NEWS OF THE ME RESEARCH YOU ARE HELPING TO FUND

breakthrough

ME RESEARCH UK

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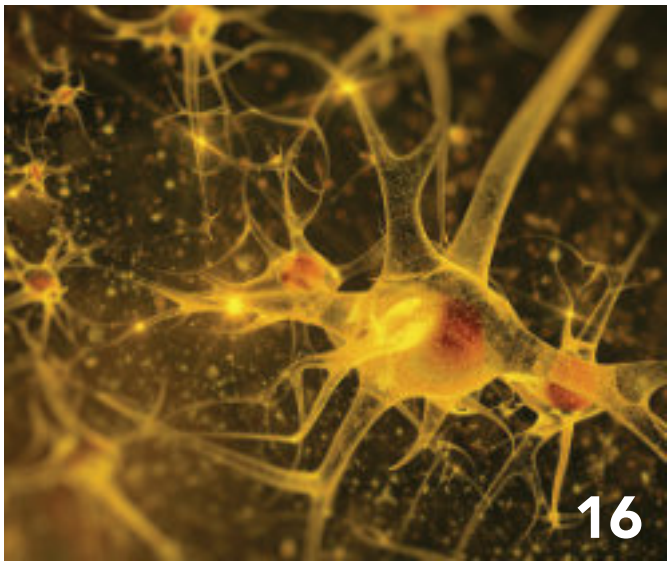

Breakthrough magazine is published by ME Research UK, a Scottish Charitable Incorporated Organisation with the principal aim of commissioning and funding high-quality scientific (biomedical) investigation into the causes, consequences and treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (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.

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In this issue

In the spotlight

What's happening in the world of ME research and funding

Editorial

"The Times They Are a-Changin'". Bob Dylan may have written this song nearly sixty years ago, but the last six months have certainly seen a lot of change.

Despite the turmoil, we remain hopeful that the initiative started by Sajid Javid will continue to fruition, and we plan to remain actively engaged in the development of a research strategy to inform a cross-government delivery plan for ME. Many challenges lie ahead, but we are committed to doing our utmost to effect positive change. There's more on pages 4 and 5.

We are delighted to welcome Dr Keith Geraghty to our team, and page 7 gives a little of his background and his new role with us. One of his first tasks was to attend the 2022 IACFS/ME conference, and his report on this large event is on page 6.

Nuno Sepúlveda has now published interesting results from his study looking for EBV biomarkers, and plans a follow-up. Full details are on page 9. We were also delighted to announce our second PhD grant (jointly funded with Action for ME) at King's College London, which is focused on the genetic basis for ME. Page 11 gives more details.

Our latest call for grant applications generated significant interest from researchers globally, and we now have over £1 million of potential research going through our review process.

Cort Johnson's latest 'postcard from Nevada' is on page 13, and provides a fascinating insight into three areas of research that warrant further exploration.

On page 16 you can read a round-up of recently published research, a common theme being the continuing need to see follow-up studies to replicate findings and provide the spur for large-scale research projects.

Of course everything we do is only possible as a result of your support. This issue, in particular, highlights some wonderful examples of the fundraising activities that help us continue our work on your behalf.

On a final note, Christmas is just around the corner(!) and our Christmas card collection is now available for purchase.

Thank you for your continued support and enjoy the issue.

Jonathan Davies
Chair, Board of Trustees

Christmas Cards 2022

Our Christmas cards are now available to order (for residents of GB, the Isle of Man and the Channel Islands only).

There's a great selection to choose from, and you can also order online at shop.meresearch.org.uk. As always, the proceeds go to help support our work.

If you would prefer not to send a physical card, dontsendmeacard.com has a good selection of digital cards and allows you to make a donation to us.

The Big Give

The Big Give Christmas Challenge is the UK's largest matched-funding campaign, and ME Research UK is taking part again this year.

Supporters have already pledged £7,000, so the first £7,000 of donations made on the Big Give's website from midday on 29 November until midday on 6 December 2021 will be matched by the pledgers. Each donation is doubled.

We may also be chosen for Charity Champion funding, which would add a further £7,000 to the pledge pot.

Information on how to make a donation will be on our website and social media during the campaign. As always, all funds we raise will be invested in ME research globally.

Rollercoaster summer

UK Government commits to ME research

ME Awareness Day, on 12 May 2022, kicked off an exciting couple of months as hopes were raised of a new era for ME/CFS research funding, and UK Government commitment to listen and believe those affected.

It started with the publication of the results of the ME/CFS Priority Setting Partnership (PSP), which aimed to "identify and prioritise evidence uncertainties in particular areas of health and care that could be answered by research".

The top ten plus priorities they arrived at are summarised in the box opposite.

At the same time, the Rt Hon. Sajid Javid, then Secretary of State for Health and Social Care, issued a very welcome statement pledging the Government's support of these priorities, and announcing a cross-Government delivery plan for ME/CFS.

The next stage was a meeting co-chaired by Mr Javid and the Chief Scientific Adviser, Professor Lucy Chappell.

This was attended by funders, researchers, charities and people with ME/CFS, and ME Research UK was represented by our Chair, Jonathan Davies.

Under discussion were the research priorities identified by the Priority Setting Partnership, the overlaps with long COVID, the need to encourage new researchers into ME/CFS, and how research funding can be improved.

The newly formed subcommittee on ME research (under the guidance of the UK Clinical Research Collaboration) then had its first meeting on 30 June.

Unfortunately, these exciting

developments were put into question with the resignation of Mr Javid on 5 July.

