

The Journal of IIMER

10
years



A New Decade of Invest in ME – Research

www.investinme.org

Science, Politics and ME

a book by Dr Ian Gibson

Dr Gibson led an inquiry into ME in 2006.

Without official funding, at a time when unbiased and independent analysis of ME by establishment organisations and the media was lacking, Dr Gibson provided a checkpoint which attempted to get publicity and change which would help ME patients



<http://tinyurl.com/hl644uh>

Publication Date
Autumn 2016

IIMEC11 - International ME Conference 2016

3rd June 2016

A New Decade of Invest in ME Research

LONDON



<http://www.investinme.eu/IIMEC11-DVD.shtml>

**Invest in ME – 10 Years
Conference DVD**

Journal of liMER

Welcome to IIMEC11	4
10 Years of Biomedical Research	8
10 Years	10
One Stupid Dot	19
Letter from America 1	20
QUADRAM	24
C of E for ME	26
EMERG	29
EMEA NEWS	30
Mike's EU Marathons for liME	33
Letter from America 2	43
Tackling ME/CFS in New Zealand	46
It's a Funny Old World	56
Speakers at IIMEC11	60
Agenda IIMEC11	75

Invest in ME - Research

(UK Charity Nr. 1153730)

PO BOX 561

Eastleigh SO50 0GQ

Hampshire, UK

Tel: 02380 643736 07759 349743

E-mail: info@investinme.org

Web: www.investinme.org

Invest in ME Research



Invest in ME Research (transitioning from Invest in ME) is an independent UK charity facilitating and funding a strategy of biomedical research into Myalgic Encephalomyelitis (ME) and promoting better education about the disease.

The charity is run by volunteers - patients or parents of children with ME – but on a professional basis with a passion for developing a scientific foundation for research into ME.

We do not receive, and have never received funding from government or government organisations.

The charity decided early on that biomedical research into ME was crucial in order to make progress in treating this disease. We also decided that education of healthcare staff, the media, government departments, patient groups and patients was to be a priority.

Our conferences and, later, our research colloquiums, were organised from the beginning in order to provide a platform for research and a means of facilitating education about ME.

In order to bring the best research to bear on ME and to bring the best education to healthcare and patients we welcome your support.

DISCLAIMER

The views expressed in this Journal by contributors and others do not necessarily represent those of Invest in ME. No medical recommendations are given or implied. Patients with any illness are recommended to consult their personal physician at all times.

Welcome from the



Chairman

IIMEC11: 11 YEARS A NEW DECADE OF RESEARCH

In 2015 Invest in ME arranged its TENTH international ME conference - an event bringing together many of the world's most renowned scientists and researchers to London to meet with healthcare professionals and patients.

In May of 2016 the charity reached its 10th year anniversary as a charity.

Ten years ago Invest in ME was formed to make a change in how

Myalgic Encephalomyelitis was perceived and treated in the media, by health departments and by healthcare professionals, and to educate, publicise and lobby regarding ME and the urgent requirement for public funding for biomedical research.

A decade of biomedical research conferences achieved - all underlining the charity's commitment to education

about this disease and to biomedical research which is the only way that the cause of ME will ultimately be found. A decade of commitment to research, education and awareness has finally succeeded in opening up new areas of research.

A strategy of high-quality biomedical research has broken the mould of the past and a new decade now brings new and possibly decisive projects which will finally overturn the barren landscape of ME research which had been allowed to exist for too long.

Ten years ago the ME research landscape was different - no platform for regularly showcasing or encouraging biomedical research - no funding and no

recognition of the need to fund biomedical research into this disease.

Yet now real progress is underway – thanks to the last ten years of effort by liME's supporters which has forced real change.

These have been the foundations upon

which we can build a sensible policy toward research into ME.

The charity has two major high-quality research projects underway – probably the two most important research projects for the future of ME research in the UK - and is building a foundation for translational biomedical research into ME – a Centre of Excellence for ME.

***By necessity Invest in ME
(Research) have had to create
and take opportunities in order
to make progress.***

***After ten years as a charity
there are good signs of real
progress and, with enough
support, we can make this
permanent.***

This strategy has been augmented with education of, and participation in our research projects by, medical students - enhancing theirs and their peers' education about ME and building a base for the next generation of researchers.

We have for many years also been introducing new areas of research and new researchers into the field of ME – a new idea initiated by the charity to mainstream research into ME.

Last year the charity proposed and facilitated the establishment of the **European ME Research Group** - a group of top European researchers who will collaborate and establish multi-site international biomedical research projects which will overturn decades of miserly funding being directed to ME research and which has discouraged good research to be formulated or performed.

The charity is at the heart of European cooperation with its participation in the formation of the European ME Alliance involving 13 countries in Europe and with the potential to achieve.

The Invest in ME strategy of bringing in researchers from other fields to help and improve biomedical research into ME has been successful and well worth the effort and cost.

Our conferences bring together patients, researchers, clinicians and healthcare staff and allow knowledge and experiences to be shared – and has been doing so for eleven years.

Our research colloquiums are bringing together high-calibre international researchers – concentrating on biomedical research - that can help us understand the cause/s and pathomechanisms of ME.

The charity's proposal for a Centre of Excellence for ME is possible to achieve and it has set a target which can be reached if enough support is given.

Our supporters deserve recognition for all their support and efforts to bring change to the landscape of ME research and perception.

Due to imaginative and positive support such as the [Let's Do It for ME](#) campaign and thanks to dedicated supporters the charity enters a new decade which promises to transition all the efforts of the past ten years into benefits for all patients

and their families - and also for healthcare staff.

All of this brings momentum which then spawns changes elsewhere - by influencing others, by interesting scientists and researchers in new research areas and establishing a change in how ME is perceived.



As we approach our tenth year as a charity we may look back to some progress and a good deal of change occurring due to the efforts and determination of the charity and its supporters. As we look forward we will continue to seek change.

If a disease is well understood then all aspects of patient care may improve whilst cures and treatments are being developed. Understanding of ME and finding the cause/s and pathomechanisms can only be achieved if research takes a clear stand of ME being a physical illness as a starting point and everything else is consequential. There are now enough clues, well presented over the ten years of liME conferences that need to be followed up.

Clinical trials such as the phase III rituximab trial in Norway and the UK rituximab trial project funded by Invest in ME Research give patients hope and make healthcare professionals take ME more seriously even before the trials have begun or results have been published.

Even the awareness of ME patients being part of proper mainstream clinical trials makes a huge difference to the perception of this disease.

This we have witnessed already.

Invest in ME Research have never had any doubt of ME being anything other than a physical illness and we do not believe there is sense or reason for mixing flawed psychosocial views of the

disease with biomedical views under one umbrella.

We hope that our ten years of focused approach and engaging with researchers that have the skills to help solve ME is beginning to bring results and will continue.

***Dear Kathleen,
I just wanted to thank you all for setting up the charity and all the hard work that you have done over the last 10 years.***

I became ill in 2005 and you set up the charity around the same time. Your charity has given me such hope that some proper biomedical research is being done.

There is a lot of positive momentum now in ME and I know the fruits of your labour over these 10 years will soon pay off big time!

Kind regards – H (ME patient)

By necessity Invest in ME (Research) have had to create and take opportunities in order to make progress. After ten years as a charity there are good signs of real progress and, with enough support we can make this permanent.

This is a good time to be involved in ME research as we are at the beginning of making discoveries. We are optimistic for the future as patient power has made

it possible for patients to show the types of research they want and need.

We believe we can look forward, and expect even more rapid progress in the future – directed by agents of change which have been or are being created.

The IIMEC11 conference and BRMEC6 research colloquium provide unique opportunities to begin this new decade of conferences with an intent to resolve ME once and for all.

And for so many patients and their families this will not have come a moment too soon.

Welcome to IIMEC11 and BRMEC6

Kathleen McCall

CHAIRMAN INVEST IN ME -RESEARCH

Let's Do Research



www.investinme.org

IIMER chairman Kathleen McCall thanks our sponsors of IIMEC11 events



10 Years of Biomedical Research - Invest in ME

Dr Leonard A Jason and Zachary Siegel

CENTER FOR COMMUNITY RESEARCH, DEPAUL UNIVERSITY, CHICAGO, USA



Leonard A. Jason is a professor of clinical and community psychology at DePaul University, director of the Center for Community Research, and the author of Principles of Social Change. - See more at:

<http://blog.oup.com/2015/02/disease-name-chronic-fatigue-syndrome-me/#sthash.OYrInLJU.dpuf>

Zachary Siegel is a research assistant at DePaul University's Center for Community Research. He is also a freelance writer.

10 years of Invest in ME's dedication to advocate for a marginalized group and the determination to allocate funds in a neglected field needs to be acknowledged and applauded.

This organization has been working in the trenches of ME, and it has been a notable and significant contribution to the field.

Invest in ME has been able to increase awareness and disseminate knowledge to scientists, clinicians, and patients within the ME community. With limited resources, but unlimited creativity and imagination, these patients and their supporters have showed the world what can be done.

They are an inspiration for the world.

Stigma is still associated with too many patients with ME, and this might be partly due to our society's infatuation with unlimited energy,

stamina, and endurance, and in fact, these entities are more alluring than money. Patients with ME continue to encounter scepticism, and this is regrettable, as patients first endure a devastating illness and then they are further victimized by our society's reaction to them. Far too many scientists and health care workers have been part of the problem, and this has to change. The status quo is not acceptable for patients with ME.

It's only by us collectively being involved in action that the situation will change. And it has changed for many other illness groups, such as people with HIV/AIDS, who demonstrated that it is possible to bring about a sea change in the treatment and respect for people with

this illness. To bring about this type change is going to involve not just the patients who have ME, but also their friends and family members who do not have this illness. The future of this field is in connecting the many patient and scientific groups into one larger body that is united for change. We welcome youth groups, civic organizations, and not-for-profits to get involved in one of the truly neglected areas needing structural changes in the way patients are treated and their availability to quality care.

In order to push forward, we need research that involves multidisciplinary efforts that will bring together scientists from different disciplines including virologists, epidemiologists, individuals who study the autonomic nervous system, genetics, computer science, immunology, and many other disciplines.

This illness represents a great challenge to medicine, and one from which we will all learn the intricacies and systems of the human body.

In addition to the massive amounts of funding that are needed to better understand this complex illness, patients living in every country need the best that medicine can offer.

The key to success is a team of health care providers working closely with patients, using services that meets all of their needs.

I continue to believe that learning how to pace and stay within the energy envelope is the key to having a better quality of life. But we need

much more basic research to find ways to cure this illness, and one day it will be possible, just as it has with other diseases that have had adequate funding for research. ME received considerable media attention over the last year, and we now need to use this momentum to bring about the changes that are so desperately needed.

There is nothing as important for our field as seeing patients as true collaborators in service programs and research that focus on better understanding this illness, and their voices and vision need to play an instrumental role in setting the agenda for the future.

By Dr. Leonard A. Jason and Zachary A. Siegel



Support Biomedical Research into ME.

Invest in ME Research wristbands

<http://www.investinme.org/liME-Wristbands.htm>

www.investinme.org



Thank you to our supporters

10YEARS

In 2006 Invest in ME was formed as a charity by patients and carers of children with ME. There were no funds let alone paid staff but lots of passion to put things right due to too much emphasis having been put on psychosocial paradigms following on from the 2002 CMO report.

The MRC annual report from 2002/03 stated

“Chronic Fatigue Syndrome/ME (CFS/ME): following the publication of a Report of the Chief Medical Officer’s Independent Working Group in January 2002, and at the request of the DoH in England, the MRC convened an independent CFS/ME Research Advisory Group to develop a broad strategy for advancing biomedical and health services research on CFS/ME.

The research strategy was published on 1 May 2003, when the MRC issued a highlight notice welcoming research proposals (investigator-initiated) covering the spectrum of research into CFS/ME.

In addition, the MRC will investigate usefulness of existing longitudinal

studies for undertaking epidemiological research on CFS/ME in the UK.

The MRC’s Council agreed the funding of two clinical trials of treatments for CFS/ME in March 2003. A trial led by Dr Alison Wearden (University of Manchester) will evaluate pragmatic rehabilitation, a nurse-led self-help intervention in the treatment of CFS patients in primary care, against supportive listening or treatment as usual.

Dr Peter White (St Bartholomew’s Hospital, London) will undertake a randomised controlled trial of cognitive behaviour therapy, graded exercise therapy, and adaptive pacing against usual medical care for patients with CFS. This latter study is funded in partnership with the DoH, the Department of Work and Pensions, and the Chief Scientist’s Office of the Scottish Executive.”

Since the CMO’s report of 2002 the debacle over the disastrous PACE Trial is the clearest illustration of the failure and the negligence shown by those who have been responsible for funding ME research.

Much of the charity’s early and continued work was concerned with

protesting the public funding policy of favouring behavioural research over biomedical one.



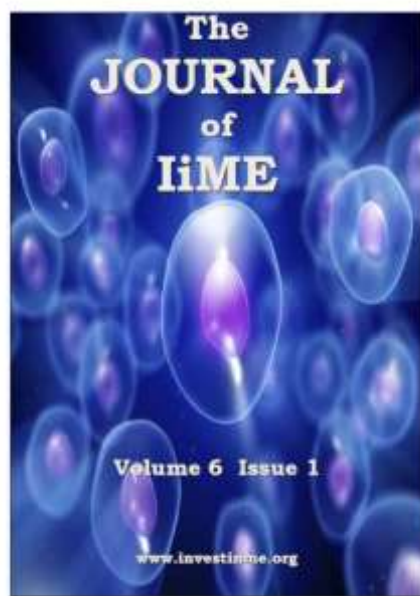
We held our first conference in Westminster, London in 2006 in the hope that politicians and other healthcare decision makers

could easily attend. Dr Ian Gibson, MP for Norwich North at the time, opened the first conference. He has been the charity's supporter and advisor ever since.

