caroline Dalton from Sheffield Hallam University.

A blood test for ME/CFS needs to be relatively inexpensive and non-invasive, and be repeatable in order to measure responses to treatment.

In a previous study, the team identified more than two hundred proteins whose blood levels differed significantly between people with ME/CFS and control subjects without ME/CFS. Many of these were replicated and were significant both for females and males and, importantly, could not be explained by inactivity.

While no single protein marker is sufficient on its own to distinguish between people with ME/CFS and those without, a combination of markers (or panel) might be used to form an effective diagnostic test.

**Name**
Prof. Chris Ponting

**Position**
Chair of Medical Bioinformatics

**Institution**
Institute of Genetics and Cancer, University of Edinburgh

**Main research interests**
Characterisation, classification and pathophysiology of neuromuscular diseases and ME/CFS; mechanisms of post-injury muscle fibre regeneration; and innovating therapies.

**More information**
edwebprofiles.ed.ac.uk/profile/chris-ponting

**Objectives**
The aim of the new study is therefore to develop a diagnostic test for ME/CFS based on the measurement of proteins in the blood.

1. Is an ME/CFS biomarker panel feasible?
2. Do these biomarkers reflect the mechanisms of ME/CFS or its downstream effects?
3. What is the accuracy of this biomarker panel in individuals?

Blood samples from 67 people with ME/CFS and 53 healthy controls have already been collected and stored, and the researchers will measure the levels of around 1,100 proteins in plasma, the liquid component of blood.

Machine-learning techniques will be used to classify the participants into those with and or without a diagnosis of ME/CFS, based on their blood measurements, and also to quantify the uncertainty of these predictions.

**Potential benefits**
The development of an accurate ME/CFS biomarker panel 'would be transformational for people with ME/CFS, placing their disease on a par with more established, and better treated, diseases such as multiple sclerosis and diabetes'.

In addition, the findings of the study, when combined with the results of genetic studies, could help provide 'a better understanding of disease mechanism, which improves future chances of finding an effective cure'.

# SCOTTISH GOVERNMENT FUNDING FOR ME/CFS SERVICES

Last year, the Scottish Government announced the allocation of £4.5 million per year to health boards in Scotland to recruit skilled staff and to develop sustainable services for ME/CFS, long COVID and similar conditions.

It is concerning that there was no mention of any commitment to ensure NICE-compliant provision for ME/CFS. This led Rhoda Grant MSP and ME Research UK to seek more details via Freedom of Information requests from the NHS boards across Scotland.

The requests asked for details of how each NHS board intends tailoring NICE-compliant services for those affected by ME/CFS, how they will ensure services meet NICE best practice, and what is each board's share of the allocated annual £4.5 million.

The detailed responses of each NHS board can be found on our website (bit.ly/4kJz2uk), but there were some general themes.

Some NHS boards will be collaborating with neighbouring boards to provide these services.

ME/CFS cover, previously lacking in Scotland, will be provided in conjunction with long COVID services.

NICE compliance is stated to be central, but services are largely being overlayed onto those for long COVID, with little appreciation of the specific needs of those with ME/CFS, especially those most severely affected.

It is also clear that NHS boards will rely heavily on outside agencies – not all with apparent ME/CFS expertise – to provide essential guidance.

With limited funding to NHS boards, limited knowledge and limited ambition, it remains to be seen how these new services will serve Scottish ME/CFS patients.

# KEEPING A LOW PROFILE

*Prof. Elisa Oltra and colleagues at the Catholic University of Valencia have published more findings from their ME Research UK-funded study investigating the role of human endogenous retroviruses in ME/CFS*

Human endogenous retroviruses (HERVs) are a family of viruses contained within the human genome – that is, their DNA has become part of our DNA and is passed on from generation to generation.

Most HERVs are thought to be inactive, but there is evidence that some may have a role in the development of diseases such as multiple sclerosis and type 1 diabetes. Activated HERVs may lead to the stimulation of an immune response, contributing to the symptoms of disease.

HERVs have also been proposed as potential triggers of ME/CFS, and two previous studies have reported overexpression of some HERV families in the immune cells of people with the disease.