The flurry of activity in the preceding couple of months meant that meetings between researchers, charities, patient representatives and the Health Department have already taken place, covering patient experience, education and training, and research.

Furthermore, a structure with a task and finish group and three sub-committees has already been established, and a number of constructive meetings held. ME Research UK attends the ME/CFS Research Working Group. It is envisaged that the process will culminate in the publication of a wide-ranging delivery plan on ME/CFS within two years.

Whatever the outcome, ME Research UK remains committed to investing in the very best ME/CFS research.

Top 10 (or 11) ME/CFS research priorities of the PSP

1. What is the biological mechanism that causes post-exertional malaise (symptoms caused or made worse by physical, mental or emotional effort, which can be delayed) in people with ME/CFS? How is this best treated and managed?
2. Which existing drugs used to treat other conditions might be useful for treating ME/CFS, such as low dose naltrexone, or drugs used to treat Postural Orthostatic Tachycardia Syndrome (POTS)?
3. How can an accurate and reliable diagnostic test be developed for ME/CFS?
4. Is ME/CFS caused by a faulty immune system? Is ME/CFS an autoimmune condition?
5. Are there different types of ME/CFS linked to different causes and/or how severe it becomes? Do different types of ME/CFS need different treatments and/or have different chances of recovery?
6. Why do some people develop ME/CFS following an infection? Is there a link with long COVID?
7. What causes the central and peripheral nervous systems (brain, spinal cord and nerves in the body) to malfunction in people with ME/CFS? Could this understanding lead to new treatments?
8. Is there a genetic link to ME/CFS? If yes, how does this affect the risk of ME/CFS in families? Could this lead to new treatments?
9. What causes ME/CFS to become severe?
10. How are mitochondria, responsible for the body's energy production, affected in ME/CFS? Could this understanding lead to new treatments?

10+. Does poor delivery or use of oxygen within the body cause ME/CFS symptoms? If so, how is this best treated?

A time for optimism

Key themes from the 2022 IACFS/ME conference

The annual conference of the IACFS/ME took place in July, and Dr Keith Geraghty, our new Science and Research Lead, attended on behalf of ME Research UK.

Taking on a new look post-COVID, the conference was hosted in a virtual auditorium for attendees to mingle and present their latest research findings. There were 58 speakers, 20 poster entrants and almost 300 attendees, including many early-stage researchers. This growth in numbers reflects increasing interest in ME/CFS among scientists and health professionals internationally.

Long COVID

The most striking difference from previous conferences was the inclusion of long COVID, with multiple talks on fatigue following acute COVID-19. One peculiar upside of the pandemic is that it has reinvigorated the scientific community to reconsider and investigate post-viral fatigue, with obvious benefits for ME/CFS research.

Prof. Akiko Iwasaki from Yale Medical School provided an especially insightful talk on the biochemical signatures of long COVID, and presented results showing how she was able to identify and differentiate long COVID patients based on blood analysis of immune markers, antibodies and hormones.

POTS

Postural tachycardia syndrome (POTS) – an abnormal increase in heart rate after sitting up or standing – was perhaps the central theme of the conference. For example, Lauren Stiles of Stonybrook University spoke about the high prevalence of POTS in both ME/CFS and long COVID, highlighting the many tests that could be performed to identify POTS, and the treatments available to treat the condition.

Inflammation upregulated

Inflammation of the brain and central nervous system was another major theme, and Dr Gunnar Gottschalk of the Simmaron Research Centre spoke about the role of ATG13, a protein involved in causing damaged or infected cells to die off. ATG13 is strongly upregulated in the blood of ME/CFS patients, indicating impairment in this process.

PEM

Another highlight was an illuminating talk by Dr David Systrom from Brigham and Women's Hospital. He spoke about the pathophysiology of post-exterional malaise (PEM), and how it can be provoked and investigated by a stress test. He believes POTS and PEM are related, and the primary cause may lie in the mitochondria.

You can read Keith's full reports from this year's conference on our website.

Dr Keith Geraghty

Meet our new colleague

We are delighted to welcome Keith onto the team as the new Science and Research Lead for ME Research UK.

His first work for the charity has been to establish a steady stream of articles on our website and social media, keeping supporters up-to-date on new ME/CFS research news.

Keith is already well known and respected in the ME/CFS field. He is an experienced health researcher who has published more than thirty papers and articles. But he also brings the perspective of a person with ME/CFS, having been diagnosed with the illness several years ago.

He grew up in Ireland, and moved to Wales to study at Cardiff University (partly due to its proximity to the Brecon Beacons and opportunities for hillwalking).

After graduating, he got his PhD and started a postdoctoral career, but then moved into clinical medicine as he wanted to do more directly with patients.

During his training Keith contracted an unexplained viral illness, leaving him very unwell and incapacitated for several years. His doctors were perplexed by his symptoms and diagnosed post-viral fatigue and chronic fatigue syndrome.

He recalls how such an illness had hardly ever been mentioned at medical school, meaning he had little understanding of his own prognosis.

Having a background in research, Keith felt compelled to look for answers for himself. He started researching ME/CFS by speaking to experts and reading the literature, and then returned to academia as a research fellow at the University of Manchester.

His work has included writing about the lack of evidence and potential harms of CBT and GET, as well as highlighting the methodological flaws in the PACE study. He advocated for a new approach to ME/CFS – one that recognises the biological features of the illness and their pathophysiologic basis. He was also commissioned by NICE to present evidence on the views of people living with severe ME/CFS during their guideline review.

