NEWS OF THE ME RESEARCH YOU ARE HELPING TO FUND

breakthrough

FANTASTIC VOYAGES

New research on the immune system

REGULARS

Research around the world
Recent fundraising
How you can help

FEATURES

AMPK activation and muscle
No update to NICE guideline
Novel treatment delivery

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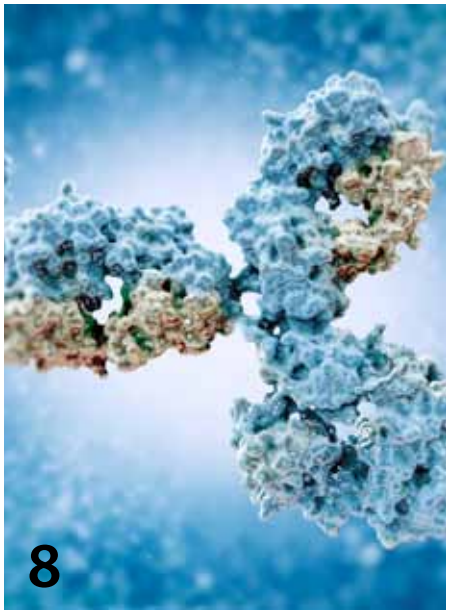
ME RESEARCH UK



Welcome

Breakthrough magazine is published by ME Research UK, a Scottish Charitable Incorporated Organisation that funds research into Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (also known as ME/CFS). The charity has an international remit, and its principal aim is to commission and fund high-quality scientific (biomedical) investigation into the causes, consequences and treatment of ME/CFS. It also aims to energise ME research by identifying potentially important areas for future biomedical research, producing high quality professional reviews and reports, and presenting research at meetings and conferences. *Breakthrough* is an open access publication and, with the exception of images and illustrations, the content may be reproduced free of charge, subject to the terms and conditions found at:

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This issue

In the spotlight

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

Many hands

ME Research UK is looking for new trustees

In the past 17 years, ME Research UK has invested over £1.5 million in biomedical research and, in terms of scientific papers published, we have funded more projects (45 to date) on ME/CFS than any other single organisation in the world outside North America.

With our small, committed team of core staff, an advisory panel of professional scientists, and a dedicated Board of Trustees, we are committed to establishing ME Research UK as a major force for change that will make a real, long-term difference to the lives and prospects of people with the disease.

We wish to develop further and to expand our current Board, and so we need volunteers who want to become trustees. As a member of the Board of Trustees, you will play a key role in developing our strategy and vision to help ME Research UK become a powerhouse of research funding into ME/CFS; to be recognised as the leading UK ME/CFS research funder; and to engage fully with supporters.

The most effective boards are those that benefit from individuals who are from a diverse range of backgrounds, experiences and skill sets. So, whatever skills you have – financial, marketing, medical, research or good old-fashioned common sense – we'd like to hear from you.

Details can be found on our website, or call 01738 451234 or e-mail meruk@pkavs.org.uk for more information and a simple application form.

Choosing a fundraising website

So, you've decided to fundraise for ME Research UK (thank you!), and chosen the event and time. The next key decision is often which fundraising website to use. We can help.

We're registered with the most popular sites – JustGiving, BT MyDonate and Virgin Money Giving. Each is designed to make it as easy as possible for your donors to donate quickly and securely, and they'll ask about adding Gift Aid automatically.

This means that you don't need to use a sponsorship form or to collect donations personally. Which site you choose is a matter of personal taste. Have a look at them and see what suits you and which features you'll use.

Where the sites differ is in their charges and therefore how much of your supporters' donations we actually receive. According to MoneySavingExpert.com, for a donation of £10 by debit card and with Gift Aid, we'd receive the most from BT MyDonate and the least from JustGiving.

This might be worth remembering before you click the button to start fundraising!

Shopping online

These days, most of us do a lot of our shopping from the comfort of our own homes. But did you know that when you're shopping online you could also be raising funds for ME research, at no extra cost to you? Here are two of the most popular ways.

Amazon – Click through to amazon.co.uk from our website (you can't miss the link on the top right of all of our pages) and Amazon will make a donation to us. It's that simple, and with Christmas approaching it will make a real difference to the funds available for research.

Easyfundraising – With over 2,700 top retailers, easyfundraising.org.uk hosts some of the UK's best online stores. Just create an account, register to support ME Research UK, and shop as usual. You can find your chosen shop via the Easyfundraising website, or install a browser plugin. The retailers donate as you buy, and every penny helps our work.

Time for a change?

NICE decides not to update ME/CFS guideline

The National Institute for Health & Care Evidence (NICE) first published Clinical Guideline CG53 on the diagnosis and management of CFS/ME in 2007, prompting an energetic critical response from patient support groups and ME/CFS charities, including ME Research UK. NICE's clinical guidelines are important because they influence national care and government policy in the UK. Ten years later, the controversy shows no signs of fading, and those same groups were in action once again when NICE recently considered updating the guideline to reflect new evidence.

You can read the content of CG53 for yourself on the NICE website and make up your own mind, but we and many others involved in ME/CFS have real concerns about its usefulness to patients. Much of this is due to the fact that the guideline's main treatment recommendations are for psychosocial management and coping strategies such as cognitive behavioural therapy (CBT) and graded exercise therapy (GET).