Prof. Elisa Oltra and her team at the Catholic University of Valencia have been investigating the role of HERVs in ME/CFS in an ME Research UK-funded study, and in a recent paper they compare HERV expression profiles between groups of women with ME/CFS and/or fibromylalgia.

**What did they do?**

The researchers compared four groups of female subjects: 8 patients with ME/

CFS (diagnosed using the Canadian and International Consensus criteria), 10 with fibromyalgia (diagnosed using the American College of Rheumatology criteria), 16 with both ME/CFS and fibromyalgia, and 9 healthy control subjects.

Blood samples were taken from all participants, and peripheral blood mononuclear cells were isolated, many of which play important roles in the immune system. RNA was then extracted from these cells. RNA is a molecule which uses the genetic information in DNA to build proteins, and some viruses have RNA as their main genetic material.

High-density microarray technology was then used to assess HERV expression profiles in these samples, characterising which specific HERVs were over- or under-expressed in each sample.

**What did they find?**

Remarkably, these profiles could accurately distinguish between the four subject groups; i.e. the patterns of over- or under-expression of different HERVs were characteristic for each disease, and different from that in healthy control subjects.

This raises the intriguing possibility that these 'HERV fingerprints' may be valuable in the diagnosis of ME/CFS and fibromyalgia. However, these findings would need to be replicated in larger groups. The results also indicate increased dysregulation of HERV in patients with ME/CFS, compared with those with fibromylagia, both conditions, or healthy controls.

## HERV fingerprints may be valuable in the diagnosis of ME/CFS and fibromyalgia

Furthermore, the ME/CFS group could be divided into two subgroups with different levels of HERV expression profiles, and associated with different levels of fatigue. The authors suggest these differences may therefore help in the assessment of ME/CFS severity.

**Conclusions**

Prof. Oltra and her team have identified 'HERV fingerprints' which can distinguish between women with ME/CFS, those with fibromyalgia, those with both conditions, and healthy controls. These may therefore have value in the diagnosis of these conditions, although the findings need validation in larger groups.

The results also give clues about the underlying pathology of ME/CFS, including the influence of epigenetic factors on HERV function.

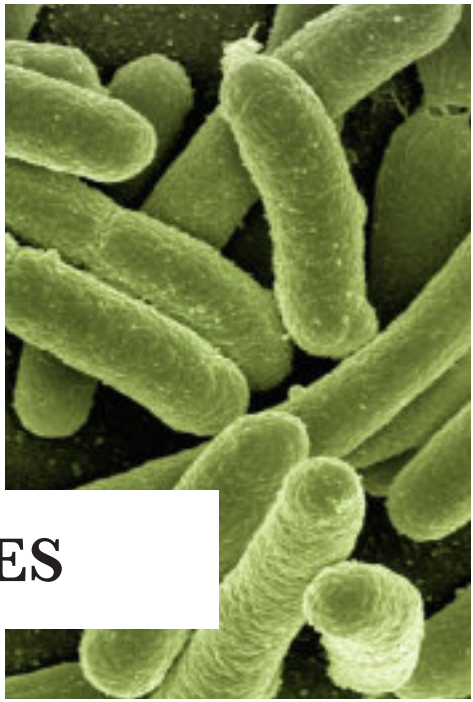
### THE BIG GIVE

Once again, we are extremely grateful to our Pledgers and to every single donor and supporter who contributed to making last year's Big Give Christmas Challenge such a huge success.

Believe us when we say that we know it was a financially tough year for so many people, and we are heartened by each and every donation received during December's event

Thanks to your support, we raised a total of £38,339 – and every penny will be invested in ME/CFS research globally.

The Big Give event raised £57.4m for 1,571 charities overall.



# RESEARCH BITES

## VITAMIN D

*Kodama, Nutrients, 2026*

Vitamin D is called the sunshine vitamin because it is produced when the skin is exposed to direct sunlight. Evidence suggests that many people with ME/CFS have a deficiency in this essential nutrient, and a recent randomised controlled trial reported improvements in several symptoms following vitamin D supplementation, including immune symptoms, pain and sleep problems. More studies are needed to confirm these effects, and it is important to consult a healthcare professional to determine whether, and at what dose, supplementation is needed.