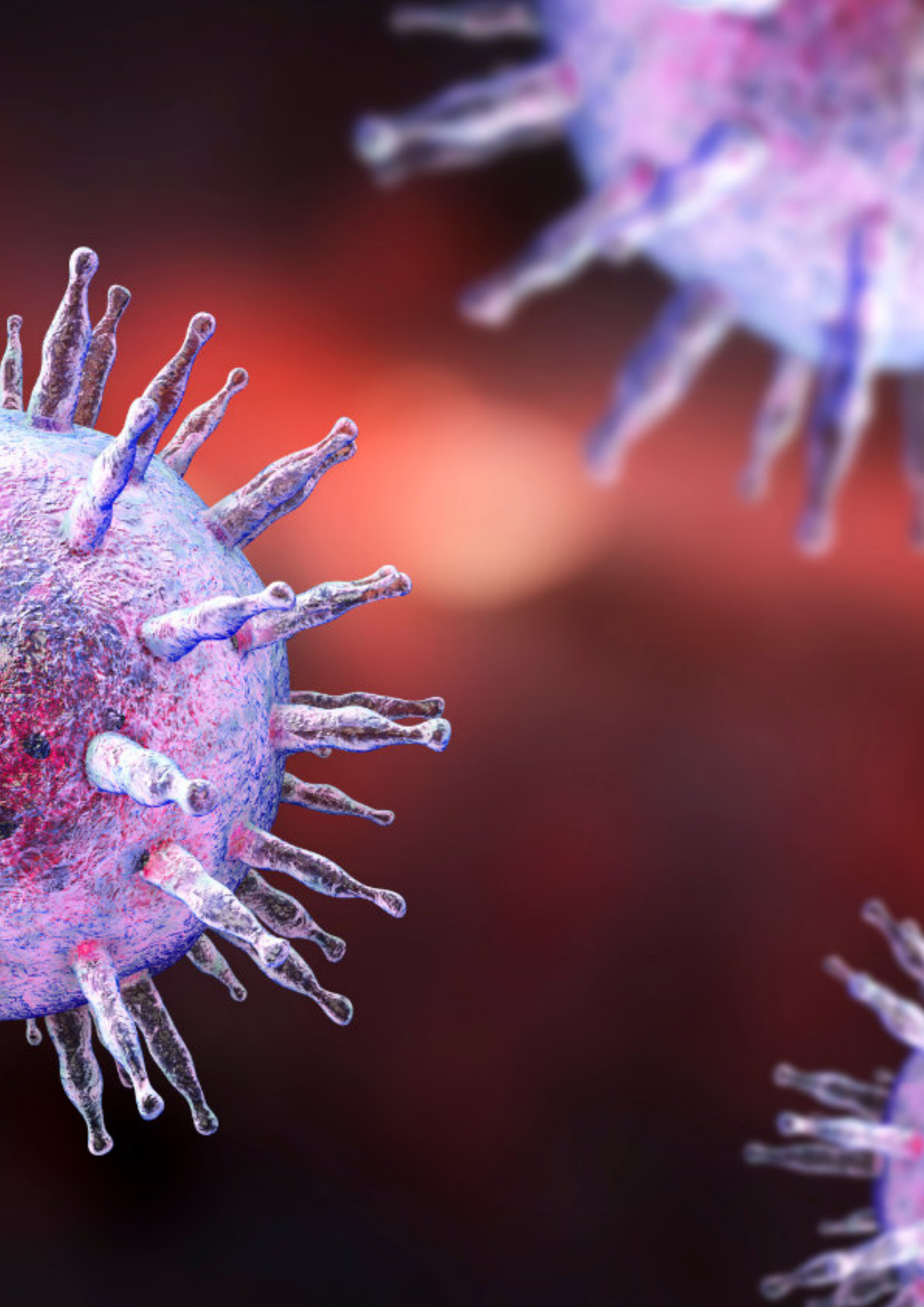
So Keith has considerable knowledge of ME/CFS, and brings a wealth of experience to his new role in ME Research UK, and we very much look forward to working with him.

Christmas shopping

When you shop online for Christmas this year, you could also be raising funds for ME Research UK, at no extra cost to you.

Visit smile.amazon.co.uk and select ME Research UK as your chosen charity, or use easyfundraising.org.uk which hosts some of the UK's best online stores.

Not only will you be accessing some great deals, but you will also be raising funds for ME Research UK without costing you an extra penny.



Signature style

Nuno Sepúlveda and colleagues have published results from their study looking for **EBV biomarkers in ME/CFS**

The emergence of long COVID has highlighted the potential long-term consequences of a viral infection, leading to symptoms such as fatigue, muscle pain and brain fog that can last for weeks or months.

These symptoms are shared by people with ME/CFS, many of whom also report a viral trigger for their illness. But which viruses are associated with ME/CFS, and how might this information help in its diagnosis?

One candidate is Epstein-Barr virus (EBV), long suggested as a trigger for ME/CFS. In his recent work, funded by ME Research UK with the support of the Fred and Joan Davies Bequest, Dr Nuno Sepúlveda from the London School of Hygiene & Tropical Medicine has been taking another look at this important pathogen.

Nearly all of us are infected with EBV at some time in our lives, and in most cases our immune system can fight it off. But the virus is known to cause several diseases (including autoimmune conditions), and people with ME/CFS are often found to have active EBV infections or antibody reactivity against EBV.