We worked with ITV Meridian and Norway's Puls programme to allow their excellent reporting on severe ME in the UK and Norway to be seen. These programs were made available for our first 2006 conference DVD set and formed a powerful and realistic statement on how disabling ME can be to patients and their families.

The 2007 we trialled a two-day public conference format in London. Dr Ian Gibson was joined by another Norfolk MP Mr Norman Lamb who opened the second day.

We also started producing the Journal of IIME, a mixture of science, education and politics and as we had no funds these were printed by ourselves using a standard, slow home printer - tedious as well as time and ink consuming all that work was.



We believe that everyone who attended the 2007 conference left not only with an enhanced knowledge gained from the conference but also with renewed hope for the future.

There were early signs of things to come from Norway when Ellen Piro and Eva Stormørken gave their presentation explaining the reasons for the Norwegian ME Association saying a firm NO to the Norwegian NICE guidelines. Their presentation received a great ovation as it resonated with patients and carers in the UK.

Invest in ME contributed to the review of the UK NICE Guidelines (both the draft version and the final version). We found both documents unsatisfactory due to emphasis on psychiatric paradigms to manage/treat ME/CFS.

Invest in ME produced a 52-page response that followed our 38,000-word response to the draft guidelines.

The charity visited the CMO's office to meet with Dr Bill Kirkup, Deputy CMO at the time. We requested that ME be treated as a notifiable illness in schools - but this was rejected.

Invest in ME have written to past and current ministers at the Department of Health and to the Medical Research Council in order to encourage more funding to be allocated for biomedical research into ME. The chief executive of the MRC contributed an article for our Journal for the 2007 conference.

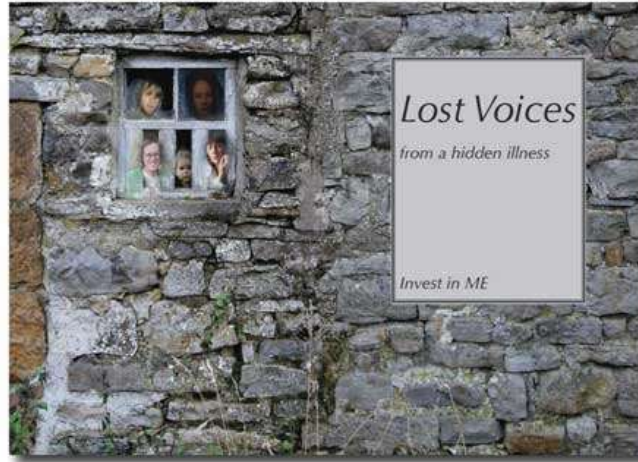
Invest in ME took over distribution of the Canadian ME/CFS Guidelines in the UK on a not-for-profit basis. The guidelines are now a basic requirement for any

service model being developed for diagnosis, management and treatment of ME.

They are widely used in research such as the Invest in ME funded B cell study at UCL and gut microbiota at IFR/UEA. The Norwegian phase III rituximab trial selects patients fulfilling these criteria also.

We translated into English the Norwegian documents describing the exciting news of the Norwegian government's intentions (MP

Laila Dāvøy was instrumental in initiating this work in 2006-2007) to treat ME more seriously and with a more strategic approach, including creation of centres of excellence for ME.



In 2009 the charity published and distributed the unique book on ME, **Lost Voices from a hidden illness**, which was compiled by Natalie Boulton and highlighted the situation of those severely affected by ME and their

families. This book has been ordered by patients, support groups, healthcare staff and researchers in twenty countries. It was also ordered for inclusion in the syllabus by Chicago University, USA.

Numerous research activities to support TV, radio and newspaper coverage of ME were performed and liME contributed to the consultation and review of the NICE Guidelines for CFS/ME.

The charity began its Biomedical Research Fund to allow donations to research projects to be made.

liME organised and hosted the fourth annual Invest in ME International ME conference in London in 2009. The focus of this conference was Severe ME, an attempt to raise more awareness of patients with severe ME - a group of patients who were not represented in research trials and completely misunderstood by healthcare services.

Prior to the conference Invest in ME arranged for the American journalist, Hillary Johnson, to visit London and give a pre-conference presentation on the evening before the conference to an audience of researchers, clinicians, patients and media people. Hillary's presentation concerned the USA CDC's

From 2008 Invest in ME began participating in the [All Party Parliamentary Group](#) discussions and sent in many submissions. Sadly, the health ministers at the time, Mr Alan Johnson and Mrs Ann Keen, both declined to take responsibility for the situation with ME and declined invitations to our conferences – demonstrating a point which has been consistent over the years – that apathy toward ME patients has no party political borders.

The charity was instrumental in forming the [European ME Alliance](#) in 2008 – a grouping of charities and patient organisations within Europe who came together to tackle issues around ME affecting European patients and their families.

influence on ME research throughout the world.

Invest in ME submitted responses to the published 5-year plan for CFS (ME) from the USA Centres for Disease Control. The charity also submitted responses to the UK All Party Parliamentary Group on ME.

In 2010, tired with continually sitting in meetings with the NHS to discuss services for ME - yet with no progress being made, Invest in ME formulated a proposal for biomedical research to be based at a research and examination facility in the Norwich Research Park in Norfolk – a Centre of Excellence for ME.

The Norwich Research Park includes multiple institutes and companies, including the University of East Anglia, Institute of Food Research and the Norfolk and Norwich University hospital as well as the Genome Analysis Centre (TGAC).

Our proposal envisaged performing translational biomedical research into ME by researchers at the university using a patient cohort which had been diagnosed by an experienced clinician using appropriate diagnostic guidelines.

Invest in ME formed a steering group to initiate our proposal and entered discussions with the university and hospital and with a renowned clinician.

We had been in discussions with Norfolk Primary Care Trust (PCT) also and had secured a promise to fund the patient

examinations. These discussions and promotion of our proposal as one of the best ways forward for securing proper research and treatments for people with ME in the UK and Europe continued.

liME organised and hosted the fifth annual Invest in ME International ME conference in London. This had the theme of “A New Era in ME/CFS Research” to reflect the new awareness and acceptance that only biomedical research will allow treatments and cures to be found for ME. The 5th liME conference (IIMEC5) was as usual CPD accredited and a platform for biomedical research.

Invest in ME continued its criticism of the NICE Guidelines for CFS/ME which we viewed as lacking in any usefulness for physicians or patients. We also continued to criticise the PACE trial as flawed science and a huge waste of public money – money which could have been far better utilised if allocated for biomedical research into ME.

From 2011 we were joined and supported in our quest for a Centre of Excellence with a new and visionary fundraising initiative – Let’s Do It For ME - formed by three house/bedbound patients. Together we quickly raised almost £10000 for our foundation project to study the gut microbiota in ME patients. For the charity this was a great deal in terms of the usual budget.

This was a turning point in encouraging people with ME and their friends and families to actively fundraise for ME as they do in many other illnesses. There is still a long way to go to get to the level of MS, cancer, heart disease etc. but it was a good start and has continued to grow.



liME organised and hosted its sixth annual Invest in ME International ME/CFS conference. This had the theme of “The Way Forward for ME – A Case for Clinical Trials” to reflect the need for clinical trials of treatments for ME which could make a difference to the lives of patients.

The 6th liME conference (IIMEC6) was the first time that Professor Mella and Dr Fluge presented on ME/CFS in public. They made a lasting impression on us and we knew straight away that these two fine Norwegian gentlemen and their research were something special and worth keeping an eye on. We are honoured to have had the chance to follow their progress year after year.



The charity organised the first Biomedical Research into ME Colloquium in 2011 – named the Corridor Conference – bringing together researchers from different continents to discuss and share knowledge about ME – and also some researchers new to the ME field. BRMEC1 was a new and unique addition to liME’s conference events.

For the first and only time the British Medical Journal (BMJ) accepted an invitation to the conference and their representative participated in the panel discussion.

Prior to the conference the charity arranged a special meeting of the APPG in parliament and took along a number of our researchers who we had brought

to London for the IIMEC6 conference. This allowed MPs to be given true facts about the disease and the research required.

Invest in ME continued to tackle the unjust media portrayal of ME and made an official complaint to the Press Complaints Commission after a series of unsubstantiated and biased articles

appeared in major newspapers in a seemingly coordinated media attack on sick and vulnerable patients. Although, predictably, the PCC did not rule in the charity’s favour the bias and inaccurate reporting in these misleading

and orchestrated articles and the unprofessional and flawed editorial control were clearly shown by Invest in ME to be present in the media – something which would be symptomatic of poor journalism shown later by the so called Leveson Inquiry.

We also wrote to the Lancet about the PACE trial and continued to argue that flawed theories should not be funded by the public.

In 2012 the three areas which have needed attention and which formed the basis of our work in order to benefit the public and society have been - funding for biomedical research, education about ME and campaigning/lobbying to ensure that ME is taken seriously and that patients receive care from healthcare staff who actually understand the disease.

To this end the 2011-2012 was a year where the charity did much work to support our objectives. Many of these

activities performed by the charity overlap.

An example was the premiere screening in the UK of a film about ME, *Voices from the Shadows*, which allowed a debate to be initiated about past treatment of ME patients with a message relating to the damage being inflicted on families by flawed and biased research. Invest in ME organised the first two showings – one in Norwich and one at the British Library in London. In Norwich the Mayor of Norwich attended along with the media, patients, and family members. In London the British Library provided an imposing setting for a serious debate on this disease which the film allowed to be initiated. Dr Nigel Speight spoke at the screening on a panel which included a local London councillor.



Our continued criticism of the PACE Trial showed how badly wrong research can go and how much money is being wasted on deleterious and flawed approaches to this disease by organisations that are unaccountable.



Invest in ME had been invited to be an observer at the All Party Parliamentary Group (APPG) for ME. The charity provided input to meetings on points concerning welfare reform, research,

NHS services, GP training, press complaints made by the charity and other activities which the charity had conducted. The charity had also written to various organisations in order to clarify errors and misinformation in publications.

Invest in ME continued with its annual conference events.

In May 2012 our seventh Invest in ME International ME CPD accredited Conference (IIMEC7) took place in London along with the Clinical Autoimmunity Working Group (CAWG) which was a 2-day research meeting, the BRMEC2 Colloquium, that IIME organised in collaboration with the Alison Hunter Memorial Foundation of Australia – working together for over six months on

designing this research meeting. The CAWG was an extraordinary meeting with world-renowned experts in different fields, not just ME and laid the foundations for our future colloquiums.

On the evening before the conference Invest in ME arranged and hosted the pre-conference dinner and the charity was delighted to have Norwegian journalist Jørgen Jelstad presenting his speech "*Words Matter*". Jørgen has closely followed ME research and his presentation provided a great deal of food for thought.

At the end of the 2012 conference we announced our intention to try to set up a clinical trial in the UK of rituximab for ME patients.

As part of our strategy to initiate high-quality biomedical research into ME that looked at causality of ME the charity was finally able to fund its first research project in 2013, the gut microbiota study at IFR/UEA involving a three year PhD studentship. This followed many years of effort and fundraising and was greatly assisted by the charity's advisor Dr Ian Gibson.

The charity and its supporters contributed to the appeal by the Australian Alison Hunter Memorial Foundation and Australian PHANU for a flow cytometer to be purchased to assist research there.

The charity organised and held its 8th annual international research conference – with the sub-title of Mainstreaming ME Research – reflecting our view that ME was now entering the mainstream research activities being considered by research establishments.

We also organised our third international research colloquium in order to encourage ME research. These events established a core working group of researchers and facilitated many new collaborations – which was the intention of the meetings. This also underlined the charity's conviction that a strategy of biomedical research into ME is possible, is sensible and will be the only way to

find treatments/cures for ME.

As part of the charity's attempt to mainstream ME research into research agendas and discussions of major organisations we invited the chair of the Royal College of GPs to speak at our 8th International ME conference. Dr Gerada's talk led to a lively discussion with some surprising statements.

Following the colloquium/conference the charity announced the beginning of its [rituximab clinical trial project](#). We also announced that our advisor on the project would be Emeritus Professor Jonathan Edwards of UCL.

During 2013 the charity organised a video conference call with Dr Martin McShane - NHS Commissioning Board Authority, Director – in an attempt to influence DoH policy on ME. In the discussion were the parents of a severely affected young adult who had themselves been victimised by the social services due to complete ignorance about ME.

We feel our strategy of biomedical research with collaboration between international biomedical researchers is bringing change and a real prospect of continued progress.

As we stated in [our newslett](#) – our motives “are to make rapid progress in translational biomedical research into ME which will benefit ME patients and their families and provide hope that something is being done for them, that there truly is a promise of better times



INVEST in ME RESEARCH

MICROBIOME



IS THIS WHERE THE CAUSE of ME LIES?

We'd like to find out!