## *COXIELLA BURNETII*

*Milovanović, Pathogens, 2025*

The bacterium that causes Q fever naturally infects many farm animals, but it may also have a role in post-infectious syndromes such as ME/CFS. A recent study suggests that *Coxiella burnetii* infection may trigger persistent autonomic dysfunction, potentially contributing to the development of ME/CFS and fainting problems in affected individuals. The autonomic nervous system regulates involuntary physiological processes such heart rate, blood pressure and respiration, and autonomic abnormalities have frequently been reported in ME/CFS.

## BREATHING PATTERNS

*Mancini, Front Med, 2025*

Researchers in New York have reported abnormal breathing patterns in a significant proportion of people with ME/CFS. They measured a variety of parameters in people with ME/CFS, and found that 42% met criteria for dysfunctional breathing during exercise, compared with 16% of healthy control subjects. Furthermore, 32% of patients had hyperventilation, compared with 4% of controls. The results suggest that breathing exercises might help reduce these symptoms in people with ME/CFS, although research is needed to assess their effects.

## BIOLOGICAL AGEING

*Nunes, Cell Death Dis, 2026*

A team of researchers has reviewed the evidence suggesting that biological ageing (senescence) of endothelial cells could be a disease mechanism in ME/CFS and long COVID. Cells enter a state of senescence following persistent stress, which might be a result of oxidative stress or viral infection. Senescence of endothelial cells can lead to blood flow abnormalities, immune dysfunction, impaired tissue repair and blood clotting problems. The authors conclude that this may be a core element of both ME/CFS and long COVID.

# MOVING FORWARD

*In November, the National Institute for Health and Care Research (NIHR) and the Medical Research Council (MRC) co-hosted a research showcase to discuss ongoing research in the fields of ME/CFS and long COVID*

The event brought together research funders, commercial and academic researchers, clinicians, and patient representatives with lived experience of the conditions. Here are some of the key themes of their discussion.

**1. Attracting new researchers into the field**

Funding opportunities specifically targeting ME/CFS and long COVID research, with requirements for the inclusion of new skills and disciplines into the field, were highlighted as a potential route to drive new activity.

Strong scientific leadership is needed to address the perceptions that the ME/CFS and long COVID pathway lacks professional viability for early career researchers.

Research culture change is needed to highlight opportunities for ME/CFS

as a viable career trajectory, and to foster more collaboration across ME/CFS and long COVID researchers across a wider range of disciplines.

Raising public and academic awareness about the importance of these conditions might attract new research teams.

Development of training and mentorship programs for early-career researchers through the NIHR Academy and with the support of NIHR RSS would be valuable.

Cross-disciplinary initiatives to make the field more accessible to researchers from diverse backgrounds should be promoted.

**2. Building a cross-disciplinary research community**

Researchers from fields such as immunology, neurology, psychology and virology should be encouraged to work with the field to establish new research collaborations and initiatives. This will help to improve understanding of the complex biological, microbiological and immunological factors underpinning these diseases.

More collaboration is needed between the ME/CFS and long COVID research communities – some of the researchers were meeting and having cross-condition conversations for the very first time.

Increasing the representation of allied health professionals at future ME/CFS events was advised, alongside considering their role in research and the formal identification of 'better care' for ME/CFS.

There was an opportunity to reframe and rebadge research efforts – for example, as 'post-acute infection conditions' – to combat stigma, attract broader support and build a cross-disciplinary research community.

Designing trials upfront with a multidisciplinary lens, including workstreams aligned to multiple disciplines, would be important. Funders have existing models for encouraging this (such as NIHR Team Science).

**3. Enhancing research collaborations**

The field requires a clear, interdisciplinary effort, bringing together clinicians, basic scientists, epidemiologists, methodologists and allied health professionals. Partnerships with clinicians and patients are deemed essential for robust study design.

Establishment of a large, inclusive virtual research hub or network in the UK to unify and consolidate efforts, which could include holding annual events, would be welcomed. The PRIME project recently funded through the MRC was proposed as a potential basis for this network.

It was recognised that the community needs strong scientific, national leadership to drive collaboration, capacity building and cultural change.

Researchers could draw on existing funding routes like the MRC Partnership Grants, NIHR Incubator and NIHR Team Science Awards.