Antibody signatures

In previous experiments – using data from Prof. Carmen Scheibenbogen's group at Charité Universitätmedizin Berlin –

Dr Eliana Lacerda

Dr Nuno Sepúlveda

Prof. Carmen Scheibenbogen

Dr Sepúlveda identified a number of EBV-derived proteins (antigens) that were increased or decreased in ME/CFS patients compared with control subjects.

He has now extended this work by looking specifically for antibody signatures that could serve as biomarkers for ME/CFS, and focusing on patients with an infectious trigger at their disease onset.

The research was conducted in collaboration with a number of other researchers, including Prof. Scheibenbogen in Berlin, and Dr Eliana Lacerda at the London School of Hygiene & Tropical Medicine.

The group analysed antibody responses against 3,054 EBV-derived antigens in 92 patients with ME/CFS and in 50 healthy control subjects. Fifty-four of the patients reported an acute infection at the time their disease began.

The first round of analyses did not find any antibodies associated with ME/CFS, but this changed when the patients were divided into subgroups based on their disease onset.

Infectious trigger

While there were still no associations among those with a non-infectious or unknown disease trigger, in ME/CFS patients with an infection at disease onset two antibody responses were stronger than seen in healthy controls.

Further analyses showed that these two responses could distinguish this subgroup from controls with a high sensitivity and specificity, and may therefore have potential in the diagnosis of these ME/CFS patients with an infectious trigger, specifically those affected by EBV.

The researchers plan to confirm these findings in other cohorts of patients from the UK ME/CFS Biobank. They also suggest that the EBV-derived antigens identified may provide some evidence of how the reactivation of EBV plays a role in the development of ME/CFS.

As Cort Johnson pointed out on our website last year, viruses haven't gone away in ME/CFS, they've just got more interesting.

A new class

New PhD-level research looking at **the involvement of RIPs in ME/CFS**

In June of this year, ME Research UK and Action for ME were delighted to announce joint funding for a PhD-level research project at King's College London.

This is our second PhD-level research project, and our first such funding collaboration with Action for ME.

The new project is being conducted by PhD student Luke Marney, under the supervision of Dr Alfredo Iacoangeli, and is focused on the genetic basis of ME/CFS.

The biological abnormalities leading to the development of ME/CFS are not well understood, but genetics are thought to play an important part. This new project will look at a specific type of genetic variation called an RIP (retrotransposon insertion polymorphism).

Retrotransposons are pieces of DNA often referred to as jumping genes because they can move around within the genome of a cell, potentially causing mutations (RIPs) that can change the function of that cell.

RIPs have been implicated in the development and progression of disorders such as motor neurone disease and Parkinson's disease, and this project aims to use genetic-sequencing data from the UK Biobank to determine if a specific RIP or set of RIPs is also involved in ME/CFS.

As well as contributing to a better understanding of ME/CFS, this research may help identify new directions for treating the disease.

Both charities are excited by the opportunity to work together, and to help support this important new research and a PhD student at the start of his career.

Call for applications

In the 22 years since our formation, ME Research UK has funded 60 research projects at a total cost of nearly £3 million. But we are certainly not stopping there.

In July, we announced a new call for applications for our research grants, and these are currently progressing through our rigorous review process.

So we hope to be able to announce more new ME/CFS research in the months ahead – more progress in understanding the disease better and in finding a cure.


BATTLE BORN
Welcome to
NEVADA

Postcard from Nevada

In his latest postcard, **Cort Johnson** looks at some of the roads not (yet) taken in ME/CFS research

This is potentially a rich time for ME/CFS research. The recent long COVID studies present a picture of a disease that – with issues relating to low cortisol, exercise, immune exhaustion, Epstein-Barr virus reactivation and blood vessel abnormalities – looks uncannily similar to ME/CFS. It seems as if broad themes are beginning to emerge.

That's good news, but ME/CFS is a complex and poorly funded disease. Its research history – now dating back almost forty years – includes some efforts that didn't pan out, some that did, and some that seemed to pan out but for one reason or another were dropped or never fully explored. Let's take a look at three of those unexplored roads.

Brains on fire?

Neuroinflammation sticks out here like a sore thumb. The 2014 Nakatomi study – which contained a mere nineteen participants – was heralded as one of the most potentially important studies in ME/CFS history. There was good reason for that: low levels of widespread neuroinflammation made sense given what we know about the disease.

Since then, neuroinflammation and activation of microglia (immune cells in the brain and nervous system) have become hot topics. They were featured prominently in three recent hypo-


Cort Johnson

theses. Researchers are currently hunting for effective microglial inhibitors, while modelling studies suggest that neuroinflammation may need to be addressed first for other treatments to succeed.

Yet despite all this interest, in the eight years since the publication of the Nakatomi study, only two small studies have been published – a Dutch study and Jarred Younger's thermography study, which produced conflicting findings – leaving the ME/CFS field in the dark about whether or not it really exists.

That's a shame. The finding of neuroinflammation would potentially align ME/CFS with well-funded neurological diseases such as multiple sclerosis, Parkinson's disease and Alzheimer's disease. Researchers are actively searching for ways to 'quench the fires' in these conditions. Documenting that neuroinflammation exists in ME/CFS could further legitimise it and ultimately open up new treatment opportunities.

Neuroinflammation studies are thankfully underway in long COVID. Perhaps Jarred Younger's ongoing, ME Research UK-funded study looking at immune cell infiltration of the brain will take a few more steps towards answering this question for ME/CFS.

The paradox

Evidence suggests there is a paradox in both ME/CFS and postural orthostatic tachycardia syndrome (POTS).