The recommendations are based on evidence from only a few randomized controlled trials, which included relatively small numbers of patients, and reported only mild to moderately positive results in many cases, and negative results in others. This is an insufficient evidence base on which to build a clini-

'The treatment recommendations of the NICE guideline are ineffective for most people with ME/CFS'

cal recommendation, and contrasts with the NICE guideline on multiple sclerosis, which is based on evidence from many hundreds of trials. Several articles in previous issues of *Breakthrough* and on our website discuss these concerns in more detail.

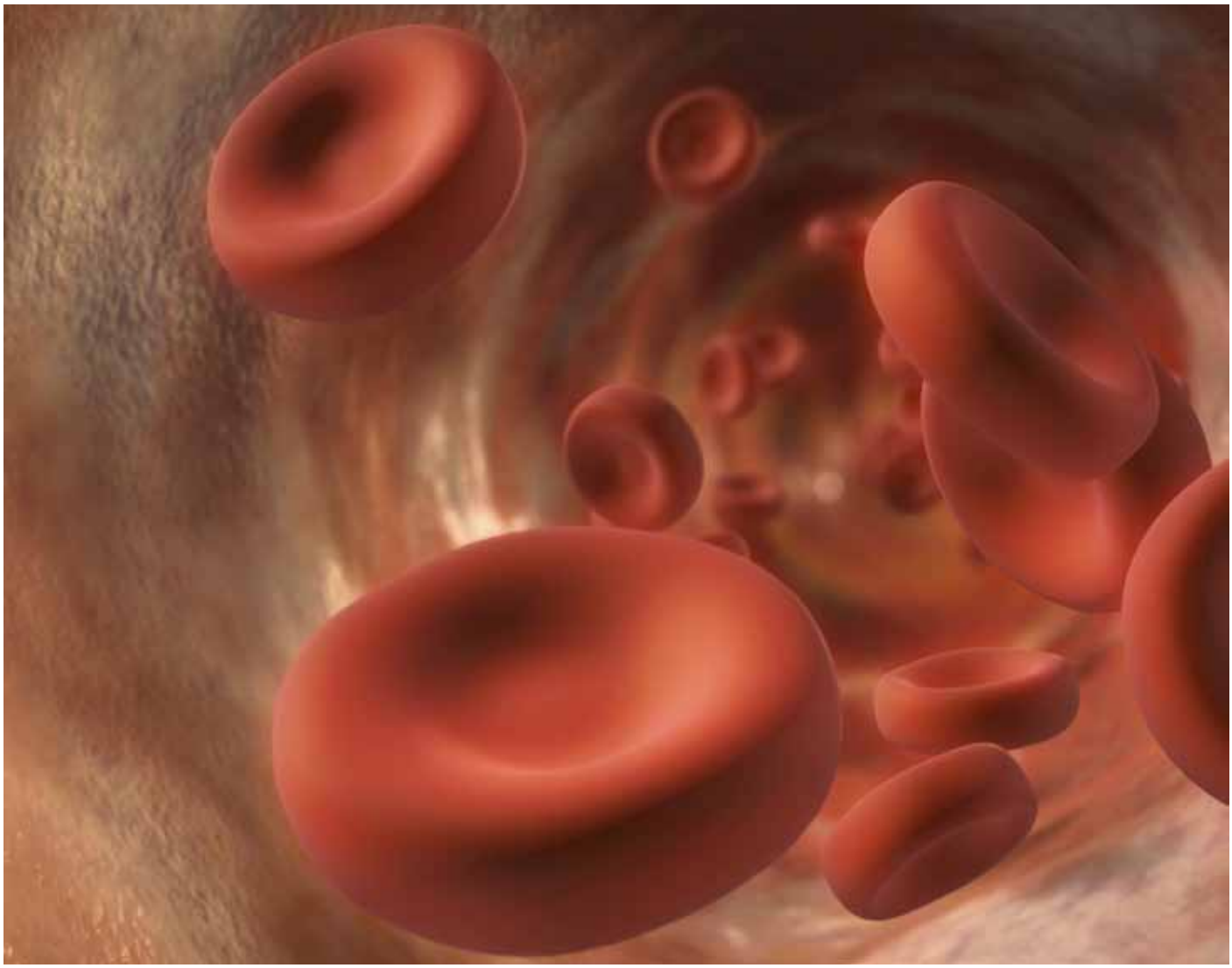
This summer, NICE considered updating their CFS/ME Guideline based on the publication in 2014 and 2015 of three reports with potential implications to the recommendations. These were from the Agency for Healthcare Research and Quality, the Institute of Medicine, and the Department of Health & Human Services, all based in the USA.

Broadly speaking, the three reports discussed the current diagnostic criteria for ME/CFS, the strength of evidence for some available therapies, and the need for further research in a number of key areas. NICE concluded that, while these reports may have implications for the CFS/ME Guideline, their proposals are still at a preliminary stage and require validation, and it would therefore be 'premature to update the guidance until there is a consensus in the UK and preferably internationally about the adoption of the proposed changes'.

ME Research UK understands these conclusions, given the lack of recently published clinical trial evidence robust enough to have an impact on the guideline. This disappointing state of affairs highlights again how ME/CFS remains under-researched.

As a stakeholder, ME Research UK was given the opportunity to comment on NICE's decision not to update the guideline, and we did so, along with many other patient groups and ME/CFS charities. We restated our position that the main treatment recommendations of the 2007 NICE guideline are ineffective for most people with ME/CFS (in the case of CBT) or may be causing actual harm (in the case of GET), and reviews and surveys published in subsequent years have only reinforced this view.