The community is keen to explore NIHR and MRC opportunities to maintain and evolve existing collaborations such as PHOSP and STIMULATE.

**4. Funding challenges and strategy**

While the success rate for funding applications is comparable to other fields, the total number of proposals is lower. A perceived difficulty in securing funding for new fields lacking preliminary data was noted as a barrier to new proposals – routes to reassure and support the community on these points were needed. Delegates acknowledged the funders' position that funding committees showed no evidence of bias but emphasised that concerns remain in the community regarding some peer reviewers' attitudes.

Several attendees requested that MRC/NIHR provide targeted funding calls (for example, by identifying post-acute infection conditions as a theme within research infrastructure) and mandate collaboration in funding applications to ensure equity and support building the growth and expertise of this research community.

A strategic approach from the community outlining the economic impact of ME/CFS and long COVID would illustrate the importance of this research for the UK government, with the long-term ambition to ensure funding and awards secured are proportionate to the level of suffering of those living with the condition.

Sandpits bringing together clinicians and scientists to agree on priorities were suggested as a good mechanism/approach for future funding in the field.

Engaging with industry for diagnostics research was a key challenge tied to sector-wide barriers for diagnostic development – the importance and value of reliable diagnostic tools both for supporting patients and for enabling future research was clear.

**5. Focus areas for future research**

***Characterising biological mechanisms***

Noting the exciting research presented at the meeting, major outstanding questions remained in the understanding of the biological mechanisms underpinning ME/CFS and long COVID, which is vital for identifying targets for future interventions.

***Diagnostic biomarkers***

There is a critical need for research to identify new biomarkers, coupled with a need for consensus on appropriate sets of accurate, reliable and accessible diagnostic biomarkers to move beyond 'diagnosis by exclusion' and help monitor disease progression.

***Case definitions***

Beyond improved accuracy of diagnosis, better case definitions are required to understand the different patient pathways and potential disease subtypes within the population, to support both patient care and research.

***Aetiology***

Observational work is needed, investigating risk factors and genetic disposition, and finding commonalities and differences across conditions to improve understanding.

***Collaborative working***
To maximise impact and reduce the burden on patients, collaborative research initiatives, such as consortia or multi-institutional studies, should be prioritised, especially when leveraging existing data, biobank samples and patient cohorts.

***Data sharing and AI***
In parallel, it is vital to encourage the sharing of interoperable data and outcomes to build a collective, robust evidence base. There is a need for a good, structured data model for longitudinal tracking. The potential of AI, machine learning and data science is recognised, but may require additional high-quality datasets for maximum benefit.

***Interventions and treatment approaches***
There is a need for clinical trials focusing on both pharmacological and non-pharmacological interventions, including the repurposing of drugs as possible new treatments. The NIHR EME drug repurposing call was discussed as a potential source of hope, and researchers were encouraged to submit applications to this NIHR development award.

**6. Conclusions**
The event highlighted the pressing need for increased focus and collaboration in ME/CFS and long COVID research.

Moving forward, continued engagement with inter-disciplinary teams, establishing wider networks, accessing research funding, engaging industry, making better use of existing data, and the involvement of lived experience contributors will be essential for addressing the unanswered questions in these fields.

# RESEARCHER CIRCLE

*Last year, ME Research UK launched the 'Researcher Circle', an online group aimed at supporting early career researchers (initially PhD-level students) working on projects funded by the charity. Here's a bit more about the group, and an article on chronic pain by one of its members, Yanthe Buntinx.*

The intention of the Researcher Circle is to:

- Create an online space for students to network and learn about each other's work.
- Provide an opportunity for skill development through talks given by members of ME Research UK staff, from established researchers in the field, and from other relevant experts.
- Provide a friendly forum to discuss challenges faced, to practise presentations, and to lay the foundations for future careers.

Supporting researchers at the beginning of their career is essential. For many, the journey starts with PhD level research, followed by a post-doctoral position or fellowship, and then working as a principal investigator on a project level grant.

At this level, the next step is often to secure grant support from government funding bodies such as the NIHR or MRC in the UK.

This progression underpins ME Research UK's approach – from PhD level through to project grants – and the charity believes that a sustainable ecosystem of biomedical research is needed to understand the causes and consequences of ME/CFS, and to discover an eventual treatment/cure.