The low blood volume found in both these conditions should trigger the renin-angiotensin-aldosterone system (RAAS) to help maintain blood pressure. This system involves an increase in renin, leading to production of angiotensin which then stimulates the release of aldosterone.

However, renin and aldosterone levels are low in these conditions. And, to make matters more confusing, angiotensin levels are very high.

Hence the paradox – in the midst of low blood volume levels, the end product of the RAAS system, aldosterone, which should be increased, is actually lower than normal.

The are two arms to the RAAS system. One turns on angiotensin II which triggers a bunch of activity (blood vessel vasoconstriction, sympathetic nervous activity and inflammation) we probably don't want happening in ME/CFS. The other (less active in ME/CFS) is anti-inflammatory. Two studies have implicated a culprit: reduced activity of the ACE-2 enzyme.

All in all, it's a pretty important system to have received almost no research in ME/CFS. But here's where it really gets interesting.

In a bizarre coincidence, it turns out that the coronavirus enters cells through the same ACE-2 receptor that appears to be malfunctioning in ME/CFS and POTS.

That's led to the same scenario being suggested for COVID-19, ME/CFS and POTS: reduced ACE2 activation and increased activation of the classical or inflammatory arm of the RAAS.

The reduced ACE2 activation could be responsible for a lot of mischief. It's been associated with impaired oxygen uptake, increased oxidative stress, leaky gut, problems with lung perfusion, reduced vasodilation of the blood vessels and inflammation.

It's even been suggested that the increased angiotensin II could be causing negative reac-

tions to the coronavirus vaccines. That's an interesting possibility given the high angiotensin II levels found in ME/CFS.

There's a big problem, though. Despite its potential for mischief, let alone its possible connection to COVID-19 and long COVID, because only two small studies of the RAAS system have been done in ME/CFS, we don't really know if the RAAS is a real problem or not. Surely though it's a research area that could use more exploring.

The gender issue

From the very beginnings of this illness, it's been clear that it strikes many more women than men. But, decades later, it's remarkable how little we know about this phenomenon.

Hampered by low funding, small sample sizes and the complexity of the hormonal system, gender has rarely been considered. Some ME/CFS and fibromyalgia research has coped with the issue simply by locking men out of their studies.

If you're not a man that's not a bad strategy as the gender issue in ME/CFS could be a huge one. Studies suggest that men and women have altered gut microbiomes, heart rate variability, responses to exercise and micro RNA patterns – and this may just be the tip of the iceberg.

There are some clues as to what is happening. An increased incidence of ME/CFS during times of major hormonal changes (adolescence, pregnancy, perimenopause) points at the sex hormones being involved. So do the higher rates of gynaecological disorders, pelvic pain, menstrual abnormalities and surgeries (especially hysterectomies).

Models suggest that the higher testosterone levels found in men may be protective, while high oestrogen levels in women may increase their risk. Likewise, high progesterone and testosterone levels appear to protect against pain in fibromyalgia, while low progesterone and high cortisol promote it.

With similar gender imbalances found in ME/CFS, long COVID, fibromyalgia, postural orthostatic tachycardia syndrome, migraine and more, it's clear we'll never fully understand these diseases until the gender imbalance is explained.

In a field scrapping for funds, the gender imbalance problem presents an added complication that most funders would understandably rather not deal with. The cure for that problem – as with all of these unexplored avenues – is a straightforward one: more funding.

Long COVID should be getting that funding. And if those scientists take the time to check out ME/CFS research, they will find some rich veins to mine.

Research bites

Our round-up of recent research from around the world

Reading the signs

Che et al., International Journal of Molecular Science, 2022

When the body breaks down nutrients to generate energy (a process called metabolism), it produces substances known as metabolites. The study of these metabolites (metabolomics) can tell us more about the activity and state of cells and tissues, and has proved useful in understanding the causes of disease and identifying biomarkers.

Some examples of its application to date include advances in knowledge about ischaemic stroke, hypertensive nephrosclerosis and glaucoma. And this is the approach used in a recent ME/CFS study conducted by researchers at Columbia University.

The investigators found that levels of a number of important metabolites were abnormal in patients with ME/CFS compared with healthy control subjects. Some metabolites were found to be at lower than normal levels, while others were higher than normal.

According to the researchers, their results suggest that lipid remodelling is impaired in these patients. Lipids are important components of every cell wall or membrane, and lipid remodelling is involved in maintaining the cell membranes, as well as signalling between cells.

These findings, if confirmed in other studies, may ultimately help us understand more about the disease process, and potentially develop biomarkers for diagnosis.

Mitochondrial supplement?

Cash & Kaufman, J. of Translat. Med., 2022

One metabolite potentially depleted in ME/CFS is oxaloacetate, and anecdotal reports suggest that an oxaloacetate supplement may improve physical and mental fatigue in some patients. When it was tested in a trial of 76 ME/CFS patients, treatment with these capsules did appear to reduce fatigue by around 25% (assessed using a questionnaire). However, the study did not have a placebo arm and it was not randomized – both considered vital in assessing the efficacy of treatments. A more rigorous trial is therefore needed to support the findings.

Is fibromyalgia similar to ME/CFS?

Ramírez-Morales et al., Autoimmun. Rev., 2022

There is much debate about whether fibromyalgia (FM) and ME/CFS are similar illnesses. While they share common symptoms such as pain and fatigue, there are differences in their apparent causes and presentation. An analysis pooling the results of 21 studies found a well-defined clinical overlap between the two conditions – almost half of FM patients met diagnostic criteria for ME/CFS. The authors say this might reflect a similar underlying cause, such as a history of viral infection leading to autonomic dysfunction and chronic inflammation.