One positive result of this process is that, although NICE has chosen not to update Clinical Guideline CG53, it has been moved from the static list to the active surveillance list. This means it will be monitored more frequently for new evidence that may have an impact on the guidance. This is perhaps a small step towards giving patients the guideline they deserve.



Hitching a ride

Delivering treatments via red blood cells

Elsewhere in this issue of *Breakthrough*, we discuss two studies, recently funded by ME Research UK, that explore the status of ME/CFS as an autoimmune disease. One is looking at the role of specific autoantibodies found in the blood, and their associations with the symptoms of the disease and aspects of blood vessel and immune function. The other is searching for an immunosignature that can predict which patients will respond to rituximab, a drug that has been used to treat some autoimmune disorders.

So, it can be worthwhile looking at research into other autoimmune diseases, to see whether advances there may translate to the world of ME/CFS at some point in the future. A good case in point is work carried out at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, USA.

A team there has been investigating how to improve the delivery of treatments for autoimmune diseases such as multiple sclerosis and type 1 diabetes. These conditions are often treated with immunosuppressants, which are designed to suppress an overactive immune response and reduce the intensity or frequency of symptoms. However, these drugs will also diminish the body's immune response to genuine invaders such as bacteria and viruses, and make patients more vulnerable to infection.

One alternative strategy to treat autoimmune diseases is to retrain the immune system so that it once again ignores the body's healthy cells that it has for some reason decided are harmful. This can be achieved by a technique known as tolerance induction, in which fragments of proteins from the cells targeted as harmful are administered to the patient regularly over time until the immune system has learned not to react to them.

A big problem with this approach is that the protein fragments can be degraded or attacked by immune cells before they reach their destination. The solution being explored by the team in

Cambridge is to use red blood cells to carry the fragments, so that the fragments are effectively disguised and left alone by the immune system.

Using this method of transport, the researchers have successfully reduced symptoms in mouse models of both multiple sclerosis and type 1 diabetes. The work is a long way from being applied to human patients with either of these conditions, and further yet from any application in ME/CFS. However, it does give one example of the way in which therapeutic developments in related areas of biomedical research may improve our understanding of the pathobiology of ME/CFS.

'developments in related areas may improve our understanding of ME/CFS'

We want to stay in touch

How to keep receiving *Breakthrough*

The rules governing how organisations hold information on supporters is changing.

The changes mean that supporters will be in control of how organisations communicate with them and for what reason.

Just like every other charity, ME Research UK will need to show that we have your explicit consent to contact you – and that includes sending you our *Breakthrough* magazine.

We want to be able to keep you posted with our research news, activities and fundraising opportunities, but we need to know that you agree to us contacting you.

That's why, with this edition of *Breakthrough*, there's a simple flyer to complete and return – we've even provided a reply-paid envelope. This will let us know the ways in which you wish us to communicate with you.

If you don't want to hear from us in a particular way then that's your choice and we'll respect it.

If we don't hear from you by May 2018, then we'll remove your details from our mailing list and we won't contact you again or send you any further issues of *Breakthrough* magazine.

It's quick and easy to change your mind at any time – just let us know.

fantastic voyages

Autoantibodies have been implicated in ME/CFS, and two newly funded studies are exploring different aspects of this area

In the 1966 film, *Fantastic Voyage*, a submarine crew is shrunk to microscopic size in order to remove a blood clot in the brain of a defecting scientist. Donald Pleasence has a particularly memorable scene when he crashes the submarine in a dastardly act of sabotage, and is subsequently engulfed by white blood cells. He has triggered an innate immune response, one of the ways the body responds to infection by foreign substances.