The Researcher Circle meets every other month, alternating between

more structured sessions with a speaker followed by time for questions, and informal 'catch-ups' which aim to provide a friendly forum to celebrate progress and discuss challenges faced, and to practise any upcoming presentations.

The first three meetings have covered a range of issues faced by early-career researchers.

- A talk from Professor Faisel Khan, one of ME Research UK's Trustees, and Professor of Cardiovascular Sciences and Associate Dean (International) at the University of Dundee, on career planning and skill development with the students.
- An informal 'catch-up' in which the students discussed topics such as career progression options, writing papers and the challenges faced when deciding where to publish an article and during the peer review process, and also the difficulties identifying sources of funding for ME/CFS research as PhD students and early career researchers.
- A session from Dr Emma Slack, Science Writer and Research Engagement Officer at ME Research UK, highlighting how important it is that researchers learn to implement methods to manage workload and wellbeing at the beginning of their careers, not only to prevent burn-out, but also to ensure that they are able to sustain high-quality research over time.

One of the goals of the Researcher Circle is to provide the students with an opportunity for skill development. Therefore, ME Research UK has created a guest blog for members of the Circle to submit a post on a topic related to ME/CFS research. Not only does writing a post for the blog offer a chance for CV development, but also for early career researchers to expand skills in areas including research communication and infographic design.

The first in the series comes from Yanthe Buntinx, who is a PhD candidate in the Pain in Motion Research Group at Vrije Universiteit Brussel Brussels, Belgium, under the supervision of Prof. Jo Nijs and Associate Prof. Andrea Polli, both of whom have received research funding from ME Research UK.

Excitingly, Yanthe's project which explores the role of T-cell dysfunction and its underlying epigenetic mechanisms in ME/CFS, recently became a joint PhD collaboration, with Prof. Lode Godderis at KU Leuven joining the supervision team.

**Chronic pain in ME/CFS: the immune system and lifestyle factors**

***Background***

Our immune system protects us from injury and infections such as those caused by bacteria and viruses. In people with ME/CFS, growing evidence shows that the immune system does not work as it should. This is important because the immune

system also plays a role in how pain develops and persists, which may help explain why many individuals with ME/CFS experience ongoing pain.

***T cells and chronic pain***

Pain is controlled by constant communication between cells of the immune system and specialised nerve endings – nociceptors – that warn our bodies of harmful signals in the environment.

Among the many types of immune cells, T cells play a particularly important role in pain: they can both increase pain and help protect against it.

Normally, T cells are carefully regulated, but when this regulation goes wrong, they can become less active. There are two important processes where T cells become less active:

- Exhaustion: where T cells become 'tired' and no longer respond properly.
- Senescence: where T cells act like 'aged' cells, similar to what happens naturally as we grow older.

Both T-cell exhaustion and T-cell senescence have been widely studied in other illnesses, such as cancer, where understanding and regulating these processes has led to new, groundbreaking treatments.

Therefore, looking closely at how T cells behave in ME/CFS could reveal important insights into the disease. Some small exploratory studies have already done this, but a large, detailed study is still missing, so no clear conclusion can be drawn yet.

In a recent article by myself and other members of the Pain in Motion research group at the Vrije Universiteit Brussel, we looked at existing information on chronic pain disorders (such as ME/CFS, fibromyalgia, rheumatoid arthritis, etc.) and immune function through a new lens: we focused specifically on T-cell

exhaustion, T-cell senescence, and everyday lifestyle factors.

***Lifestyle factors and chronic pain***

Chronic pain is shaped by [but not caused by] many aspects of daily life, including sleep, stress, physical activity and diet. Each of these factors affects pain but also influences how well our immune system works. This suggests a strong connection between a balanced lifestyle, the immune system and chronic pain in ME/CFS.

Understanding this link could help researchers uncover the biological processes that drive chronic pain, especially those related to the immune system. We found that some features of T-cell exhaustion and T-cell senescence may be linked to lifestyle factors, but current studies often show unclear or conflicting results. That's why we proposed several ways to improve how future research is designed.

***Improving future studies***

So far, many studies have looked at the immune system in ME/CFS in a very broad way. While this has helped to reveal immune dysfunction as a key contributor to the disease, it does not yet explain why or how it happens in these individuals.