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. This is one project ME Charity Invest in ME wishes to initiate to determine whether changes in the gut microbiota contribute to ME. Other biomedical research projects will follow. Please support our proposal for an examination and research facility for ME in the UK and help us to help people with ME. Let's Do It For ME. See - <http://www.investinme.org/research.htm>

Invest in ME (UK charity nr. 1114035)
www.investinme.org email: info@investinme.org

RITUXIMAB



One Event Can Change Everything

One small charity – one BIG cause
A rituximab clinical trial for ME
www.ukrituximabtrial.org

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. A UK trial of rituximab for ME is being initiated and organised by Invest in ME and University College London. The charity wishes to establish a Centre of Excellence for ME in the UK. Please support us and help us to help people with ME. Let's Do It For ME. Let's Do Research.

Invest in ME (UK charity nr. 1114035)
www.investinme.org email: info@investinme.org lidfira.org

Possibly the two most important research projects for ME in the UK
 Both initiated and funded by Invest in ME and our supporters

With two of the most important ME meetings scheduled for 2016 -
<http://www.investinme.eu/IIMEC11.shtml>

Let's Do It For ME
Let's Do Research

ahead and not just further delaying tactics to waste more years”

By 2014 we could say that the charity's work had made an impact.

After a year of attempting to gain interest in setting up a clinical trial of the drug rituximab, following promising results from the Norwegian Fluge et al. study, the charity initiated a project for the trial and related B cell research in association with University College London.

We began a fundraising campaign with the help of the Let's Do It For ME team of volunteers. An initial target amount of £350 000 was set and we thus started a crowdfunding project into ME which had not been tried before in the UK. This was a daunting task but not one the

charity thought impossible to achieve – and IIMER's supporters rose to the challenge with positive campaigns which raised funds and awareness for this disease.

The supporters of the charity have been a credit to the community of ME patients and carers and have demonstrated the resilience of this population of sick people.

We were privileged and grateful to the **Hendrie Foundation** who agreed to pledge funding toward the rituximab trial. This allowed patients and carers renewed hope in tackling this disease and is now an international project – both in the crowdfunding aspect and in the research itself.

The charity has received donations and support from many different countries around the world. After an impressive campaign lasting a year, in August 2014 the charity secured the initial target amount (with pledges) of £350,000. To allow the promising B-cell study into ME to continue, and as part of the overall research portfolio that Invest in ME has with UCL and the consultants from Epsom and St Helier University Hospital and UCLH, the charity committed itself to fund a new PhD studentship at UCL that began in 2015.

The charity organised and held its 9th annual international research conference – with the sub-title of Synergising Research into ME – illustrating the objectives of the charity in organising and facilitating international collaboration in research into ME.

Following the IIMEC9 international conference the charity agreed in principle to fund further PhD students at UEA/IFR and also two intercalating medical students who would assist in the research underway at UEA/IFR. One student spent time at Cornell University with Professor Maureen Hanson and one at Oxford University under the guidance of Professor Angela Vincent.

The charity also formed an Advisory Board to help the charity plan a strategy for research and provide advice on what research to fund. We are very pleased to have renowned researchers from UEA, IFR, Oxford and UCL in our Advisory Board.

In 2015 the charity made submissions for the NIH Pathways to Prevention Report (P2P). We also made an analysis of the Institute of Medicine

(IOM) “Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness” report.

We continued our advocacy and support for people with ME by formally complaining to the BBC regarding poorly researched and unbalanced reporting. The BBC to its shame failed to respond to any of the complaints made – underlining the fact that although we had begun to change the research landscape it was still difficult to change the practices of a publicly-funded establishment organisation that is unaccountable regarding the truth. One

can bring a horse to water but the horse has to be thirsty to drink.

2015 saw the fifth international biomedical research Colloquium and our tenth international ME

conference. And both events were the best to date. A landmark achieved.

Over ten years only a small proportion of the work that the charity and its supporters has performed can be mentioned. And in truth we never imagined that it would take so much effort to make the changes now being seen.

Yet we enter a new decade of Invest in ME research – better equipped than ten years ago, more knowledgeable of the disease itself and as passionate as ever to produce a solution which will finally see an end to the misery which people with ME and their families have been forced to endure for the last two decades or more.



One Stupid D^ot

Stacy Hart aka @MamaChill hip hop/rap artist, diagnosed with M.E. in 1991.
Stacy still has M.E., 24 years after being diagnosed.



ONE STUPID DOT

ME & M.E Same Letters Separated By A Dot
 One's Who I Am, One's What I've Got
 One's Who I Used To Be, One's What I'm Not
 Oh I'm Still ME, There's Just A Dot Inbetween
 But It's A Dot That Can Stop You From Living A Dream
 It's A Dot That Separates The M From The E
 And While It's Sat There It's Hard To Be ME
 The ME I Was In Healthier Days
 Before The Dot Came Forcing The Parting Of Ways
 I'm Nothing As M And Empty As E
 But Side By Side Again I Could Be ME
 That Dot Has Got A lot To Explain
 How Can Something So Small Cause So Much Pain?
 So Much Devastation? Seem Endlessly Cruel?
 It's Just One Stupid Dot After All
 Why Does It Have To Be Stuck In The Middle
 Causing Complex Symptoms That Read Like A Riddle?
 I Have To Believe That Just As It Came
 The Dot Will Mysteriously Vanish Again
 Every Night Before Sleeping I Hope And I Pray
 That I'll Wake Up As ME Without A Dot In The Way.



Letter from America 1

By Zaher Nahle PhD, MPA,
Vice President for Research and
Scientific Programs

Solve ME/CFS Initiative –
Los Angeles, California

Within the spectrum of human diseases, ME/CFS is “...one of the most challenging.” That is how the Director of the National Institutes of Health (NIH), Dr. Francis S. Collins, described this disease in a press release in late 2015 when he announced efforts to bolster ME/CFS research at the NIH. Collins, as the head of a \$32 billion research agency investigating hundreds of complex diseases, has a unique perspective on medical challenges worldwide, which makes his characterization of ME/CFS especially telling.

But why is this disease so challenging, “most challenging” in fact? The answer is not simple yet the challenges can be classified in two categories. “Human-made” challenges resulting from inept policies and a lack of leadership and “nature-made” challenges stemming from the complex, multifactorial nature of the disease itself:

First, solving medical mysteries historically, particularly stubborn ones, has been proportional to investment in clinical investigations and basic

research. Lessons from polio to HIV have taught us that repeatedly. It is, therefore, consequential that the

meager research spending on ME/CFS to date continues to sustain, if not fuel, the challenging attributes of this disease.

Second, there is no US national strategy yet to tackle the disease in a focused, comprehensive way. Such strategy would create an aggregate mass of scientists,

including the necessary infrastructure, for studying this incredibly stimulating area of science. Elements of such strategy would include: (i) Making ME/CFS a viable career path for investigators by funding federal grant opportunities in this area; (ii) Supporting clinical and research mentorship programs in ME/CFS; (iii) Developing centers for excellence dedicated to ME/CFS clinical and basic research; (iv) Fast tracking FDA approvals of promising drug candidates; and (iv) Redefining the illness as one of the “most challenging” diseases in medical school curricula and other medical education platforms, including those associated with influential federal agencies such as the CDC.



Third, the serious deficit in comprehending the natural history of the disease is another key challenge. Case in point are statements in the February 2015 Institute of Medicine (IOM) report indicating that the committee **“was unable to define subgroups of patients or even to clearly define the natural history of the disease”** recommending that **“Studies aimed at assessing the natural history of the disease and its temporal characteristics (onset, duration, severity, recovery, and functional deficits) are essential for a better understanding of ME/CFS and also are important to further refine the diagnostic criteria proposed in this report.”**

Fourth, the reluctance of most pharmaceutical companies to invest in the ME/CFS field absent reliable biomarkers is a challenge. In effect, this virtually eliminates the bulk of the financial and technological contributions from the private sector. Therefore, clever public/private partnerships to stimulate such endeavors are needed.

These four issues define the “human-made” impediments to solving this disease.

The complex nature of the disease is a challenge itself; the biological pathways associated with ME/CFS pathophysiology are hard to investigate since by all indications they affect systems that are pleotropic by nature, i.e., regulating multiple interweaved networks and targets. Let’s illustrate this last point with an example: Take Cortisol, which is now being studied in depth at the CDC through its ME/CFS clinical multi-site program. It is a critical steroid hormone regulator within neuroendocrine signaling but also regulates a myriad of key components in the cellular energy production machinery (i.e., bioenergetics) and influences essential genes of inflammatory cytokines as well, hence altering our energetics capacity

alongside our immunity and inflammation status. Clearly, a singular factor can potentially control complex functions and systems that are intertwined and interconnected. When it goes awry, the consequences become multifactorial. One can list many more examples associated with ME/CFS, from mitochondrial dysfunction, to pathogenic factors to neurological abnormalities to autonomic deregulations that are all, by design, complex, pan-disciplinary elements crucial for our cognitive and physical



Solve ME/CFS Initiative

Leveraging patient-centered research to cure ME/CFS

functioning.

At our organization, the Solve ME/CFS Initiative (SMCI) and under the leadership of Carol Head, SMCI president, we work to mitigate these challenges in several ways:

- I. One, we **continue to put resources into projects that accelerate the discovery process.** We promote this function by:
 - i. Supplying any investigator studying ME/CFS the research materials (specimens) they need, using our **Solve CFS BioBank**; Our BioBank and Patient Registry™ holds a repository of physical samples from ME/CFS patients to supports the work of qualified researchers. This important aspect of services that our organization provides to researchers, also represents our efforts to link patients directly to researchers and facilitate the use of human materials in the process of investigating ME/CFS.
 - ii. Funding meritorious grants through a competitive peer-review process to identify innovative technologies,

concepts and biomarkers. This program is named the **Ramsay Research Grant Award Program** in honor of the Myalgic Encephalomyelitis pioneer Dr. A. Melvin Ramsay, who was the recognized authority in ME from 1955 until his death in 1990. His sound descriptions of the disease have stood the test of time. This grant program part of our organization's overall research strategy to encourage participatory investigations, accelerate new discoveries and reduce barriers for entry into the challenging yet rewarding field of ME/CFS. The Ramsay program has three main objectives:

- INVEST in original ideas that will clarify the nature, progression and root causes of the disease.
- CREATE environments through these pilot grants to help awardees generate preliminary data and compete for long-term federal grants with the hope of retaining these researchers in the ME/CFS field.
- FACILITATE collaboration among individuals committed to solving this challenging medical issue through our organization's network.

II. Two, we **engage with government leaders and policy makers**. This engagement in advocacy is driven by two fundamental beliefs: one, that it is the responsibility of the government to find cures for the up to 2.5 million ME/CFS patients in the US alone and not the other way around; and two, that major breakthroughs will be accelerated

with significant funding from the federal government, most importantly NIH and CDC. These discussions with key government officials, which we consider essential to our core mission, establish a healthy partnership with national and public health organizations while simultaneously maintaining the pressure aimed at finding real solutions to our disease.

- III. Three, we are taking the lead in developing a **national registry** that can clarify the natural history of the disease. This is done in partnership with Genetic Alliance PEER program and the Robert Wood Johnson Foundation, as well as the ME/CFS community. Such initiative will also facilitate performing longitudinal and cross sectional studies, informing clinical trial design, sharing information with organizations and researchers for educational and research purposes, collecting demographic, epidemiological, genetic, social sciences, health disparity, comorbidity and treatment outcome data, conducting relevant and targeted surveys and creating an information hub that will benefit the ME/CFS community as a whole.
- IV. Four, we **maintain vigilance against misleading information** and poorly designed studies and disseminate information through our multi-communication channels (e.g., e-newsletter, print publication, social media) to refute suspect science and keep the community up to date on current

affairs. We also bring thought leaders from government, academia and the private sector to our patient community through regular webinars and forums.

- V. Five, we developed an investigation framework of high-priority targeted research initiatives focusing on **original research**. Initiated this year, this program leverages in-house expertise to help close the knowledge gaps in our organization's three key research focus areas: **bioenergetics, neuroendocrine biology and immune dysfunction**. We conduct these targeted initiatives through well-defined projects initiated at our organization, either independently or in collaboration with researchers or medical centers. Projects are typically high risk/high reward and likely to generate information useful to the broader medical and scientific ME/CFS community. Results of these initiatives will be shared with the community to spark further studies. Currently, we have several targeted initiatives in the areas of bioenergetics, metabolomics, functional genomics, immune-senescence and RNA interference that were developed with commercial entities like Metabolon, research centers like Memorial Sloan Kettering Cancer Center and individual academic laboratories at leading medical centers nationwide.

To achieve all these ambitious goals, we leverage other key assets at the organization including:

- a Research Advisory Council made up of highly respected experts drawn from diverse fields
- a broad-based network of patients as partners
- deeply committed board members, each of whom has a personal connection to the disease.

We work to add value in our research endeavors by pursuing the most innovative applications and ideas in the ME/CFS field to make this disease understood, diagnosable and treatable. We are always looking for collaborations and partnerships in the United States and abroad.

The Solve ME/CFS Initiative (SMCI), based in Los Angeles, is the major nonprofit, US-based organization focused on the debilitating disease Myalgic Encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS) since its founding in 1987 (then under the name of CIFS Association of America). SMCI's mission is to serve ME/CFS patients through making the pathophysiology of the ME/CFS understood, diagnosable and treatable. With emphasis on transparency and rigor, the organization pursues its work in a number of ways, including grant making, bio-banking and patient registry support, the design and implementation of research programs in the basic and translational sciences as well as national advocacy, engagement and multi-channel communications on the most pressing and current ME/CFS affairs.