Predicting severe ME/CFS

Jason et al., Journal of Rehabilitation Therapy, 2022

Around 10% of individuals with infectious mononucleosis (mono) meet diagnostic criteria for ME/CFS six months later. To investigate whether they could predict this, researchers looked at several factors in college students who had developed ME/CFS following mono. Patients with gastrointestinal symptoms, an irritable bowel and abnormally low immune markers at the time of mono had an almost 80% chance of developing severe ME/CFS six months later. These findings support the importance of these factors in the development of ME/CFS.

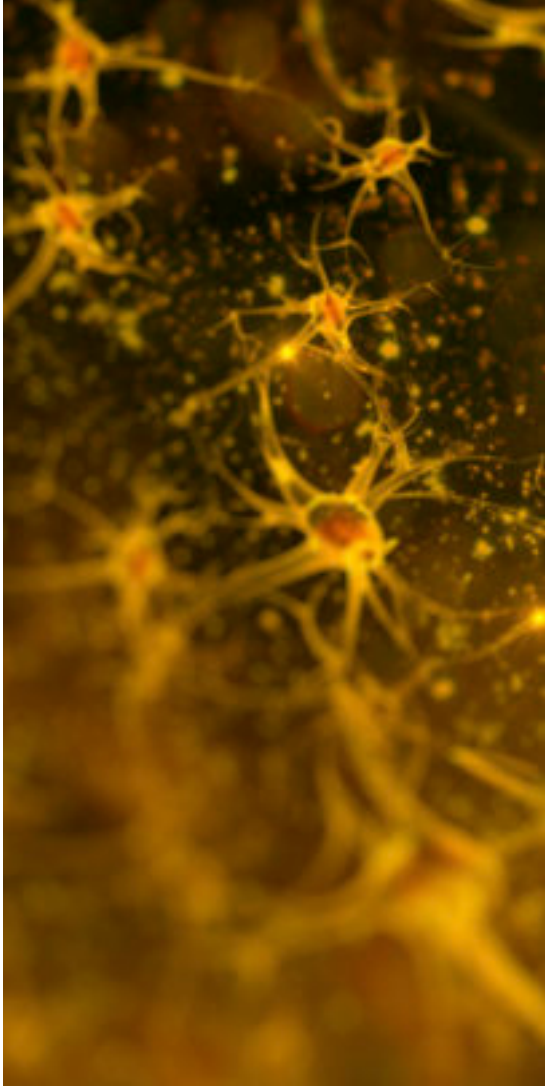
Transmission electron microscopy

Jahanbani et al., PloS One, 2022

Transmission electron microscopy (TEM) represents a step up from traditional light microscopy because the beam of electrons used can provide much higher resolution images and so capture much finer details. But what can the technique tell us about ME/CFS? Researchers at Stanford University used TEM to look at immune cells from people with the illness, and their findings suggest that an increased number of these cells are dying due to apoptosis (programmed cell death) or necrosis (caused by damage). They also found abnormalities in the mitochondria (which generate energy in the cell).

Changes in the hippocampus

Thapaliya et al., J. of Neuroscience Res., 2021



Recent research from Australia suggests that symptoms of ME/CFS such as fatigue, pain and sleep disturbance may be linked to structural changes in a part of the brain called the hippocampus. This region is involved in cognition, memory and regulation of the hypothalamus. Using a technique called magnetic resonance imaging, the researchers found that volumes of specific areas of the hippocampus were greater in ME/CFS patients who met the strict International Consensus Criteria (ICC) than they were in healthy control subjects. This was not the case in patients who met only the more general Fukuda diagnostic criteria for ME/CFS.

Furthermore, increases or decreases in the size of different areas of the hippocampus were associated with symptoms including fatigue, pain, sleep disturbance and physical function, and these links were stronger in ICC patients. The researchers suggest that their findings indicate the hippocampus may be involved in some of the symptoms of ME/CFS, including brain fog, memory problems and the ability to do complex tasks. However, the results need to be replicated on a larger scale to confirm this.