To better understand the connection between the immune system and chronic pain in ME/CFS, future studies should use more consistent approaches. This includes:

- Studying larger and comparable groups of people, while carefully taking differences such as age, sex or other health conditions into account.
- Considering variations in illness severity, and changes in symptoms over time.
- Using research methods which better take into account the differences between people (known as heterogeneity) may reveal different causes or processes that contribute to ME/CFS.

> **"Looking closely at how T cells behave in ME/CFS could reveal important insights into the disease**

Transparent reporting of research methods and use of consistent definitions will make it easier to compare results across studies, and new technologies, such as single-cell RNA sequencing and advanced immune cell analysis, can also provide much more detailed insights; for example, into how T cells behave.

Finally, it is crucial to look at the role of lifestyle factors in future research. Standardised questionnaires about stress levels, sleep quality, exercise and a healthy diet will help researchers link biological findings to the real-life experiences of people living with ME/CFS.

# ONE BATTLE AFTER ANOTHER

*Prof. Bhupesh Prusty and his team have recently published results from their ME Research UK-funded study investigating how viral infections may influence the development of ME/CFS*

The group's research ties together three areas that are potentially important in the development of ME/CFS: the endothelium, the mitochondria and autoimmunity.

First, the endothelium. This is a thin layer of cells that lines the inner surface of every blood vessel. It is one of the largest organs in the body and is essential in regulating several important processes.

It controls blood flow by contracting and relaxing blood vessels, it regulates the passage of fluids from the blood to the tissues which allows the movement of immune cells, and it produces substances to prevent blood clotting.

There is a considerable body of evidence implicating endothelial dysfunction in the development of ME/CFS; in fact, some of the first studies funded by ME Research UK were in this area.

Second, the mitochondria. These are structures which are responsible for generating energy in every cell, and mitochondrial abnormalities have been implicated in ME/CFS, although their exact role is not yet clear.

Endothelial cells are highly reliant on mitochondrial signalling, so alterations in the mitochondria could have serious implications on endothelial function.

Third, autoimmunity. Immunoglobulins (also known as antibodies) play a key role in the immune system.

They are proteins produced by the white blood cells which recognise and attack harmful invaders such as bacteria and viruses.

Autoantibodies are immunoglobulins which target the body's own proteins, cells or tissues. They do have many useful functions such as destroying cancer cells or removing waste, but they can also lead to the emergence of autoimmune diseases such as multiple sclerosis or lupus.

The effects of autoimmunity may also play a role in the development of ME/CFS. However, there is a lack of clear evidence for this link, partly because the disease is so complex and because there is considerable variability between individuals.

Prof. Prusty's hypothesis is that changes to the mitochondria seen in people with ME/CFS may be due to immunoglobulins transferred in the blood plasma, and this is what his team investigated in their recent study.

**What did they do?**

The researchers obtained immunoglobulins from blood samples from 106 individuals, including 39 people with ME/CFS that had developed following an infection, 15 people with ME/CFS following COVID, 20 people with multiple sclerosis, and 41 age-matched, healthy control subjects. ME/CFS was diagnosed based on the Canadian Consensus Criteria.

These immunoglobulins were then mixed with endothelial cells which had been obtained from heathy individuals and kept in carefully regulated laboratory conditions.

The effects on the mitochondria in the endothelial cells were assessed us-

ing a high-resolution microscope to examine their structure, and other techniques to look at cellular energy use and metabolism, and the secretion of proteins that cause inflammation.

**What did they find?**

In short, the researchers found that immunoglobulins from the blood of people with post-infectious ME/CFS caused disruption to the mitochondria of the healthy endothelial cells.

Specifically, they observed fragmentation, where the mitochondria divided into smaller parts. Mitochondrial fragmentation can occur as a normal response to stress or exercise, to allow damaged parts of the mitochondria to be removed. However, uncontrolled fragmentation has been linked to neurodegenerative diseases such as Parkinson's disease.

It is worth noting that fragmentation was only seen in response to immunoglobulins from a subgroup of ME/CFS patients, and was more common using samples from women and those with post-COVID ME/CFS. Fragmentation was not seen when cells were exposed to immunoglobulins from patients with multiple sclerosis.