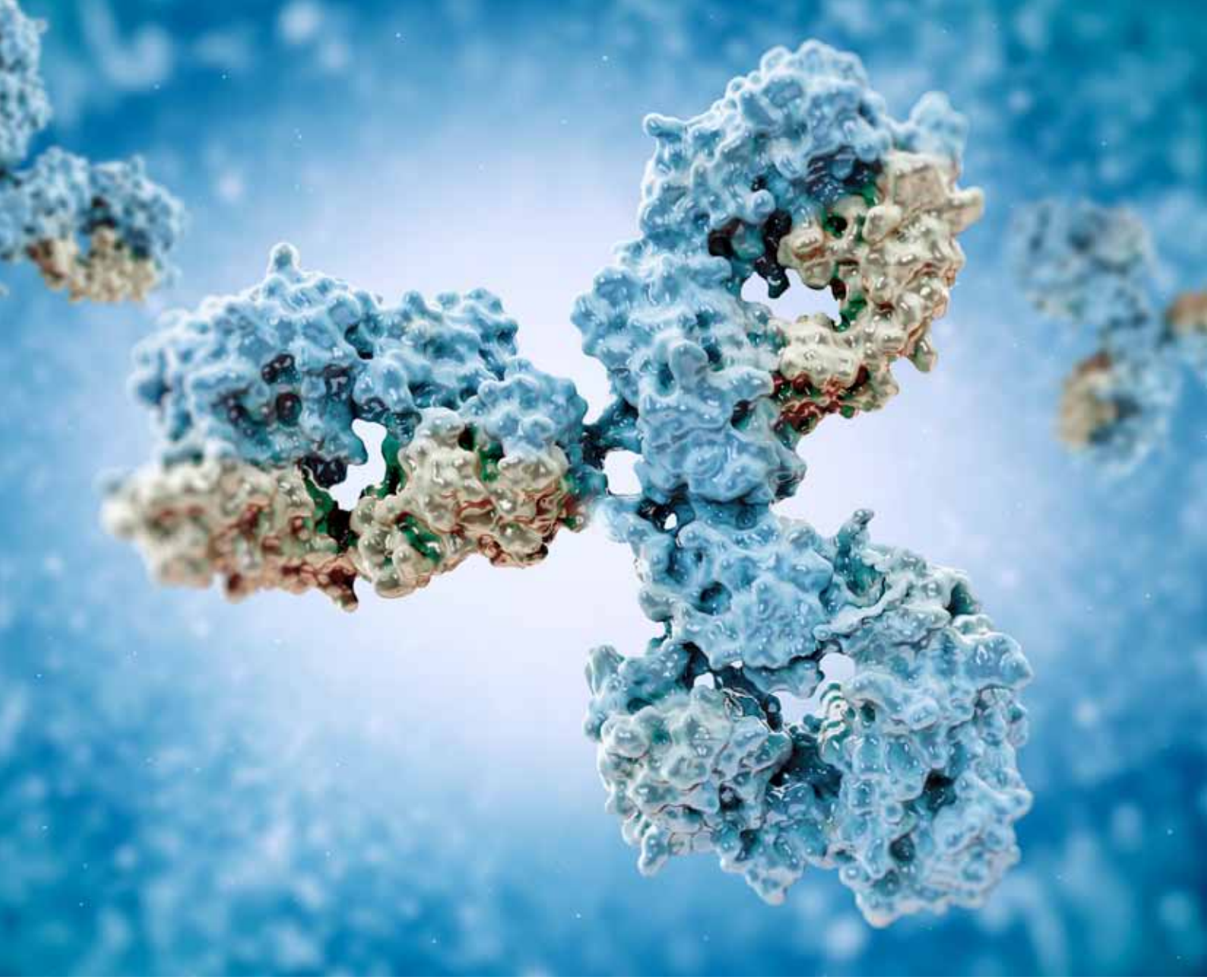
The other type of protection is adaptive immunity. In this situation, B cells (a type of white blood cell) produce proteins called antibodies which can recognise and attack harmful invaders such as bacteria and viruses. It is therefore highly specific to a particular organism, and can provide long-lasting protection against invasion from outside.

A role for autoantibodies

Autoantibodies, on the other hand, occur when the immune system wrongly identifies the body's own healthy cells as harmful and produces antibodies against them. This can lead to the development of a so-called autoimmune disease such as multiple sclerosis or lupus. A couple of recent findings suggest that autoantibodies may also have a role in ME/CFS, at least in some patients.

Firstly, autoantibodies against adrenergic receptors (which are involved in the sympathetic nervous system) have been found in people with postural orthostatic tachycardia syndrome or orthostatic hypotension, disorders also seen in ME/CFS patients.

Secondly, two clinical trials of the antibody rituximab (which attacks B cells and is often used to treat autoimmune conditions) in ME/CFS patients reported significant benefits to around 60% of participants. Their responses were delayed by five months, suggesting that the clinical effects of rituximab only occurred when the autoantibodies produced by the B cells had been washed out.



'Which symptoms and immune abnormalities might be affected by these harmful antibodies?'

Two new studies exploring this area in more detail have recently been awarded funding by ME Research UK and are currently underway. Neither involve a miniaturisation ray, high-tech submarines or Donald Pleasence, but they are fascinating nonetheless!

Symptoms and function

Last year, Dr Madlen Löbel and Prof. Carmen Scheibenbogen at the Institute of Medical Immunology in Berlin found that nearly a third of ME/CFS patients they studied had increased levels of autoantibodies against adrenergic receptors. Furthermore, these autoantibody levels decreased in individuals who responded to treatment with rituximab (see below for more about this drug). This unexpected finding suggests that, in a subgroup of patients, some of the symptoms of ME/CFS may be caused by these autoantibodies, although their exact role in the illness is not yet clear.

ME Research UK is therefore supporting Dr Löbel and Prof. Scheibenbogen as they continue their investigations by looking at the function of β2 adrenergic receptor autoantibodies in ME/CFS. They will identify patients with these autoantibodies and those without, and compare a wide range of clinical and immunological measures between the two groups. These measures will include clinical symptoms such as fatigue, physical function and signs of autonomic dysfunction, as well as blood vessel function, immune marker expression, and the proliferation of T and B cells. In this way, the researchers hope to discover which

of these symptoms and abnormalities of the immune system might be affected by the presence of these potentially harmful autoantibodies.

Immunosignature for rituximab

Rituximab is an antibody that attacks B cells and has been used to treat some cancers and autoimmune disorders. A scientific report in 2011 raised the possibility that the drug could be used to treat ME/CFS, and showed 'lasting improvements in self-reported fatigue' over 12 months of follow-up in 67% of ME/CFS patients on rituximab, compared with a response rate of 13% among those on placebo. Rituximab was also associated with significant improvements in some quality-of-life measurements.

The investigators subsequently reported promising results in another group of ME/CFS patients over a longer period, and are now working on a randomized, placebo-controlled trial of the drug at five centres in Norway. Since rituximab appears to be effective in only a proportion of patients, it would be valuable to identify these individuals, so that those unlikely to benefit can be spared unnecessary treatment and possible serious side effects.