Norwich to be Home to the Quadram Institute

The Quadram Institute is a new centre for food and health research to be located on the Norwich Research Park. Under one roof the Quadram Institute will integrate research teams from the current Institute of Food Research (IFR) and University of East Anglia's (UEA) Faculty of Science and Norwich Medical School with the Norfolk and Norwich University Hospital's (NNUH) gastrointestinal endoscopy facility.



The Quadram Institute is the name of the new hub for food and health research to be located at the heart of the Norwich Research Park, one of Europe's largest single-site concentrations of research in food, health and environmental sciences. Building of a new facility to house the Quadram Institute began in February 2016, with an anticipated opening in 2018.

The Quadram Institute's mission is to develop solutions to worldwide challenges in human health, food and disease.

The opening of the new building will be in 2018 quadram.ac.uk

The initial investment for the Quadram Institute is being provided by the Biotechnology and Biological Sciences Research Council (BBSRC) together with its three Norwich-based partners: the Institute of Food Research (IFR); the Norfolk and Norwich University

Hospitals NHS Foundation Trust (NNUH); and the University of East Anglia (UEA).

The Quadram Institute will integrate research teams from the IFR and UEA's Faculty of Science and Norwich Medical School with the NNUHs' gastrointestinal endoscopy facility under one roof.

To be led by Professor Ian Charles, currently Director of the IFR, the Quadram Institute's mission will be to develop solutions to worldwide challenges in human health, food and disease. The concept for the institute is to enable a step-change in food and health science research by providing new insights and accelerating innovation that will deliver new foods and treatments as well as proactive health and lifestyle interventions, for the benefit of society and the bio-economy.

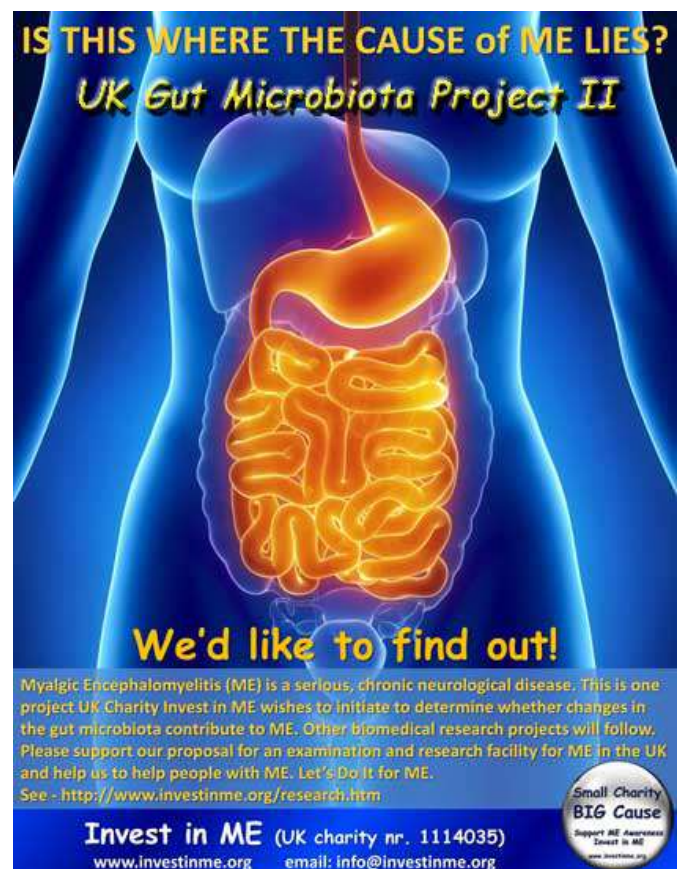
The creation of the Quadram Institute underlines the collaboration of the four founding partners and reflects its strategy to work across four research themes: the gut and the microbiome (the gut flora); healthy ageing; food innovation; and food safety. These research themes will link closely to the world-class plant and crop research at the John Innes Centre and bioinformatics at The Genome Analysis Centre, both also located at the Norwich Research Park, creating a powerful plant-food-health pathway to deliver clinically-validated strategies to improve human nutrition, health and wellbeing. The Quadram Institute will work closely with the food industry, healthcare and allied sectors to transfer its scientific knowledge into practice.

“There is a unique set of resources and expertise at the Norwich Research Park enabling the new Quadram Institute to be a world-leading innovation hub across our areas of interest, namely the gut, microbes, food and health. This is an exciting time to have the opportunity to be truly at the forefront of an emerging new discipline of health and food research. Recent understanding of how food and our gut flora interact is creating a fundamental shift in the way we will understand and address the impact of food on health. We will be engaged in fundamental and translational research, alongside clinical studies and endoscopy and our goal is to become recognised globally for research excellence and clinical expertise, and impact on patient care and outcomes” said Professor Charles.

Professor Melanie Welham, BBSRC Director of Science said, “The UK is a recognised leader in bioscience research, with Norwich being well known for its strengths in food and plant

sciences, as well as microbiological and gastrointestinal research. The Quadram Institute will enable us to bring together world-leading scientists in custom-built facilities to develop an integrated approach to food, diet and health research. The challenges these scientists will be tackling are some of the most important for people around the world, socially and economically.”

UEA Vice-Chancellor Professor David Richardson said: “The Quadram Institute will be a unique multidisciplinary hub for world-leading research in the important fields of food, diet and health. This partnership will give Norwich Research Park researchers the opportunity to make cutting-edge contributions at the forefront of this emerging discipline.”



IS THIS WHERE THE CAUSE OF ME LIES?
UK Gut Microbiota Project II

We'd like to find out!

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. This is one project UK Charity Invest in ME wishes to initiate to determine whether changes in the gut microbiota contribute to ME. Other biomedical research projects will follow. Please support our proposal for an examination and research facility for ME in the UK and help us to help people with ME. Let's Do It for ME.
See - <http://www.investinme.org/research.htm>

Invest in ME (UK charity nr. 1114035)
www.investinme.org email: info@investinme.org

Small Charity
BIG Cause
Support ME Awareness
Invest in ME
www.investinme.org

A Centre of *Excellence* for ME

An Opportunity for Major Progress in Diagnosis, Treatment and Research into Myalgic Encephalomyelitis

Since 2010 Invest in ME have been promoting the concept of a Centre of Excellence for ME and we have been steadily building a foundation of research that can be the basis for such a Centre.

Our Executive Summary for MPs has been updated and is here –

<http://www.investinme.org/Documents/CofE/Invest%20in%20ME%20Research%20-UK%20Centre%20of%20Excellence%20for%20ME%20Executive%20Summary%20for%20MPs%20Status%20June%202016.pdf>

This is a summary of the current status regarding the Invest in ME Research proposal for a Centre of Excellence for ME Research and Treatment based in Norwich, UK.

Background

- A seriously inadequate standard of medical care exists for ME patients in UK
- Very little and fragmented biomedical research into the condition

- Confusion between ME and chronic fatigue has led to unscientific research and ineffective treatments
- Medical professionals lack understanding of, and training in ME – a serious risk of mis-diagnosis and missed diagnoses exists
- Medical students are taught from a curriculum which uses flawed or out of date information about ME
- ME identified as both highlighted area and high priority by MRC – yet MRC has continually failed to fund adequate biomedical research into ME
- ME is leading cause of long-term absence from school due to sickness for students and teachers
- ME is recognised by the Department of Health as a chronic neurological illness yet official guidance and management are aimed at mainly changing patients' "false illness beliefs"
- In 2015 The USA Institutes of Medicine (IOM) recognised ME as a serious, chronic disease

Our Objective

A Centre of Excellence for ME in East Anglia, within the Norwich Research Park, utilising and based on existing facilities and resources would provide a hub of scientific and clinical excellence for ME within Europe

The research arm would be funded initially by private/charitable donations but these preliminary research projects, coordinated in a strategy, would lead to grant applications to major public research funding bodies

The clinical diagnosis and treatment arm would be funded eventually by the NHS - a key objective is that treatments are made available for all.

Service Commissioning

A GP referral, via normal NHS channels to a consultant-led service that links with GPs with special interest. Treatment of patients would be based on sound scientific evidence

A hub and spoke model would exist which would allow dissemination of expert knowledge to GPs and/or ME clinics nationwide and internationally.

Out of area referrals would generate income.

Training opportunities for medical students and other consultants, nurses etc. would exist.

A unique training establishment would be possible

Benefits

Our proposal is a unique opportunity to establish European hub of scientific and clinical excellence in Norwich Research Park

Early and correct diagnosis of patients would apply for all UK patients.

The establishment of standard protocols for effective diagnosis and clinical trials would be complemented by development of effective treatments, leading to highly significant public savings.

The hub and spoke model would address seriously inadequate levels of clinical service for ME in East Anglia and nationwide

The development of a network of domiciliary services to support severely affected patients (currently seriously neglected by the health service and previously left out of research into ME).

Savings on existing consultant referrals and staff - ME examination focused in one area

The project is financially viable – the Centre can start small and grow as further funding becomes available

Current status

All elements of the centre model exist and are ready to be integrated, with the exception of a lead ME consultant that the charity is progressing in discussions with relevant parties.

The Foundation project at IFR/UEA examining the gut microbiota in ME patients started in October 2013. In the autumn of 2016 there will be two more PhDs starting and a further PhD student funded by liME is currently being advertised.

B-cell research as part of a rituximab clinical trial project began at UCL in 2014 and continues with a PhD currently working and a student being funded later in the year.

Several medical students funded by liMER have been intercalating in their medical degrees and we will continue to do this with more already planned. More plans exist to develop a strategy of research involving international collaboration

The inaugural meeting of The European ME Research Group (EMERG) – initiated and funded by the charity - has opened the possibility of a European-wide collaboration which seeks national and EU funding.

The charity is actively looking at complimentary projects which will increase the research knowledge base and translate research into treatments.

The foundations are therefore already set to establish a Centre which can act as a hub for UK and European research and work with other academic organisations and researchers, as well as other Centres of Excellence in Europe and USA, Canada and Australia and New Zealand.

LET's C Research – A C of E for ME

Now the charity is launching a campaign to raise awareness of the possibilities with the Centre of Excellence and gain more support for the firm establishment of this biomedical research and treatment facility for ME.



So we ask supporters to begin getting major support from MPs, GPs, media, celebrities, schools, businesses, research organisations, families, friends.

Our logo will appear everywhere. We are having t-shirts made for events in which our supporters raise funds and awareness.

A web page will be set up for this shortly and progress will be published as and when possible.

Already it is good to see some early support for this campaign -



Our Twitter hashtags are

#LetsCresearch

and

#CofEforME

Our Big Give page is here –

<https://secure.thebiggive.org.uk/projects/view/9169>





Creating a New Vision of Research into ME in Europe

For a long time it has been the objective of Invest in ME to forge international collaborations between researchers.

liME is a member of the European ME Alliance (EMEA) and recently EMEA has joined the European Federation of Neurological Associations in order to promote ME in Europe.

With our EMEA colleagues we also had discussions on forming a European Advisory Board which would allow EMEA to discuss, initiate and fund biomedical research into ME. This led to further development of the idea.

During the Invest in ME BRMEC5 Colloquium in May 2015 discussions with European researchers were conducted about the future of ME research and how better to coordinate and link together research activity in several European countries.

Based upon these conversations there appeared to be overwhelming support and enthusiasm from the group of researchers whom liME/EMEA have brought together to work cooperatively and more effectively.

Forming a group or consortium of European researchers represents a very progressive step in not only helping to establish new collaborations and cement on-going ones but also in developing new research ideas and

priorities and bidding for funds that would allow us to work together on joint projects.

This is the genesis of EMERG - The European ME Research Group

liME convened the inaugural meeting in London in October 2015 to bring this together in the hope that rapid and lasting progress can be made in the research, treatment and cure for myalgic encephalomyelitis.

EMERG has a vision of working collaboratively to increase biomedical research into myalgic encephalomyelitis (ME) in order to find cause(s), treatment(s) and understanding about the disease.

This provides a powerful combination of campaigning and raising of awareness, building new research and accumulation of data based on collaboration and sharing of experiences and knowledge, which will allow rapid progress in the building up a strategy of high-quality research into ME.



The European ME Alliance (EMEA) is now composed of thirteen countries in Europe – working together to create change.



RISK OF SUICIDE DUE TO NEGLECT AMONGST PEOPLE LIVING WITH MYALGIC ENCEPHALOMYEILITIS/CHRONIC FATIGUE SYNDROME IN SPAIN: FIRST SPANISH STUDY

LigaSFC May 12, 2016

*“We will not be a just, advanced nor democratic country as long as there are people who have Myalgic Encephalomyelitis who continue being ignored and **INVISIBLE**”*

- Juan Jimenez-Ortiz

Another International Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Day is here.

But do people with ME/CFS in Spain Have we anything to celebrate?

No, it does not seem so.

That is why the Spanish association of PWME (people with Myalgic Encephalomyelitis), LigaSFC, is launching this very important study by Juan Jimenez-Ortiz on the effects of neglect, mistreatment and lack of proper medical and social care which people with ME/CFS in Spain live with.