Orthostatic intolerance

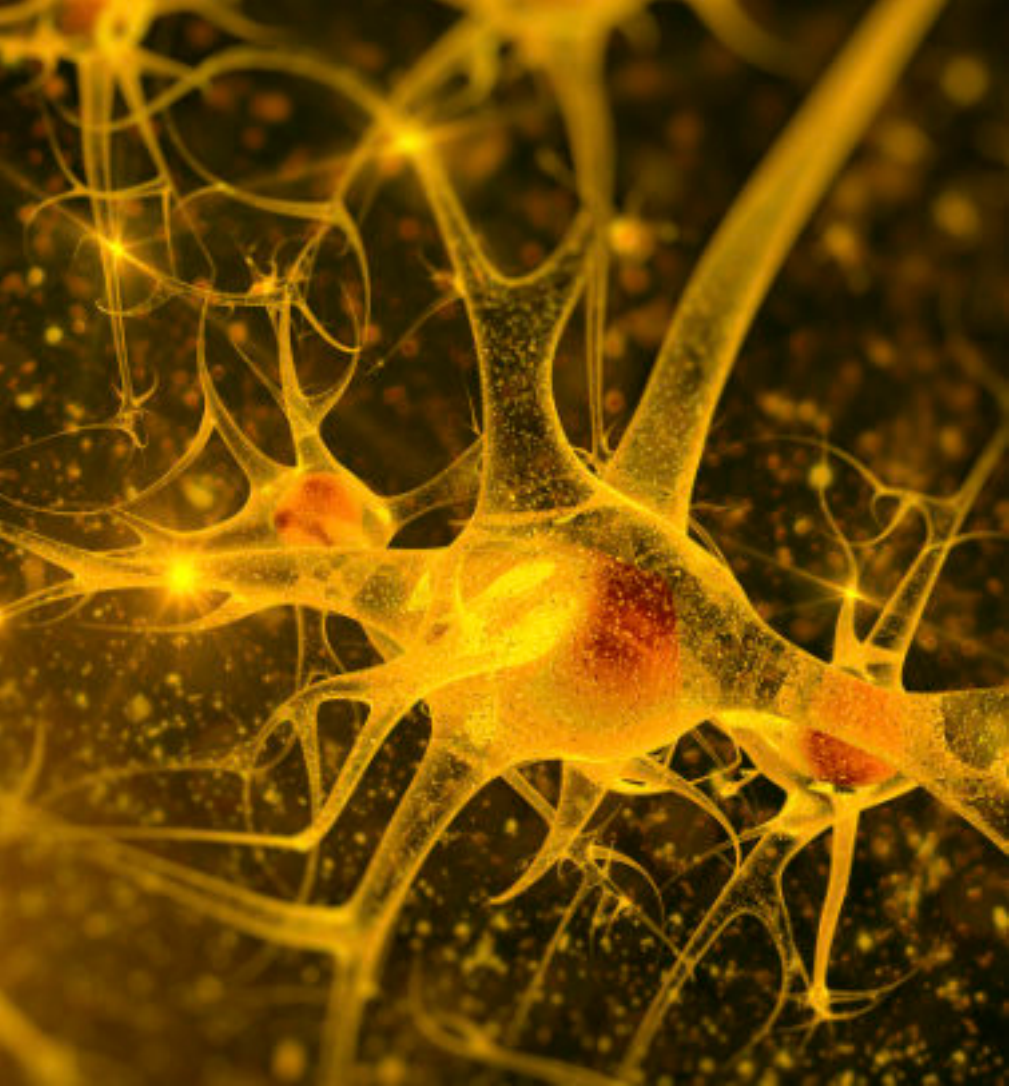
Vernon et al., Frontiers in Medicine, 2022

ME/CFS and long COVID may both be associated with orthostatic intolerance – abnormal dizziness or fainting after standing. In this study of patients with either illness, symptoms and other measures were assessed following a NASA Lean Test involving periods of sitting up, lying down and standing up. The test worsened symptoms in both patient groups (but not in controls), and caused narrowing of the pulse pressure and worse cognitive reaction times. The researchers therefore recommend an orthostatic stress test for all patients with ME/CFS or long COVID.

Measuring sleep

Yang et al., Quality of Life Research, 2022

Sleep disturbances are a significant but perhaps under-researched symptom of ME/CFS, so it is important to be able to measure sleep quality and its impact on quality of life in people with the illness. The patient-reported outcome measurement information system (PROMIS) has been designed to assess sleep disturbance, sleep-related impairment, pain interference and pain behaviour. This study from the USA shows that the system performs well in patients with ME/CFS for all four of these measures, and the authors suggest it could be used both in research and in clinical practice.

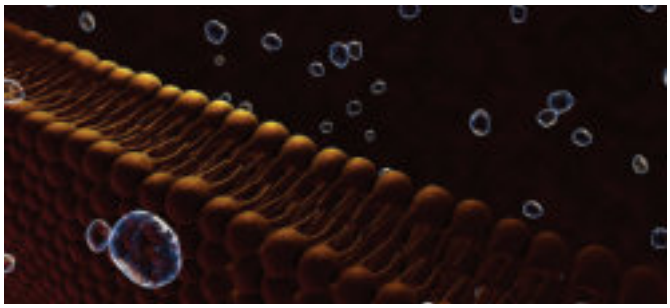


"hippocampus may be involved in some of the symptoms of ME/CFS"

Immune function in adolescents

Jason et al., Chronic Illness, 2022

There is some evidence of immune dysfunction in adolescents with ME/CFS, although this is varied. To investigate the question more closely, researchers in Chicago took blood samples from youths aged 5 to 17 years with ME/CFS, including a group with severe disease. An analysis of the cytokines in the blood (which are involved in regulating the immune system) identified a pattern suggesting active inflammatory responses, and this was particularly strong in those with severe disease. The researchers suggest this may help in identifying a biomarker for paediatric ME/CFS.



Ion channel function

Sasso et al., Molecular Medicine, 2022

TRPM3 is an ion channel responsible for transporting ions such as calcium between cells – a process which is crucial for their normal function. The finding of impaired TRPM3 activity in immune cells from patients with ME/CFS suggests that this may be an important feature of the illness, and could potentially be treated using a drug to restore the influx of calcium into the cell. Now, research from Australia has found similarly impaired TRPM3 ion channel activity in cells from patients with long COVID – more evidence of the similarities between ME/CFS and long COVID.

Fundraising stories

Recent fundraising activities by our supporters.
To support ME Research UK, please visit our website for ideas.