This is where Prof. David Patrick comes in. One of the specialities of his group at the School of Population and Public Health, University of British Columbia, is the development of immunosignatures. An immunosignature uses an array of chemical compounds called peptides to give information about the antibodies present in an individual's blood. Prof. Patrick acquired some samples from the Norwegian team with which to develop an immunosignature capable of distinguishing ME/CFS patients likely to respond to rituximab treatment from those who will not. This issue is important because rituximab is associated with potentially serious side-effects and requires clinical monitoring, and it is also an expensive drug.

The preliminary results were promising (200 peptides differentiated responders from non-responders 92% of the time), so ME Research UK has awarded Prof. Patrick a grant to see if the results can be confirmed in a blinded study using a larger number of samples from all of the participants in the Norwegian trial. If the immunosignature pattern for the response to rituximab is sufficiently sensitive and specific, it may represent a useful biomarker for ME/CFS patients' responses, helping to predict those who will and those who will not benefit from rituximab treatment. ●

'A useful biomarker helping to predict patients who will respond to rituximab'

Prof. David Patrick at the University of British Columbia in Canada


YOUR
STRENGTH
300
TOP
DOG
250
NICE
TRY
200
GOOD
GIRL

test your strength

Continuing work on muscle abnormalities, a team from Newcastle University is exploring the **role of the enzyme AMPK**

Abnormal muscle fatigue is one of the most common symptoms reported by people with ME/CFS, and can occur even after periods of only mild exercise. In fact, patients often highlight the importance of muscle fatigue (including reduced muscle power) in their experience of the illness. So this is a particularly important area on which to focus research.

Since 2006, ME Research UK has provided pilot funding for a number of projects at Newcastle University exploring the mechanisms underlying muscle fatigue in ME/CFS. One of their early findings was of a higher than normal build-up in acidity during exercise, and a slower recovery back to resting levels afterwards. This suggests abnormalities in the way muscle cells handle acid in ME/CFS.

Following this, Prof. David Jones and Prof. Julia Newton from the Institute of Cellular Medicine went on to look more closely at the function of muscle cells. To achieve this, they took muscle cell biopsies from ME/CFS patients, and cultured them to provide sufficient numbers of cells to examine in standardised laboratory conditions without the influence of other complicating factors. A series of electrical pulses was applied to these cultured muscle cells to simulate the muscle contraction that occurs during exercise, and the researchers found two notable defects.

AMPK activation and glucose

Firstly, activation of AMP-activated protein kinase (AMPK) was impaired (as reported in the autumn 2015 issue of *Breakthrough*). AMPK is an enzyme with an important role in regulating energy in muscle cells and it is normally activated during muscle contraction. Secondly,

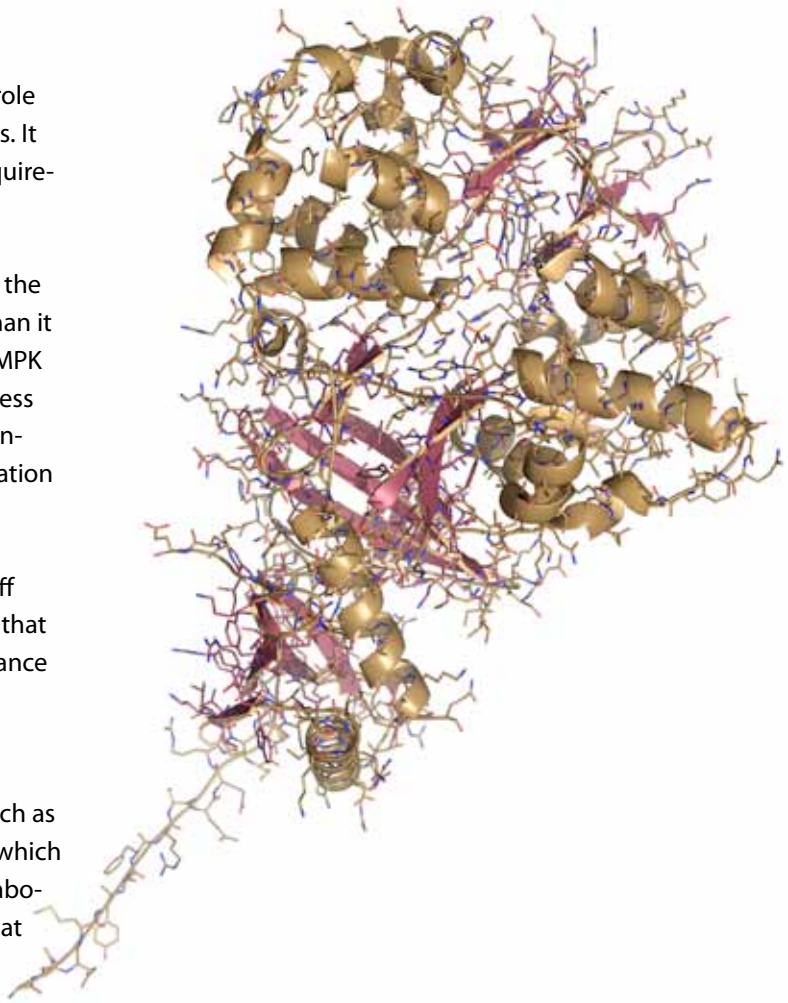
What is AMPK?