For several decades, PWME in Spain, their associations and their lawyers, have been denouncing that this very serious neuroimmune illness, which

affects one in 200 people, live with a great number of social and political factors which, added to their illness, severely reduce their quality of life and put them at risk of suicide (see the numerous articles by the Collectiu Ronda Lawyer’s Cooperative in Barcelona). These factors include, mainly, a lack of access to relevant medical care and a precarious economic situation due the lack of pensions and other help which people too sick to work are entitled to in Spain. Also the lack of proper care of this illness by the health administrations results in a general lack of social support for PWME.

PWME in Spain have spent decades saying that all they want is what other people who are ill with other pathologies have. But they don’t seem to be listened to.

Socially aware and concerned Spanish psychologist, Juan Jimenez-Ortiz, has carried out a research study (for his PhD thesis by the University of Valladolid) with the title: “Depression, hopelessness

in people with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Risk factors and protection” (2016).

The results of this research study are highly worrisome. The high level of risk of suicide, depression and hopelessness in these patients is much higher than in the rest of the Spanish population due to, mostly, the lack of relevant health care services.

STUDY AND RESULTS

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is one of the Central Sensitivity Syndromes (CSS). Although there are still some questions regarding its etiology, the research done up to now attributes it to a significant alteration in the Central Nervous System which affects the immune and the endocrine systems. This produces severe symptoms of fatigue that is not solved by resting, immune dysfunction, cognitive problems, inflammations, and many more organic alterations.

Due to these dysfunctions and symptoms, PWME's lives are severely disrupted. All activities of daily life are affected. Many studies, including this one by Jimenez-Ortiz, show that the effects of this illness as well as the institutional abandonment (health care and social care), added to the losses that such an illness produces (work, family and social relations) are related to depression, hopelessness and risk of suicide.

The objectives of this study by Jimenez-Ortiz were the following:

To measure the incidence of depression, hopelessness and risk of suicide in a sample of Spanish PWME.

To identify which sociodemographic variables or circumstances were related to suffering depression, hopelessness and risk of suicide.

Concretize which variables could be modified to reduce the incidence of depression, hopelessness and risk of suicide.

Propose a model of probability of depression, hopelessness and risk of suicide amongst PWME.

Jimenez-Ortiz proposed the following hypothesis:

There is an incidence amongst PWME higher than the rest of the population of depression, hopelessness and risk of suicide.

There is significant sociodemographic and clinical data (circumstances) regarding depression, hopelessness and risk of suicide amongst PWME.

There are variables which can affect in a positive manner these circumstances.

In this study, 205 Spanish people participated, all of them diagnosed with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, 187 women and 18 men, between 27 and 71 years of age.

The participants were from the following Spanish Regions: 7 from Andalucia, 1 from Aragon, 1 from Asturias, 5 from the Canary Islands, 4 from Castilla La Mancha, 15 from Castilla y Leon, 102



from Catalonia, 7 from Galicia, 22 from Madrid, 1 from Murcia, 14 from Navarra, 5 from the Basque Country, 3 from La Rioja and 18 from Valencia.

The most significant result in this study is the incidence, amongst PWME, of risk of suicide which is 12.75%, compared to the incidence in the general Spanish population which is 2.3%. The incidence of depression amongst these PWME is 57.25%, compared to the incidence in the general Spanish population which is 4%. And the incidence of hopelessness amongst these PWME is 66.85% (there are no studies of hopelessness in the general Spanish population).

Some of the reasons which have been found to be associated in a significant manner to depression, hopelessness and risk of suicide amongst PWME, include:

To risk of suicide:

Not having medical care.

Having ME/CFS affect their capacity to earn a living and the worsening of the economic situation of their family unit.

Having to turn to family members for help with activities of daily life.

Not being listened to by doctors.

To depression and hopelessness:

Having been put down and not treated properly by the health care system.

Not having regular medical follow-up.

Having been sent for psychological or psychiatric treatment and been labelled as "rebellious patient".

Having lost their job.

Having lost friendships due to the illness.

Not being believed when mentioning the effects on their health of chemical agents (chemical sensitivities).

Having had their intimate (sexual) relationships affected by ME/CFS.

Having had ME/CFS affect their economic situation.

CONCLUSIONS AND RECOMMENDATIONS

The results of this study are very important because they show that:

PWME have the most significant areas of their lives affected by this illness.

PWME feel invisible in all aspects of their daily life.

The disruption created by the symptoms of ME/CFS added to the negative experiences lived by PWME are related, in a very significant manner, to depression, hopelessness and to risk of suicide.

Spanish PWME have higher levels of depression, hopelessness and risk of suicide than the rest of Spanish society.

Some of the Preventive Measures that the author, Juan Jimenez-Ortiz, proposes are:

The abandonment and neglect that Spanish PWME live with from the health care system, from the employment world and from their social and family lives has to be denounced and taken seriously. This abandonment and neglect generates suffering among these PWME.

There is an urgent need to organize and carry out educational and training activities about ME/CFS for health care workers, families and society in general.

FOR MORE INFORMATION:
info@ligasfc.org

Mike's EU Marathons

My name is Mike Harley; I'm from Bristol and I'm about to run my 6th of 28



planned EU marathons for charity, that's one in every member state.

On Saturday 4th June 2016 I'm heading out to run the Stockholm Marathon before another 2 marathons

this year: Gdansk in Poland and Toulouse in France.

I want to raise the profile of ME all over Europe and connect charities, researchers and patients together to share resources and lobby their governments for biomedical research and progress.

Ultimately I want to help affect a change in the UK/across Europe but also a real shift in the perception of this awful, indiscriminating illness.

The icing on the cake for me would be to make it through all the marathons in one piece and see some of my friends well on the road to full recovery.

I hadn't heard of ME really before my friend Ian came down with it over 9

years ago. Ian is one of my oldest mates and even though for much of the last decade he's been too ill to work and lost some of the best years of his life to ME, he's always been the same positive person throughout.

After a few years of no real improvement and not seeing him as much as before, I wanted to find out a bit more about what was making him ill and what could be done. He's taught me a lot about the inconsistencies in treatment, both the lack of up-to-date knowledge from GPs and funding for biomedical research from governments not just in the UK.

It wasn't until he told me about *Invest in ME* and the work they're doing with the top scientists and researchers that I started to learn more about ME and how

'well folk' can potentially help them to find a cure.

Around the time that I got involved with fundraising, Invest In ME were already on the way to



crowd-funding enough to set-up a Rituximab trial, B-Cell research and beginning to finalise plans to create a UK ME treatment and research centre in Norwich drawing upon their strong ties with some of the best researchers and scientists from around the world.

I was very impressed with what they had achieved given the fact that the work is done entirely on a voluntary/non-salaried basis; compared to other charities they seemed to be the only ones doing anything really pro-active to help people get better.

It's not my first sponsored challenge for biomedical ME research; I led a team to visit [92 football grounds in 92 hours](#) in

2014 on a trip where we raised over £4000, were featured in 11 TV regions, BBC radio and over 70 football club matchday programmes.

It was on this trip that we felt a huge wave of support from ME patients and their families, not just on social media where they really kept us going, but also when they turned up at the grounds to wish us well, often with food, sponsorship and their stories to tell.

We met sufferers in wheelchairs, really ill young children, people of all ages and severities. It really was a life-changing experience: they were all such nice people who through no fault of their own were ill and weren't getting any help. When the challenge was done, I felt that I really couldn't just leave things there. Most weren't well enough to fight for funding and attention themselves and with very few people around to stand up for them I had to find something bigger and carry on; I think the injustice of their

situation really angered me (and still does) if I'm honest.

On to this challenge and I can tell you that I've done 5 so far: London (UK), Prague (Czech Rep), Helsinki (Finland), Dublin (Ireland) and Thessaloniki (Greece).

I've met with charities, media and patients and it's been an incredible experience; everyone has been really receptive and super-friendly.

Since I started the challenge last May, I've acquired over

1000 followers, £3200 in donations and clocked up nearly 2000 miles in training. I'm not a natural runner by any stretch, I'm short, not very sporty and pretty ignorant when it comes to technique (mental and physical).

But like all good underdogs, as with the people I run for and represent, I'm determined and up for the challenge despite the cost, lifestyle change and commitment required.

I'm driven by the good wishes and support from the friends I've made within the community as well as the gross injustice that I'm seeing with regards to the treatment of ME patients. The support I've had makes it really easy to carry on.

Having done the UK previously (I may well do it again at the end to wrap things up!), my 1st race and return to running was in Prague. Prior to the race I met the family of an ME patient there with connections to their leading ME charity.



I had patients come to cheer me on in the race and I found the same sense of frustration and injustice that I had read about in the UK.

I met patients and ME charity representatives in Finland and Ireland also and interviewed an ME patient of 25 years from Greece; all were the same –their governments classified ME as a psychological problem and refuse to support biological research.

I'm always keen to write a blog where I find out more about the treatment and perception of ME in each country. These pieces are by far and away the most viewed posts; patients and their families are really keen to see what is happening in other countries and join together in solidarity.

The people that I interview have explained that they need to remain relatively anonymous and not to publish their names as they fear investigation by social security/insurance companies who might claim that they are 'working'.

It's a desperate situation in my view when patients aren't able to publicly fight for their right to treatment. The UK PACE trial and its legacy clearly has had a huge impact on the rest of Europe and the way ME is viewed and (not) treated.

I've tried hard to raise awareness of ME on the challenge so far. I've had blogs published and interviews on Running Bug (300K followers), BBC Radio and regional newspapers. It has been difficult though. ME sadly still seems to be viewed with suspicion and huge ignorance by national media –perhaps the government agenda of neglect and denial is being adhered to there too.



One national newspaper approached me to write a piece on the challenge but have failed to publish it despite claiming to be happy with the quality.

In any case, I'm here to do everything I can to help Invest in ME.

I'm strongly urging anyone who is doing a sponsored event to pick them as their charity, we all know someone with ME and biomedical research is the way that you can help them.

Big thanks to everyone who has supported and sponsored me so far, I'm really enjoying the challenge and feeling that I'm doing something worthwhile to help my new friends and, of course, my good friend Ian. Find me on Twitter **@mikesEumaras** If you'd like to sponsor me, text 'IIME82' and £5 to **70070**

I can also be found at www.justgiving.com/mikeseumarathons and at www.mikeseumarathons.eu and on Facebook at www.facebook.com/mikeseumarathons



www.justgiving.com/mikeseumarathons

News from NO^Wrway

On 10th of April the Norwegian Research Council announced that they would be inviting mainly patients and family members but also healthcare practitioners to submit suggestions for research topics into ME. The deadline for these submissions was 3rd May.

The Research Council acknowledges that there are different names being used such as CFS and ME and considers it a serious and fairly common condition with or without pain. The cause/s are unknown, biomarkers for the condition have not been found yet and there is disagreement on the symptom based criteria.

As a consequence there are no effective treatments.

The Norwegian Health Directorate estimates that there are between 10 000 and 20 000 patients with CFS/ME in Norway. Many experience considerable health problems over a long period of time and feel that they are badly served by the healthcare system. The research activity has increased over the last few years, both in amount and approaches, but the need for research and better understanding of CFS/ME is still extensive.

Why this approach?

There are many ways of identifying the knowledge requirement. The health programmes within the Norwegian Research Council now trial an approach which has been named 'needs identified research'. It will be research that gathers knowledge that is particularly called for by healthcare users, and which can provide benefit in a relatively short time period. The Research Council therefore invited participation to identify research areas that can form a basis for new research projects.

News from Norway

What happens after 3rd May?

The Norwegian Research Council will set up a broad based user panel that consists of patients, family members, healthcare professionals, healthcare authorities and researchers who will advise on the research need and type of research that would be useful for patients with CFS/ME.

This will be achieved through a three stage process toward prioritising concrete research projects.

The first task of the user panel would be to evaluate proposals or research questions that have been received by the 3rd May deadline (stage 1). Based on the user panel's prioritisation of proposals the Research Council will send out a call for researchers to respond to.

In the first instance researchers are invited to send in a simple application with a short project description (stage 2).

The user panel evaluates and grades the applications on the basis of how they answer the need and expected benefit set out in the call. A selection of researchers who have sent in applications will be then invited to send in full applications (stage 3).

These applications will be treated in a similar manner as ordinary applications to the health programmes. The planned deadline for a simplified application will be 7th September and for the full application 23rd November 2016.

The Research Council will publish a short general report on the research proposals that have been received. The announcement and invitation for a simplified application (stage 2) is scheduled to be published on the Research Council's website in June.

None of the user panel members can submit or be involved in an application for a research project. Names of the panel members will be announced in early May.

News from N rway



The Norwegian ME Association works to improve the condition for ME-patients through informing both patients and health care workers, health authorities and politicians about ME and about new research on ME. The association also arranges talks and conferences as well as informal meetings where patients can meet other in the same situation. The association has local chapters in almost all counties.

During 2016 the Norwegian ME Association has responded to calls for input regarding new laws concerning child protection services, services for disabled persons and education for disabled children.

In January the association published the report from a large survey of ME patients experience with Nav. NAV administers a third of the national budget through schemes such as unemployment benefit, work assessment allowance, sickness benefit, pensions, child benefit and cash-for-care benefit.

Many ME patients report that they find it difficult to get the benefits to which they are entitled. The report showed that the treatment of patients varies wildly between offices, and that there is little knowledge of ME within Nav. Since the report was published, the association has been invited to present it at several Nav offices, and we hope to go to many others.

We are very pleased to see a growing interest in ME as experienced by the patients.