Viking Coastal Trail

Watching out for longboats on the horizon this August were Grace Mitchell and her mum Tracey, who walked the eight-mile Viking Coastal Trail to raise funds for ME Research UK. The Trail begins near Ramsgate, following clifftop paths to link numerous bays through Margate and along the sea wall to Westgate-on-Sea, until it reaches Reculver Country Park. Thank you so much to Grace and Tracey and their supporters for fundraising for us, and for keeping the coast of Kent safe from marauders.

100 miles done

Terry Smith and his daughter Poppy continue their adventure crossing the country from Liverpool to Goole by canoe. Taking it section by section, as of writing they had completed more than 100 miles of the 162-mile trip. Terry's blog has kept supporters up to date with their progress and sights along the way, including lots of birdlife such as ducks, geese, herons and swans. Keep going Terry and Poppy! You can support them here: bit.ly/3odEvg9.

Wakeboarding for ME

Congratulations and many thanks to Finlay Scott who completed his challenge to wakeboard 50 km in one day to raise awareness and money for research into ME/CFS, which has had a devastating impact on his younger sister.

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01 Terry Smith reaches 100 miles by canoe

02 Finlay Scott wakeboarding for ME

03 24 hours of solid sport

04 Kathryn Aveyard faces up to her challenge

Mont Blanc

Kathryn Aveyard has set herself the monumental task of climbing Mont Blanc in aid of ME Research UK. This multi-day hike is a significant challenge requiring the use of specialised equipment such as crampons and ice axes. "I have been training to try and improve my endurance and lung efficiency. Supposedly, due to the altitude, the summit day is more challenging than running a marathon." Thank you and good luck, Kathryn. You can support her here: bit.ly/3zDvvrA.

24-hour warriors

From 9 a.m. on Friday 27 May, as part of Team 24 Hour Sportathon Warriors, Chrissy Nazif completed a 24-hour sportathon to raise money for ME Research UK and The Link Foundation (which supports local children and families in Maidenhead). Over the course of this period, the team took part in more than 24 different sports – "a dream come true for some, a nightmare for others!" Thank you so much to Chrissy and the rest of the warriors for their efforts, which raised a terrific total for the charities.

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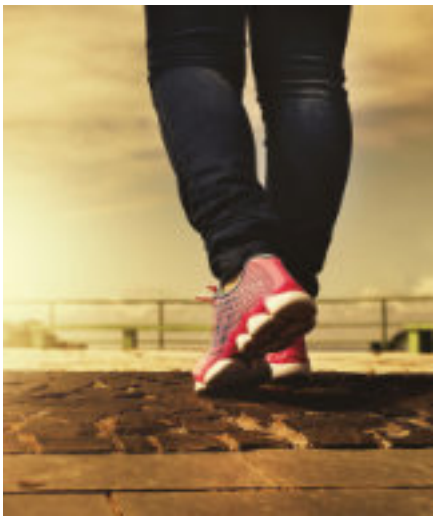

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01 Joe, Tom and Will heading in for their last day of swimming

02 What will you read next?

03 Racking up the miles this May

Mega May Miles

May was a huge month for fundraising as the Mega May Miles for ME team walked, ran, swam and cycled a total of more than 1,000 miles over the course of the month, in aid of two ME research charities including ME Research UK. Congratulations and thank you to everyone who took part.

Swimming the Lakes

Joe Welton, Will McCausland and Tom Gilbertson have recently completed their challenge to swim the full length of every swimmable lake in the Lake District over the course of one week – a total distance of 66 km across thirteen lakes. The three friends join only a handful of people to have managed this feat. What a fantastic achievement – we are so grateful for their fundraising efforts.

An autumn of reading

Here are some suggestions if you're looking for your next read. The authors are all donating some or all of their royalties to our work. Robert McMullen's *Stranger and Stranger* tells of an encounter in the life of a man with ME (amzn.to/XDVnyK). In Jack Croxall's acclaimed *Tethers Trilogy*, Karl and Esther discover an anonymous journal filled with bizarre scribblings (amzn.to/1oqY9N2). Merryn Fergusson's *What is Wrong with ME* is a story of ME through the experiences of her son Chris and his family (amzn.to/X1Hw5w).

Standing Order Form

To support our work, please consider setting up a standing order by completing this form and sending it to: **ME Research UK, The Gateway, North Methven Street, Perth, PH1 5PP**

☐ Please tick this box to indicate you are happy for us to collect and store your personal information, in accordance with our Privacy Policy at meresearch.org.uk.

Name of account holder(s)

Instruction to your Bank or Building Society

To the manager, Please arrange to debit my/our account with the amount detailed below, once every month until further notice.

Account number

Branch sort code

Address and postcode

Debit amount (£)

Payment date each month

Telephone number

Date of first payment

Name of Bank or Building Society

Pay to: Virgin Money, St John's Centre, Perth, PH1 5UH, UK, Account: ME Research UK, a/c no: 50419466, Branch code: 82-67-09

Branch address and postcode

☐ **Tick** if you would like us to treat this, any future donations to ME Research UK (SC036942), and all payments in the previous 4 years, as Gift Aid donations, meaning your donation can increase in value by a quarter at no extra cost to you. You confirm that you are a UK taxpayer and understand that if you pay less Income Tax and/or Capital Gains Tax than the amount of Gift Aid claimed on all your donations in that tax year it is your responsibility to pay any difference. Please notify us if you wish to cancel this declaration, change your name or home address, or no longer pay sufficient tax on your income and/or capital gains. If you pay Income Tax at the higher or additional rate and want to receive the additional tax relief due to you, you must include all your Gift Aid donations on your Self-Assessment tax return or ask HM Revenue and Customs to adjust your tax code.

Signature

Date