AMP-activated protein kinase (or AMPK) has a key role in the regulation of the supply of energy inside cells. It is particularly active in tissues with high energy requirements, such as the liver, brain and skeletal muscle.

AMPK is activated by a drop in the energy status of the cell, such as when energy is being used up faster than it is being produced. During exercise, for example, AMPK activity increases as muscle cells experience the stress caused by the increased demands for energy. This involves a cascade of processes, including the stimulation of glucose and fatty acid uptake and oxidation.

Overall, the effect of AMPK activation is to switch off pathways that use energy and switch on pathways that generate energy, helping to restore the energy balance within the cell.

Although much remains to be discovered, AMPK is thought to be an important player in conditions such as type 2 diabetes, metabolic syndrome and obesity, which are all associated with disturbances of energy metabolism. AMPK-activating drugs are already used to treat type 2 diabetes.



'Could pharmacological activation of AMPK improve muscle function in ME/CFS?

glucose uptake was diminished. Glucose is an important energy source for the body, particularly during exercise which requires energy production at a faster rate than can be provided with oxygen. The researchers concluded that these results point to a muscle abnormality at the level of AMPK, or in other regulatory enzymes further up the biochemical pathway.

Although AMPK was not activated by simulated muscle contraction in these cells from ME/CFS patients, later experiments showed that it could be activated by treatment with metformin, a drug known to have this effect in healthy cells and commonly used in the treatment of diabetes. This raises the possibility of whether a therapy such as this could improve muscle function in patients.

Exploring mechanisms

Following on from these intriguing results, ME Research UK has awarded further funding for Prof. Newton and her team to continue investigating these abnormalities in AMPK activation. Their new project will use specific AMPK activators (used in the treatment of other diseases such as diabetes) to explore the mechanisms through which AMPK is activated pharmacologically (i.e., by drugs), but is not activated by muscle contraction. The researchers will also examine the function of the mitochondria (the powerhouses of the cell) in ME/CFS patients and healthy control subjects.

These results may help to determine whether pharmacological activation of AMPK could improve muscle function in ME/CFS, and help identify potential new targets for treatment. ●

Prof. Mark Walker, **Dr Audrey Brown**, **Prof. Julia Newton** and **Cara Tomas** at Newcastle University

A guide to some of the terms used

Biopsy
Biopsies involve taking a small sample of tissue from the body in order to analyse it more closely under a microscope or using laboratory tests. They are commonly used to test for the presence or extent of a disease such as cancer.

Cell cultures
A biopsy may not provide enough cells to perform certain tests, in which case more cells can be grown under controlled conditions. This usually involves culturing the existing cells in a medium that can supply the nutrients, growth factors and other substances required for cell division.

Enzyme
An enzyme is a protein that stimulates a biochemical reaction between other organic molecules. Examples include amylase which is involved in the digestion of food, and urokinase which breaks down blood clots.

Metformin
This is a drug used to treat type 2 diabetes. It works by activating AMPK, thereby suppressing the production of glucose in the liver.

Mitochondria
These microscopic structures inside each cell are often described as the powerhouses of the body. They convert oxygen and nutrients into ATP energy, which drives metabolism.

Muscle contraction
The contraction of a muscle fibre is stimulated by an electrical impulse from a nerve, which causes the two filaments of the fibre (actin and myosin) to bind and then slide past each other. This generates tension in the muscle, with either a change in muscle length causing movement of the limb (i.e., lifting a weight) or no change in length (holding the weight still).

Research bites

Our round-up of recent research from around the world

The search for a biomarker

Lidbury et al., Journal of Translational Medicine, 2017

It's a recurring theme, but the diagnosis of ME/CFS is severely hampered by the lack of a test to distinguish people with the illness from those without. This is a challenge in many diseases, but particularly in ME/CFS which affects so many different systems of the body. Researchers have looked at a number of different measures as potential biomarkers for ME/CFS, including brain imaging findings, ECG abnormalities, and immunosignatures based on antibodies in the blood. Now, new research from a team in Canberra, Australia, led by Prof. Brett Lidbury, has added another potential biomarker to this list. Prof. Lidbury has a longstanding interest in the search for biomarkers for ME/CFS, and ME Research UK is currently funding one of his projects (see the spring 2017 issue of *Breakthrough*).

In this recently published study the team focused on activin. The two types of activin (A and B) are produced in several organs and have a number of different roles, including regulation of the menstrual cycle, and involvement in metabolism and wound repair. Of particular relevance to ME/CFS is its control of inflammation and muscle mass. The team found that levels of activin B in the blood were markedly higher in ME/CFS patients than in healthy individuals, while levels of activin A and follistatin (which regulates activin levels) were no different. This interesting finding suggests that the combination of elevated activin B and normal activin A may represent a useful biomarker for the presence of ME/CFS, although this result would need to be confirmed in larger groups of patients.

Childhood obesity

Norris et al., Archives of Disease in Childhood, 2017

We are often told that obesity rates in children are rising, and this is important because it contributes to the risk of conditions such as heart disease and type 2 diabetes. Children with ME/CFS tend to be less physically active than their healthy peers, so it might be assumed they are more likely to become obese. This possibility prompted researchers in Bristol to look at 1,685 adolescents with ME/CFS severe enough to require a visit to a specialist ME/CFS service, and 13,978 other adolescents participating in a study, including some with ME/CFS and some without. As expected, obesity was significantly more prevalent in children with more severe ME/CFS (9.3% at age 13) than in either of the other two groups (3.7 and 4.2%, respectively).