Representatives for the association has also talked at ME conferences, both arranged by patients and by the health authorities

The Norwegian ME Association is often asked to provide background information for articles in magazines and newspapers. Representatives for the association has also been on the news on national radio several times. The association has a large website filled with information on ME. The website is updated regularly, both with research news, and “human interest” stories. A guest blog has become very popular.

Recently, the Research Council of Norway invites patients to tell them what research into ME was needed. They received more than 700 replies. A board of researchers and patient representatives, two from the ME Association, will soon start to look through the ideas and identify projects.



From Norway Haukeland University Hospital: Brief status of the Project on Genetic Predisposition to ME / CFS

A published study shows a clear genetic predisposition to ME (Albright et al, 2011).

This was a population-based study in which risk of ME was 2.7 times higher in first-degree relatives of CFS patients, 2.3 times higher in second degree relatives, and 1.93 times higher in cubic relatives, compared with the risk of ME in the general population.

Our research group at the Department of Oncology, Haukeland University Hospital, has in recent years been contacted by several independent families with striking incidence of ME and they all have wanted us to do further analysis on mapping of genetic predisposition.

We believe mapping of gene changes in affected patients will be an important step forward in the understanding of disease mechanisms.

We conducted exome sequencing from both CFS patients and healthy family members, where all the coding regions of the genome, including the flanking intron regions were characterized. This technique is considered experimental diagnostic / research and is not considered a full investigation of all genetic variants

that exist in a human. Initially we will only answer the question of what is the molecular genetic predisposition to ME disease in our patients. Exome that constitutes the coding parts of genes including the flanking intron portions, is approximately 1.5% of the total DNA of a human cell, but about 85% of all known mutations is still located therein.

We imagine that some families may have genetic variants of immune genes such as HLA genes, where it is known that specific HLA types are correlated with various autoimmune diseases. HLA genes in ME are being examined in a specific project at OUS, led by Benedicte Lie, Marthe Viken and Torstein Egeland.

At Haukeland Hospital, we are most concerned about families with significant incidence of ME disease, often with multiple siblings with onset relatively early age, often with a relatively severe illness, and preferably with ME disease in successive generations.

We believe some such families may have genetic variants directly in the "effector system" for symptoms (which symptoms are created), and where the detection of such variants can tell us about disease mechanisms.

We have completed exome sequencing in a total of 18 people, from two different families with significant incidence of ME disease among first and second degree relatives. We have started analysing a third family.

Regarding the two families for whom we have completed exome sequencing and subsequent analysis, we have several relevant gene variants that are being investigated further.

Currently we have focused on an interesting genetic variation (mutation) that all the sick persons in one family have, and which occurs in approximately 2/1000 of a European general population.

The variant also occurs in a few of the patients included in our clinical trial.

We focus our efforts towards this variation now and have taken skin biopsies (all cells in the affected have the same gene variant) for cultivating cell cultures and closer examination of energy metabolism.

We have created cells in which the mutation is "inserted" by means of gene transfection, and where we can "turn up" the expression of the mutated variant significantly, and see the implications for the cells.



We believe the version we're dealing with now may be relevant to the disease, and data so far fits in well with the work we otherwise perform now, to identify disease mechanisms of ME closer.

04/15/16

Øystein Fluge Olav Mella Ove Bruland

<http://me-forskning.no/oppdatering-fra-haukeland-om-prosjektet-pa-genetisk-predisposisjon/>

10 May 2016

Update, RituxME study

Multi-centre study RituxME completed enrolment of all 152 participants in September 2015.

By the summer holidays, all patients in Bergen, Trondheim, Notodden and Oslo will have completed their course of treatment, and study centre in Tromsø provides final treatment in September.

As known RituxME is a double blind study, meaning that neither the patient nor treating personnel know whether the individual patient is receiving active medication or placebo.

Blinding is maintained until the last participant has finished one year of follow-up after stopping treatment, and we will therefore be able to break the code in September 2017.

The results of RituxME study will be published in a scientific paper during 2018.

Research biobank at Haukeland University Hospital has been expanded with blood tests before treatment from all participants, and together with samples from previous studies and the ongoing cyclophosphamide study, these blood samples form a unique source for research on disease mechanisms and a possible biomarker.

There is currently a lot going on in the laboratory at Haukeland, and there is collaboration with several national and international institutions on studies such as autoantibodies, immune signatures, cell metabolism and genetics, where samples from the biobank are being used.

We continue to collect samples for the Biobank at fixed time points during the trial, right until the last patient has completed follow-up.

Kari Sørland
Programme coordinator

<http://me-forskning.no/oppdatering-fra-haukeland-om-rituxme-studien/>

One Event Can Change Everything

A rituximab clinical trial for ME

Let's Do Research
www.ukrituximabtrial.org

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. A UK trial of rituximab for ME is being initiated and organised by Invest in ME and the charity wishes to establish a Centre of Excellence for ME in the UK. Please support us and help us to help people with ME. **Let's Do It For ME. Let's Do Research.**

Invest in ME (UK charity nr. 1114035)
www.investinme.org email: info@investinme.org idifme.org

Small Charity
BIG Cause
Support ME Awareness
Donor in ME
www.investinme.org



Letter from America 2

When the hoof beats are zebras

By Maureen Hanson

An analysis [by Johns Hopkins researchers](#) claims that a third of all deaths in the US annually are due to medical errors. This finding not only [calls for better reporting](#) of such errors, but also for better medical training to prevent them. But death is not the only outcome of medical errors—instead, unnecessary patient suffering can result.

Anyone who binge-watches the TV show [Discovery Life: Mystery Diagnosis](#) will soon detect a pattern, one that demonstrates the need for improvements in medical training. A typical show might have a young woman suddenly taken violently ill with an apparent stomach flu. But instead of getting better, she continues feeling nauseated and weak. She has to drop out of college. At home she develops a myriad of symptoms—such as night sweats, sore throat, swollen glands, and difficulty reading and speaking. She visits a doctor, who tells her she has strep throat. Despite antibiotics, she doesn't get better, then goes to an internist, who tells her she should see a psychiatrist.

Professor Maureen Hanson is Professor of Molecular Biology and Genetics at Cornell University and conducts NIH-supported research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. She is with The OpEd Project's Public Voices Fellowship at Cornell.

This continues on for several more scenes—sometimes several years in the life of the ill person whose story is being told—as one after another wrong diagnosis is made. The mistaken doctors are always played by actors, as no doctor who gave the incorrect diagnosis would like to be identified.

Finally, a smart doctor figures out what is wrong, and is identified by name and appears on the show. The grateful young woman now has a diagnosis, and sometimes a treatment, often leading to a happy ending.

Such could be a show made to describe Laura Hillenbrand's journey to a diagnosis of chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis, as described in [her vivid, and often shocking, New](#)

Yorker article. But while she eventually did receive the correct diagnosis, she didn't get a happy ending. For there is no effective treatment for most victims of the disease, and she remains ill and rarely able to leave her house.

As a researcher who surveys CFS patients who volunteer as experimental subjects, I have learned that a long journey to be diagnosed with chronic fatigue syndrome is not unusual.

In fact, it is common for individuals with symptoms of CFS to go through multiple years of misdiagnoses, most seeing **an average of 4-6 doctors or more**, often being told they have a psychiatric disorder, before they find a doctor who has learned enough about CFS to identify the disease.

The **Centers for Disease Control estimates** that fewer than 20% of Americans who have CFS have been diagnosed. Part of the blame for this problem lies in medical training, in which students are told the famous adage: "If you hear hoofbeats, think horses, not zebras." In other words, if symptoms appear to fit a common disease, then that is the best diagnosis.

This idea, when not applied properly, is the origin of many of the errors chronicled by the Mystery Diagnosis TV show. Because though some diseases are less common than others, that doesn't mean they don't exist—every rare disease has its victims.

Another lesson from the show's episodes: advocating for yourself can save your life. A striking number of the patients or their caregivers came to a suspected diagnosis or consulted a knowledgeable physician through researching their own symptoms on the web or in the library.

Standard blood tests are given to someone who arrives complaining of long-lasting fatigue, malaise, and muscle pain. But no abnormalities are seen in such tests of patients with CFS. This leads to the favorite diagnosis of doctors who don't want to spend time dealing with a patient with unexplained symptoms: depression. Indeed, some CFS patients do become depressed—after being ill for years, losing their jobs, being maligned by friends and family, and repeatedly being told that there is nothing physically wrong with them. But not all CFS patients become depressed, and even those who have psychological problems also have a physical illness of unknown origin. More sophisticated tests, ones more often found in research labs rather than medical testing labs, have revealed immunological and neurological abnormalities in CFS patients. But these are difficult to translate into a simple, easily administered test.

Why is a diagnosis important, given that there is no effective treatment for most CFS victims that can restore their prior functioning? Because recommended therapies for misdiagnosed illnesses often can do harm, increasing the severity of CFS. Inappropriate drugs or lifestyle changes—such as types of exercise harmful to people with CFS—can cause patients to become worse, sometimes with long-term detrimental effects.

Improved training of physicians about CFS is needed if patients are not going to continue being unwilling characters in real-life episodes of Mystery Diagnosis.

A **2010 survey of medical textbooks** revealed that only 40% even mentioned CFS. Until recently, little has been done to dispel early and

stubbornly persistent notions of the psychological basis of the illness.

Fortunately, the National Institute of Medicine undertook [a year-long study](#) of the scientific literature, and concluded that that CFS is a “serious, chronic, complex, and systemic disease that frequently and dramatically limits the activities of affected patients.”

The report provided a [simple set of diagnostic criteria](#) that could be applied by a physician in general practice or any speciality to determine whether a patient should be diagnosed with CFS.

A [Clinician's Guide](#) the Institute produced should reduce the time to diagnosis—and help knowledgeable patients advocate for themselves.

Originally printed in *THE HILL*
<http://thehill.com/blogs/congress-blog/healthcare/279089-when-the-hoofbeats-are-zebras>



From **IT's A FUNNY OLD WORLD - MEDICINE and ME**
<http://www.investinme.org/IIME-Cartoons-2013-01.htm>

Tackling ME/CFS in New Zealand

by the

Principles of Precision Medicine

Within its population of 4.5 million, New Zealand has an estimated 20000-25000 ME/CFS patients¹. An advantage of this nationwide number is that a significant proportion of these have been evaluated and diagnosed by a single general health practitioner, Dr Rosamund Vallings, of our team who specialises in ME/CFS in her Auckland medical practice. Moreover, with her specialised clinical knowledge of this illness and international role her patient contact extends nationwide and she facilitates training for other health practitioners throughout the country. There is also an effective national ME/CFS organisation, ANZMES, and various regions within the country have their own support groups that are invaluable for affected patients. This means for study purposes in depth information is available for at least a proportion of New Zealand patients. For this patient group variables beyond

Warren P. Tate¹, Eiren C. Sweetman¹,
Alex J. K. Noble¹, Christina D. Edgar¹,
Grace Bateman¹, Angus Mackay¹,
Margaret M. Ryan², Lynette D.
Hodges³ & Rosamund Vallings⁴

¹Department of Biochemistry,
²Department of Anatomy, University
of Otago, Dunedin & Brain Health
Research Centre and Brain health
New Zealand, ³School of Sport and
Exercise, Massey University,
Palmerston North, & ⁴Howick Health
and Medical Centre, Auckland

the design of a study, like ethnicity, that can confound subsequent evaluations can be managed by careful selection of patients. Our New Zealand environment brings into play the concept of 'precision medicine' where intense study of a small number of

patients can balance the disadvantage of having only a limited base number of patients available for recruitment. 'Precision medicine' is being applied to 'rare diseases' internationally where patient numbers are naturally small, and yet intense molecular studies are starting to reveal new biological insights into these illnesses².

Despite the advantages of a small well-characterised patient group, those health practitioners in New Zealand who understand that most ME/CFS patients do not recover from their illness, are often reluctant to take more than a very small number of such patients into their practices. Additionally, until very recently, medical students received no formal training in ME/CFS, and so graduated without the necessary knowledge to assist their professional response when confronted with a potential ME/CFS patient. There are still pockets of practitioners who remain sceptical of the validity of ME/CFS as a distinct illness. This often leads to frustrated patients looking constantly for an empathetic health practitioner in their own town or city who has some knowledge and understanding of their illness.

The confusing and conflicting publicity in 2015 from opposite sides of the Atlantic on the nature of ME/CFS has not helped this situation in New Zealand. On the one hand, the Institute of Medicine of the National Academy of Sciences in the United States published a report in February³ that emphasised the serious and chronic nature of the illness. The authors expressed regret that many practitioners had not taken patients



more seriously. It further concluded the disease needed a new name to replace the name used in the United States, Chronic Fatigue Syndrome (CFS). The well-meant suggestion of Systemic Exercise Intolerance Disease (SEID), emphasising post exertional malaise as the key characteristic of the illness,

Professor Warren Tate

however, would be unlikely to add more gravitas to perceptions of the disease from either the public or the health profession. On the other hand, a conflicting Lancet Psychiatry report was published in October, updating⁴ the PACE study of 2011⁵ arising from Oxford University, which together with associated publicity advocated exercise and positive thinking as the best mix for alleviating ME/CFS symptoms

For those chronically affected patients here in New Zealand who have tried everything possible to manage their ME/CFS over a long term of the illness, the additional apparent quotes in the publicity surrounding the follow up PACE study article from the authors - that it was a minority who thought ME/CFS was a chronic illness and was caused by a virus - were not well received. Indeed, many believe their illness to have been triggered by a viral infection - often Epstein Barr-mediated glandular fever. Such ME/CFS patients have often used highly innovative ways to achieve a constructive life despite the serious restrictions to their life choices because of the symptoms of the illness. Post activity malaise has been a real part of these debilitating effects. As discussed in one of our pilot studies below, this can be documented after exercise by physiological testing. Ironically, medical students in training, and the wider group of health professionals in New Zealand, regard the Lancet as an iconic fount of medical knowledge, and have enormous respect for Oxford as a research University. Therefore, those who rely on such sources, and have no prior contact with ME/CFS patients or appreciation of the often lifetime debilitating features of the illness, will be left with a distorted view of ME/CFS not helpful to the management of their patients.