Immunoglobulins from people with ME/CFS also changed the cellular energetics of the endothelial cells; that is, the way in which the cells produce and use energy. However, the cells' ability to generate ATP (often called the energy currency of the cell) was not altered.

Finally, immunoglobulins from ME/CFS patients also caused the production of chemicals known to stimulate inflammation, although it was not clear whether this finding was also linked with the mitochondrial fragmentation.

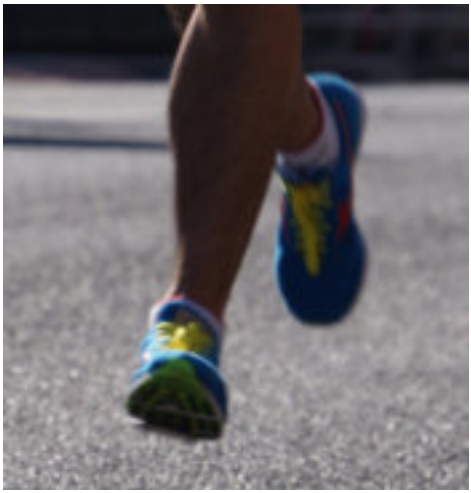
**"changes to the mitochondria seen in people with ME/CFS may be due to immunoglobulins transferred in the blood plasma**

**Conclusions**

In summary, Prof. Prusty and his team found that immunoglobulins from a subgroup of people with post-infectious ME/CFS (including following COVID) caused fragmentation of the mitochondria in healthy endothelial cells. This did not affect the cells' ability to generate ATP.

These results indicate that autoantibodies may therefore play a role in the development of ME/CFS following an infection, and give further support to the idea that autoimmunity is involved in the disease. The researchers therefore suggest considering treatment strategies for ME/CFS that target these autoantibodies.

ME Research UK is funding Prof. Prusty to follow up this work by looking more closely at the molecular mechanisms by which immunoglobulins can cause mitochondrial dysfunction (see page 5).



# FUNDRAISING

## MARATHON RUNNERS

We have several supporters taking part in marathons across the UK this year to help raise funds for ME Research UK. They include: Florence Law and Molly Davies who are running the Manchester Marathon, Chloe Tribe who is running the Brighton Marathon, and Kellie Farmer who is running in the London Marathon. Thank you so much to those four and to everyone else running for us in 2026. And good luck to you all. You can read all about them on our website, where there are also links to their JustGiving pages. bit.ly/4rvlkgb

## EDINBURGH'S SANTA

Meet Nick, the Edinburgh resident who keeps Santa alive in the capital. Throughout December last year, Nick wrote 189 Santa letters to fundraise in aid of ME Research UK. 'I've been writing these letters from Santa for 6 years now, so they've become as part of the Christmas tradition to me as mince pies, paper chains and leaving carrots out for the reindeer! I'm a firm believer in the idea of Christmas spirit though. People are kind across the year, but are extra kind at Christmas, and the donations they have made shows this. Thank you to everyone who supported the letters. I'll see you next Christmas to do this all again.'


## WALK FOR ME

This year's Walk for ME fundraising scheme has been launched, and ME Research UK is grateful to be chosen once again as one of two charities to benefit. The initiative invites people – especially the family and friends of people living with ME – to do a sponsored walk, run, swim or ride of whatever length they feel comfortable with. Since it started in 2013, Walk for ME has raised well over £238,000 for ME research charities. Please visit our website to learn more about the scheme and to see a handy guide on how you can take part. bit.ly/4chsbq9

## DESK DOLLS

Do you want to support ME Research UK with a new friend on your desk? Then look no further. Fun Notty Artefacts are selling crochet patterns for ME Awareness Desk Dolls, with all the proceeds donated to ME charities in the UK, including ME Research UK. The designer says, 'I was diagnosed with ME in 2001 and created a beginner-friendly crochet pattern during periods of illness as a gentle, creative way to cope.' You can buy the pattern via Etsy. etsy.me/3OyQ0zJ

*For more inspiration about ways you can help raise funds, please visit* ***meresearch.org.uk/support-us***.


Scan to donate to
ME Research UK
via Wonderful.org