Local anaesthetics

Staud et al., Journal of Pain Research, 2017

Lidocaine is a local anaesthetic commonly used to numb the skin to treat minor injuries and before some surgical procedures. It works by blocking tissue receptors responsible for transmitting sensations and pain, and there is some evidence that, in the muscle, these receptors are oversensitive in people with ME/CFS. So, could injections of lidocaine into the muscle help relieve some of the pain and fatigue associated with the illness? A recent study from Florida reported that, compared with placebo, injections of lidocaine improved patient-rated fatigue by around a third, although pain and other ratings were not altered. So, perhaps lidocaine does have some potential, although we'll need to see a lot more data before getting too excited.

Patient experiences

Stormorken et al., BMC Family Practice, 2017

It is easy to focus on the biology of an illness such as ME/CFS and forget about the patients themselves. Hence the value of studies such as a recent collaboration between researchers in Oslo and Chicago, who looked at the experiences of patients with post-infectious fatigue syndrome (a subtype of ME/CFS), and how these changed as the disease developed. Asked to describe their life over the four years since they had become ill, participants described experiencing initial symptoms and a decline in physical and cognitive function until they reached rock bottom, followed by a period of slow improvement to reach a more stable condition. The complete article provides valuable insights into the real, lived experiences of people with ME/CFS.

Sleep and the brain

Shan et al., NMR Biomedicine, 2017

Most of us take for granted that, at the end of a long, tiring day, we can enjoy a good night's sleep and wake recovered and refreshed for a new day. But this is not so for many patients with ME/CFS, who do not benefit from good quality sleep and often wake unrefreshed. What might be causing this? Scientists in Australia used magnetic resonance imaging of the brain to see if they could detect any abnormalities that might be to blame. Interestingly, they found structural differences in the medial prefrontal cortex in patients compared with control subjects, and these differences correlated with measures of sleep quality as assessed by questionnaire. The medial prefrontal cortex is thought to help mediate normal sleep.

Internet-based CBT?

Ghatineh & Vink, Behavioural Sciences, 2017

ME Research UK has long contended that there is not enough evidence to support a recommendation for the use of cognitive behavioural therapy (CBT) as an effective treatment for ME/CFS. Yet, CBT is enshrined in the UK's NICE Guideline on CFS/ME and still attracts considerable research funding. In particular, the imminent FITNET-NHS study aims to investigate the efficacy of home-based CBT delivered via the Internet to children who do not have access to a specialist ME/CFS service.

The study is based on the design of the Dutch FITNET study which reported a recovery rate of around 60% after 6 months of treatment, compared with 8% in those who received usual care. However, a recent article raises serious questions about the design of this study. According to the authors, the treatment received by those in the usual care group was not specified (some received no treatment), and may have varied in intensity and how often it was delivered, which would have had a significant effect on its efficacy. Furthermore, the outcomes evaluated (fatigue severity, physical functioning and school attendance) were mainly subjective and assessed via questionnaire, making them vulnerable to bias. They conclude that these and other problems may have led to a false conclusion that the treatment was effective in this group, with potentially serious implications for the validity of the forthcoming FITNET-NHS study.

HPV vaccination

Feiring et al., Vaccine, 2017

Vaccination programmes have transformed public health, but they can still be the subject of controversy, including suggestions of involvement in ME/CFS. A potential link between human papillomavirus (HPV) vaccination and ME/CFS symptoms was discussed in the spring 2017 issue of *Breakthrough*, and researchers recently performed a thorough investigation of the risk of ME/CFS in Norwegian children given the quadrivalent HPV vaccine. Using data from several registries, the team calculated annual incidence rates for ME/CFS over six years. Although the incidence of ME/CFS increased over that period, there was no difference between girls who had undergone HPV vaccination and those who had not been vaccinated.

Vitamins and minerals

Joustra et al., PLoS One, 2017

Many ME/CFS patients take vitamin and mineral supplements, and you can find plenty of websites recommending their use and offering to sell them to you. But is the illness associated with any vitamin or mineral deficiencies that actually need correcting in this way? A systematic review performed recently by a team in the Netherlands would suggest not. They looked at a total of 45 published studies (many of low quality) reporting vitamin or mineral status in ME/CFS and fibromyalgia patients, and, when the results were collated, found very little evidence of any vitamins or minerals consistently linked to either disease. Furthermore, trials investigating supplements generally showed no clinical improvements. You may be able to save your money.

'potentially serious implications for the validity of the forthcoming FITNET-NHS study'

Cytokine signature

Montoya et al., Proceedings of the National Academy of Sciences, 2017

Elsewhere in this issue, we discuss a newly funded study in Vancouver looking for an immunosignature to distinguish patients likely to benefit from rituximab therapy. Nearly 1,000 miles down the Pacific coast, a team of scientists in Stanford, California has also been investigating the immune system in ME/CFS patients, this time measuring a range of cytokines (proteins which help control immune responses). Seventeen of these cytokines (most involved in promoting inflammation) were raised in the group of 192 patients studied, and were correlated with the severity of disease. These findings provide further support for the idea that ME/CFS involves an inflammatory process which contributes to the symptoms experienced.