Despite this confusion, the situation in 2016 in New Zealand is looking promising for New Zealand patients. Now, at the University of Otago Medical School, in a module on unexplained diseases, teaching and discussion on the topic of ME/CFS is facilitated by WPT to what has proven to be a highly

responsive young audience of 3rd year medical students. The most common question asked, albeit with some anxiety by the medical students in their sessions on ME/CFS is 'How do I respond to an ME/CFS patient?' My (WPT) simple response has been 'Acknowledge that the patient is ill and needs your empathy and help - while you are determining whether their illness is consistent with the clinical guidelines for ME/CFS'. They, and all General Practitioners in New Zealand now receive the 2014 edition of the international 'Primer for Clinical practitioners'⁶ to which Dr Vallings contributed as part of the international writing panel. In addition, Dr Vallings has written two excellent books, one for adult patients and their practitioners⁷, and one for teenagers⁸ bewildered by an ME/CFS mediated dramatic change in their health status. It is anticipated the situation for ME/CFS patients countrywide will improve as tomorrow's young doctors graduate and spread throughout the workforce. The students were surprised that, despite the lack of general community knowledge and understanding of ME/CFS, the number of New Zealand patients is about half of those diagnosed with Alzheimer's disease in New Zealand⁹. In common with ME/CFS, Alzheimer's disease still has no simple molecular diagnostic test, and as yet no effective therapies. ME/CFS however, receives much less publicity, less national and international focus, and considerably less research funding than Alzheimer's disease, and so there is critical need for better knowledge and a higher public profile.

However, despite ongoing confusion as to the nature of ME/CFS, much new exciting global research and

serendipitous observations have been made in the 4- 5 years since the unfortunate focus on the retrovirus XMRV¹⁰, a false lead that appeared at the time to be so promising. The Norwegian trials of rituximab as an antibody therapy for lymphoma that serendipitously gave ME/CF patients a period of remission is an exciting observation that can direct our focus to better understand the disease¹¹. Recent important ME/CFS studies on plasma cytokines¹², and on miRNAs in plasma¹³ and Natural Killer cells¹⁴, as well as a miRNA study for a biomarker signature in the related disease, fibromyalgia¹⁵, have added valuable information. Given the environment described above in New Zealand, we have initiated a research programme on ME/CFS that is patient focussed, and is leaning towards the principles of precision medicine for understanding each patient, by using comprehensive molecular studies in the hope that this paradigm might reveal new information on the illness that is of national and global significance.

An illustration how a detailed molecular focus on individual patients - precision medicine - can provide valuable information for such an unexplained disease as ME/CFS was starkly illustrated by the personal intense molecular study published in *Cell* in 2012¹⁶ with over 40 authors by a Stanford University medical geneticist Michael Snyder. He followed his own molecular profile over ~ 2 years and related it to relatively minor illnesses such a common cold and an upper respiratory infection. The title of the paper was 'Personal omics profiling reveals dynamic molecular and medical and phenotypes'. Apart from

determining the sequence of his genome, Snyder carried out complex analyses like exome sequencing, transcriptome sequencing, small RNA sequencing, shotgun proteome sequencing and metabolome analysis repeatedly through the 2 year period on samples of plasma and blood cells, and these were linked with clinical tests. Informative changes in gene expression profiles were revealed in response to the viral illnesses and they could be related to specific molecular pathways that were affected.

Such a profound longitudinal study and analysis is beyond what can be done even with a small group of ME/CFS patients because of cost alone. Nevertheless, a distilled down study is possible that could still provide valuable information. Changes in the expression of genes, proteins and plasma metabolites in a chronic disease like ME/CFS that has acute, steady state, and relapsing phases might be highly informative to reveal a deeper layer of understanding. The costs of genome sequencing have plummeted to ~\$2000 - \$5000 per genome depending on whether detailed analysis of the results is included, and while providing valuable information it seems as yet not to provide compelling data that would immediately improve the situation for individual ME/CFS patients.

In line with these concepts, we are now in the data collection stage for two small pilot studies, each with 10 patients, recruited in two separate regions of New Zealand. They are matched by age/gender with healthy controls, with one of the studies having

a comparative cohort of multiple sclerosis (MS) patients, as an example of a 'fatigue illness' distinct from ME/CFS. Our goal is to examine and correlate changes in plasma cytokines and miRNAs, with the cellular transcriptome, and the proteome in purified immune cells. In the second study we are planning to link these molecular analyses to an exercise regime that measures physiological parameters before and after exercise. These two pilot studies in turn are preliminary to a planned larger study with 40 carefully evaluated patients from Dr Vallings health practice.

To understand the disease mechanism of ME/CFS in our NZ cohort at a molecular level, a comprehensive analysis has been undertaken in an initial pilot study group. Peripheral blood samples were taken from the study participants and plasma, lymphocytes and neutrophils extracted. From the plasma and lymphocyte immune cells total RNA (including small RNAs) was isolated using a *mirVana*[™] *PARIS*[™] RNA and Native Protein Purification Kit. Total protein was also obtained from the lymphocyte and neutrophil cells for western and proteome analysis. So far we have obtained and analysed data on both cytokines and microRNAs from plasma in one of our pilot studies, and are awaiting the results of analyses on the transcriptome encompassing

coding, small and large noncoding RNAs, and initiating a study of the proteome.

We have become acutely aware that the key to validating results from small patient studies, whether it be for rare diseases or the pilot studies we are conducting, are appropriate biostatistical analyses. This is a dynamic field and new ways of analysing data are constantly being developed that can extract richer information from low numbers of patients, providing random variables outside the study design can be controlled. It is sobering that of the 750 000 studies that have suggested

statistically significant leads for therapy development only a handful have stood up to rigorous testing and development¹⁷. That is a challenge for us in taking a 'precision medicine' approach to these studies. In consultation with an experienced biostatistician we are exploring a number of mainstream statistical approaches in an attempt to ensure apparent molecular differences between ME/CFS patients and controls have validity. There is an advantage in having two independent statistical tests so that if an effect is found with one test it can be confirmed with the other. Since our studies are discovery tests,



the ability to confirm a result derived from one patient cohort with the other cohort of our second pilot study supports further analysis. MicroRNAs are of great interest as potential disease biomarkers since they are present and highly stable in virtually all biofluids, and appear to be acutely sensitive to changes in various physiological processes¹⁸⁻¹⁹. They have emerged as important biomarkers and modulators of numerous pathophysiological processes. Our approach, guided by the 'precision medicine' methodology aims to investigate any correlation between circulating cytokines and miRNAs in plasma samples from individual patients within our two study groups. In our ME/CFS pilot studies for example, we have found differences between multiple cytokines and a particular microRNA. This implies a connection between these cytokines with the microRNA. Of interest for our initial results is a recent study by Su et al. 2015²⁰ where two cytokines were shown to induce a microRNA in macrophages in chronic inflammation.

Recently, perhaps relevant to ME/CFS a number of dysregulations in microRNAs have been reported in patients suffering from pain - in complex regional pain syndrome, cystitis-induced chronic pain, and irritable bowel disorder, both in the affected tissues, and reflected in the circulation. Such microRNAs are implicated functionally in pain processing based on studies in animal models of inflammatory and neuropathic pain, and in vivo studies have found dysregulated microRNAs influence the post-transcriptional

modulation of genes implicated in pain generation and maintenance²¹.

Several clinical studies have highlighted the potential of plasma microRNAs to be biomarkers for complex regional pain syndrome and for fibromyalgia. For example, Orlova et al. (2011)²² used whole blood samples from 41 patients with complex regional pain syndrome and 20 controls in a study analysing miRNA, cytokines and correlations with numerous clinical parameters. Unsurprisingly, expected cytokines such as VEGF were elevated in the disease group compared to controls and a miRNA-signature was evident. Extensive correlation analyses revealed that 4 miRNAs were positively correlated with disease-associated pain level, one other was correlated with the occurrence of migraine within the patient cohort and an extensive array of miRNAs was found to correlate with the levels of circulating cytokines²². A similarly designed 2013 study investigated the miRNA profile of the cerebrospinal fluid in fibromyalgia patients²³, a disease with many commonalities to ME/CFS, identified 10 miRNAs differentially expressed between affected patients and healthy controls. Most notably, the study found that decreased levels of miR-145-5p in the CSF were associated with reported symptomatology such as pain intensity and fatigue²⁴.

To investigate changes in miRNA expression, we used TaqMan® Array MicroRNA cards to assay for 754 human miRNAs in the plasma samples. Megaplex™ RT Primers complement the assays on the cards

and were used to convert the miRNA to cDNA. To improve assay sensitivity and account for the limited abundance of some miRNAs, a preamplification step using Megaplex™ PreAmp Primers was included. Data was assessed using the BioC/R package HTqPCR (high-throughput qPCR)²⁵. MiRNAs with 'undetermined' ct values or ct values >35 were removed from the analysis. A norm rank invariant method was used to normalise the data. The two study groups have initially been compared using a non-parametric Mann Whitney U test to determine statistically significant miRNAs.

To complete our molecular study of the pilot study group we are also completing full transcriptome and proteome analyses of the ME/CFS and healthy control individuals. At present, as stated above, transcriptome analysis of the 20 participants in our first pilot study is underway. Total RNA was extracted from lymphocytes purified from the original blood samples, using the same extraction kit as for the miRNA analysis. We are investigating by HiSeq analysis both small RNA (NEXTflex small RNA libraries), including miRNA, and total RNA (TruSeq stranded total RNA libraries (ribozero human/rat/mouse)). The proteome analysis will analyse total protein extracts from the patient and control subject's lymphocyte cells. Samples will be compared by sensitive global proteomics profiling using the mass spectrometry facilities in the Centre for Protein Research, University of Otago. The approach will allow for a semi-quantitative comparison of protein profiles using for example spectral counts or extracted peak intensities. It will be of significant interest to see if the results of these

analyses correlate in any way with our miRNA and cytokine investigations to suggest disease mechanisms or pathways.

Our second pilot study conducted by exercise physiologist, Dr Lynette Hodges at Massey University, aims to link exercise performance with molecular analyses. The exercise part of the study has examined differences in fatigue parameters among three study groups, ME/CFS patients, MS patients and healthy controls. Each group performs repeated incremental exercise tests separated by 24 hours. Incremental exercise tests utilised an increased power requirement each minute and measured oxygen consumption, carbon dioxide production, respiratory exchange ratio, and power output, among other parameters. Each incremental exercise test was followed by a steady state 5 min exercise test conducted at the anaerobic threshold, measuring cardiac output. In contrast to the other two groups ME/CFS patients uniquely had lower power output on the day 2 re-exercise test, consistent with the reported characteristic of the disease, post-exertional malaise. Cytokine analysis data on plasma samples from these subjects have just been collected. Applying miRNA analysis in this collaborative exercise study is appealing; it has been shown that circulating miRNA-signatures are distinct enough to enable discrimination between eccentric and concentric exercise²³ and so they also may provide valuable indicators of the post-exertional malaise experienced by ME/CFS sufferers. It is hoped that we can also add data on the expression of coding genes, and of small and larger noncoding RNAs, together with altered protein profiles to give a more

comprehensive understanding of the compromised physiology in ME/CFS relating to this post exercise malaise.

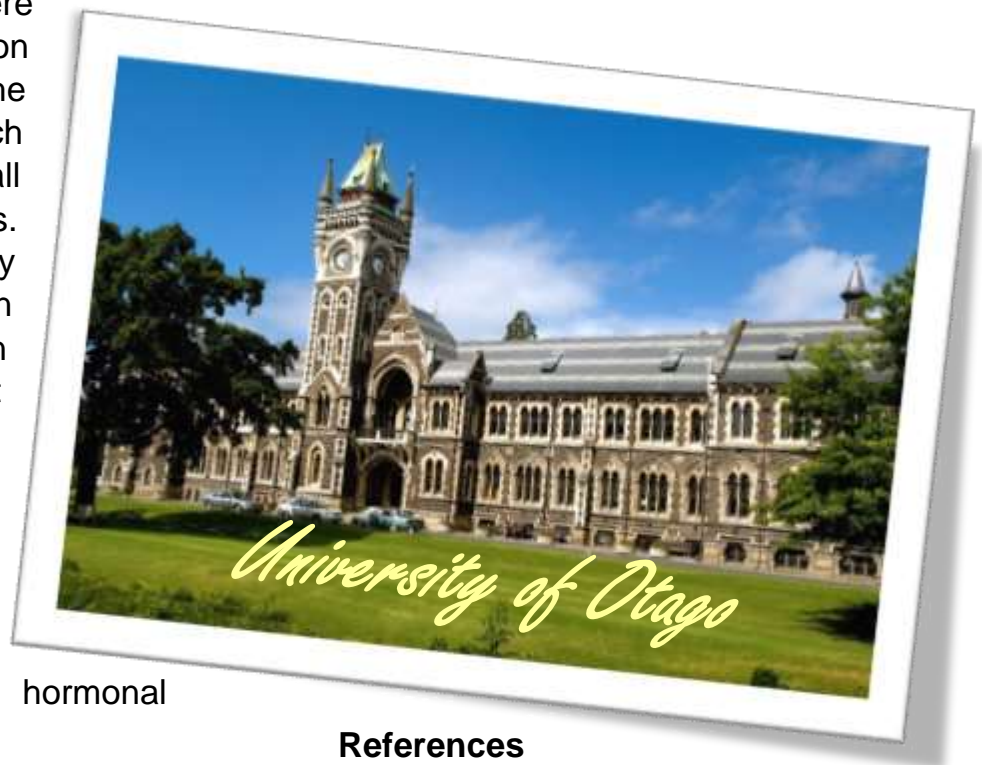
ME/CFS lends itself to longitudinal intensive molecular study to understand fluctuating health through relapse and recovery and steady state health periods, just as the Snyder study described above monitored molecular changes through compromised health episodes with viral illnesses. The precision medicine approach can be used to analyse what is happening in individual ME/CFS patients, and determine whether there are common mechanisms behind the relapses in each member of a small cohort of patients. Additionally, pregnancy in some women ME/CFS patients can lead to a significant alleviation in symptoms, perhaps because of increased blood volume, suppression of allergic responses, and their changed hormonal profile.