Video games

Ferrar et al., JMIR Research Protocols, 2017

We generally think of video games as being sedentary, involving little more than twiddling fingers and thumbs for a few hours. But of course there's a new breed of active video game, in which players compete in a virtual tennis match or copy dance moves. There isn't yet a consensus on whether these games actually lead to sustained increases in physical activity in the general population, but there have been suggestions that they may benefit patients who have difficulties participating in real physical activity. This is the question being addressed by a new study in Australia which will look at several health-related outcomes after 6 months of active video gaming in ME/CFS patients, and we look forward to seeing the results in the future.

Tom Whittingham proudly shows off his London Marathon medal

Friends united

Some of the many activities undertaken by our supporters to raise funds for ME research.

Crossing the finish line

This year's Virgin Money London Marathon took place in April, with the women's and men's races being won by Mary Keitany and Daniel Wanjiru, respectively. But of far more interest to us were two runners finishing a little later in the day, but no less delighted with their achievements. India Lewis Thompson and Tom Whittingham were both running to raise funds for ME Research UK. Tom had our guaranteed charity place, and our Facebook followers were able to keep track of his training regime. 'It was the best race I have ever been involved in. Support from start to finish, iconic landmarks and fantastic organisation. Thank you so much to everyone for all your kind messages of support and donations.'

India was accompanied by her dad, also fundraising for a charity, and she too reported back on the big day: 'It's been an amazing experience, and it was a huge privilege to be part of the run. I also managed to get home to Bristol in time to do my maths exam at uni the next day, so it's been a busy few days!' We'd like to thank India and Tom for everything they've done to support our work.

Hair today...

In August this year, supporter Laura Crane sacrificed her crowning glory in aid of ME Research UK. Laura has been affected by ME since 2014, and so was determined to raise funds to help us support more research projects. As a bonus, the lost locks were donated to the Little Princess Trust, which pro-

01

02

03

04

01 Tina Boswell celebrates finishing the Brighton Marathon

02 The pilgrimage is complete for **Hamish**, **Jen** and **Steve.**

03 A fantastic achievement for **India Lewis Thompson** and her dad

04 Laura Crane before and after the chop

vides real hair wigs to children who have hair loss due to illness. Thank you, Laura, for going to these lengths. We hope your hair is back for the winter!

Buen camino

Tradition has it that St James the Great is buried in the Cathedral of Santiago de Compostela in northern Spain, and each year many make the pilgrimage there via the Camino de Santiago. Walking the 500-mile route for other reasons this summer were Jen, Hamish and Steve, raising funds for ME Research UK. They completed the trek on 30th June, and their adventure was featured in the Dundee *Courier*. You can read much more about the journey on their blog at icouldwalk500miles.org. A fantastic experience and fundraising effort!

Luck of the draw

We'd like to give huge thanks to everyone who entered our Spring Prize Draw, the proceeds of which will be used to fund more biomedical research to add to our current projects. Lynsay, the Management Support Officer of PKAVS (where we are based), was kind enough to draw the tickets, and the prize winners spanned the British Isles, from Dunfermline to Hexham to Southampton.

Hot runnings

On the hottest day of the year up to that point, around 12,500 runners took to the streets of Brighton for the city's eighth annual marathon. Among them was Tina Boswell, running to raise funds for ME Research UK. The hot weather added a few minutes onto her predicted time, but it was a splendid performance from someone who describes herself as not a natural or experienced runner. 'I am more than happy just having finished. The charity is very close to my heart, and if [my run] can benefit those who suffer from this debilitating illness in some small way, I have achieved my goal.'

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05 Tracey James and her faithful companion

06 Finishing the 100-mile Prudential RideLondon is **Jonathan Davies**

07 Charlotte Booth jumps for joy after finishing her ride

08 Some of the tough guys who completed this year's Knobbler

London pride

Taking part in Prudential RideLondon this year were two supporters raising funds for ME Research UK. Jonathan Davies said, 'I managed to do the ride in 5 hours 44 min and hopefully raised awareness of the terrible illness that is ME. A huge thank you to everyone who supported me.' Likewise, Charlotte Booth completed the course in an amazing 6 hours 45 min, and her fundraising efforts were very generously matched by her employer, Hodkinson Consultancy. Many thanks to them both.

Tough enough?

We were delighted to learn that ME Research UK was chosen as this year's charity for The Knobbler. This 60-km mountain bike ride is sponsored by Knobblies Bike Shop in Exmouth, and takes place over some tough terrain. The event had amazing support, and we'd like to give special thanks to Bruce McGlashan (whose son Finn has ME) who nominated us, and got round the course fuelled by cake, jelly babies and energy drink. Thank you also to all who rode on the day, and to the staff at Knobblies for organising the ride.

200 miles to go

Over the past few months, we have been following Tracey James as she racked up Boot Miles on her Walk 1,000 Miles campaign in aid of ME Research UK. Tracey has been living with ME for 30 years, so this is a particular challenge for her. At the time of writing, she had completed 800 miles by making the climb up Brown Clees Hill, Shropshire's highest point. Who knows where the next 200 miles will take her!

Standing Order Form

To allow us to press ahead with our mission to Energise ME Research globally, 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**.

Name of account holder(s)

Address

Postcode

Telephone number

Name of Bank or Building Society

Branch address

Branch postcode

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

Debit amount (£)

Payment date each month

Date of first payment

Pay to: Clydesdale Bank, 158/162 High Street, Perth PH1 5PQ, UK, Account: ME Research UK, Account no: 50419466, Branch code: 82-67-09

☐ ***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.*

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