Understanding what dysregulated pathways are reversed in this situation through molecular analysis may give further insight into the nature of ME/CFS. Additionally, new technology is now available that can assess mitochondrial functions in isolated blood cells and that may be additional information that can be added.

We work towards a goal of providing a diagnosis that combines multiple molecular biomarkers linked to

dysregulated biologically plausible pathways, and understanding the compromised physiology and can lead to more effective treatments for the heterogeneous symptomology of the ME/CFS patient group, not only aiding clinicians in choosing treatment options, but perhaps also helping in the stratification of patients in clinical trials.

Acknowledgements: We are grateful for support from ANZMES the national ME/CFS group of New Zealand, Lottery Health Fund of New Zealand, H S and J C Anderson Charitable Trust, a private bequest.



References

- 1) Welcome to ANZMES. The Associated New Zealand ME Society Inc, Auckland, New Zealand. <http://www.anzmes.org.nz>
- 2) Newman SK, Jayanthan RK, Mitchell GW, Carreras Tartak JA, Croqlio MP, Suarez A, Liu AY, Razzo BM, Oveniran E, Ruth JR, Fajgenbaum DC (2015) Taking Control of Castleman Disease: Leveraging Precision Medicine Technologies to Accelerate Rare Disease

Research *The Yale Journal of Biology and Medicine* 88:383-388.

3) Committee on the Diagnostic Criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Board on the Health of Select Populations; Institute of Medicine. (2015) *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness*. Washington (DC): National Academies Press (US). Available from: <http://www.ncbi.nlm.nih.gov/books/NBK274235/> doi: 10.17226/19012

4) Sharpe M, Goldsmith KA, Johnson AL, Chalder T, Walker K, White PD (2015). Rehabilitative treatments for chronic fatigue syndrome: long-term follow-up from the PACE trial. *Lancet Psychiatry* 2: 1067–1074.

5) White PD, Goldsmith KA, Johnson AL, Potts L, Walwyn R, DeCesare JC, Baber HL, Burgess M, Clark LV, Cox DL, Bavinton J, Angus BJ, Murphy G, Murphy M, O'Dowd H, Wilks D, McCrone P, Chalder T, Sharpe M (2011) Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. *The Lancet* 377: 823 – 836.

6) Friedberg F, Bateman L, Bested AC, Davenport T, Friedman KJ, Gurwitt A, Leonard LA, Lapp CW, Stevens SR, Underhill RA, Vallings R (2014) ME/CFS: A Primer for Clinical Practitioners. Chicago, USA: International Association for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.

7) **Vallings R (2012) *Chronic Fatigue Syndrome M.E. Symptoms, Diagnosis & Management* Calico Publishing Ltd, New Zealand, edited by Linda Cassells, pp1-350.**

8) **Vallings R (2015) *Managing ME CFS A Guide for Young People*. Calico Publishing Ltd, New Zealand edited by Linda Cassells, pp1-145.**

9) Dementia Economic Report 2012. Alzheimers New Zealand. <http://www.alzheimers.org.nz/news-and-events/nz-information/dementia-economic-report-2012>

10) Lombardi VC, Ruscetti FW, Das Gupta J, Pfof JD, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, Mikovits JA (2009) Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome. *Science* 326: 585–589.

11) Fluge Ø¹, Bruland O, Risa K, Storstein A, Kristoffersen EK, Sapkota D, Næss H, Dahl O, Nyland H, Mella O (2011) Benefit from B-lymphocyte depletion using the anti-CD20 antibody rituximab in chronic fatigue syndrome. A double-blind and placebo-controlled study. *PLoS One*. 6(10):e26358. doi:10.1371/journal.pone.0026358.

12) Brenu EW¹, van Driel ML, Staines DR, Ashton KJ, Hardcastle SL, Keane J, Tajouri L, Peterson D, Ramos SB, Marshall-Gradisnik SM (2012) Longitudinal investigation of natural killer cells and cytokines in chronic fatigue syndrome/myalgic encephalomyelitis. *Journal Translational Medicine* 9:88. doi: 10.1186/1479-5876-10-88.

13) Brenu EW, Ashton KJ, Batovska J, Staines DR, Marshall-Gradisnik SM (2014) High-throughput sequencing of plasma microRNA in chronic fatigue syndrome/myalgic encephalomyelitis. *PLoS One* 9: e102783

- 14) Petty RD, McCarthy NE, Le Deiu R, Kerr JR (2016) MicroRNAs hsa-miR-99b, hsa-miR-330, hsa-miR-126 and hsa-miR-30c: Potential Diagnostic Biomarkers in Natural Killer (NK) cells of patients with Chronic Fatigue Syndrome (CFS)/Myalgic Encephalomyelitis (ME). *PLoS One* 11: e0150904
- 15) Cerdá-Olmedo G, Mena-Durán AV, Monsalve V, Oltra E (2015) Identification of a microRNA signature for the diagnosis of fibromyalgia. *PLoS One* 10: e0121903
- 16) Chen R, Mias GI, Li-Pook-Than J, Jiang L, Lam HYK, Chen R, Miriami E, Karczewski KJ, Hariharan M, Dewey FE, Cheng Y, Clark MJ, Im H, Habegger L, Balasubramanian S, O'Huallachain M, Dudley JT, Hillenmeyer S, Haraksingh R, Sharon D, Euskirchen G, Lacroute P, Bettinger K, Boyle AP, Kasowski M, Grubert F, Seki S, Garcia M, Whirl-Carrillo M, Gallardo M, Blasco MA, Greenberg PL, Snyder P, Klein TE, Altman RB, Butte AJ, Ashley EA, Gerstein M, Nadeau KC, Tang H, Snyder M (2012) Personal Omics Profiling Reveals Dynamic Molecular and Medical Phenotypes. *Cell* 148 :1293–1307.
- 17) Manning A (2016) Precision Medicine and Autoimmune diseases - presentation
- 18) Jung M., Schaefer A., Steiner I., Kempkensteffen C., Stephan C., Erbersdobler A., Jung K. (2010) Robust microRNA stability in degraded RNA preparations from human tissue and cell samples. *Clinical Chemistry* 56, 998–1006.
- 19) Tomaselli S., Panera N., Gallo A., Alisi A. (2012) Circulating miRNA profiling to identify biomarkers of dysmetabolism. *Biomarker Medicine* 6, 729–742.
- 20) Su S, Zhao Q, He C, Huang D, Liu J, Chen F, Chen J, Liao JY, Cui X, Zeng Y, Yao H, Su F, Liu Q, Jiang S, Song E (2015) MiR-142-5p and miR-130a-3p are regulated by IL-4 and IL-13 and control profibrogenic macrophage program. *Nature Communications*. 6:8523. doi:10.1038/ncomms9523.
- 21) Anderson HH, Duroux M, Gazerani P (2014) MicroRNAs as modulators and biomarkers of inflammatory and neuropathic pain conditions. *Neurobiology of Disease* 71, 159–168.
- 22) Orlova IA, Alexander GM, Qureshi RA, Sacan A, Graziano A, Barrett JE, Schwartzman RJ, Ajit SK (2011) MicroRNA modulation in complex regional pain syndrome. *Journal Translational Medicine* 9, 195. doi: 10.1186/1479-5876-9-195.
- 23) Bjersing JL, Lundborg C, Bokarewa MI, Mannerkorpi K (2013) Profile of cerebrospinal microRNAs in fibromyalgia. *PLoS One* 8, e78762. <http://dx.doi.org/10.1371/journal.pone.0078762>.
- 24) Banzet S, Chennaoui M, Girard O, Racinais S, Drogou C, Chalabi H, Koulmann N (2013) Changes in circulating microRNAs levels with exercise modality. *Journal of Applied Physiology* 115, 1237-1244.
- 25) Dvinge H, Bertone P (2009) HTqPCR: High - throughput analysis and visualization of quantitative real - time PCR data in R. *Bioinformatics* 25: 3325.

It's a Funny Old World

#thingsdoctorsaytopeoplewithME

With a disease such as ME humour can sometimes help in balancing the absurdity of the patient's situation with hope for a better way forward.

When the establishment organisation responsible for using public funding to research diseases such as ME has failed consistently (influenced by vested interests), where the Department of Health and Chief Medical Officer avoid taking any responsibility for treating the disease with any serious action and where successive health ministers do not even register the disease on their worklist of important subjects – then what is left for a patient or his/her family to do?

All of the above, of course, influences how many healthcare professionals still continue to view and treat the disease – sometimes showing an immense talent for ignorance and insensitivity that might be candidates for some record book, were it not for the negligence that it so clearly illustrates.

Hopefully conferences such as IIMEC11 and the [resulting DVD](#) can dispel some of this ignorance and neglect – and increased knowledge and education are weapons that the patient community can use to counter this.

But humour can help one deal with it. So here, thanks to Ali Head and

friends, are a selection of quotes from patients who have been on the receiving end of some awkward, some ridiculous, some incomprehensible and some just downright stupid observations from healthcare staff – and others.

“well, I'm going to have to give you the



CFS diagnosis. But no employer will want you.”

“well if you don't follow your GET/CBT plan it means you want to keep yourself ill”

GP: "ALL my patients complain of tiredness".

- Exactly. Doctors & patients need diagnostics for this disease

"there's no such thing as CFS"

After neg bloodwork: "I've tested you for everything I can treat." - Infectious Disease Specialist

“Oh dear you must be very tired...”

Follow up with Gastroenterologist 'U need to take a step back and address your mental state'

"Well a lot of that will be because of your weight"

At cardiologist for myocarditis, cardiomyopathy, POTS, - "so you're here because you're fatigued? 3x week sport will cure you!"

Psychotherapist when challenged "WE think it's something in your PERSONALITY that keeps you ill" (tied to 'benefits' situation)

GP: "I don't think there is anything wrong with your heart, You Just have ME GP: but I don't believe in ME"



"finally going to GP due to worsening symptoms from consistently overdoing it& being referred for GET for deconditioning"

'No illness could be that complicated - you must have imagined it!'"

- I wish ! !

Doctors attributing any new symptom to your ME diagnosis, making them miss other ailments/illnesses f.ex. breast cancer

Apparently my fibromyalgia is caused by childhood trauma, according to ME clinic psych.

At ME clinic with psych. I told of woman who died from ME. She replied "no one dies from fatigue"

My GP often dismisses my symptoms and labels me with health anxiety. who wouldn't want answers to symptoms?

I asked about poss POTS diagnosis, GP told me no point in testing as it's just another label with no cure.

Why don't you just go for a run around the block!

In a consultation with my GP, she said: "Shall I pray for you? We could do it now!"

"You just have an atypical depression"

"The death of your boyfriend is probably holding you back to full recovery."

"I suffer with Fibromyalgia & M.E. One Dr told me it doesn't exist."

"I can try you on these new meds and if they help you I can try them on my other ME patient".

"Part of it is that you're getting older too! (Thanks, I'm 53 not 73. I see old people more fit than I am.)"

"You def have a fatigue/pain syndrome but I don't want to label you. (Thanks, my boss will love that)"

"u either choose2get better or continue2live like this. Rheumy said this2me.I have ME&fibro"

"So how is your relationship with your parents?"

"I am completely baffled by your symptoms" one of the more honest Drs.

"Do you believe in ME?" – Psychiatrist

"It's mind over matter". If only I'd known, I'd have thought myself better years ago!

"Well ME and Fibro are all just terms for pain and fatigue that is unexplained, I can't help you"- neuro!!"

"Everyone gets tired. You need to push through it." Went from moderate to severe within weeks...

"I've never heard of ME. I'll google it"
Medical Assessment Unit doc trained in Ireland."

When asking if anything could with excessive sweating. "No it's just the chronic fatigue"

"You need to see a psychiatrist" Went to psychiatrist, got clean bill of MH
"It was psychotherapist I meant"
Neurologist; "FM? That doesn't exist, neither does that other thing what do you call it? ME?"

"People who work here think it's a mental illness" (CFS clinic)

"The only thing I know about ME is Graded Exercise Therapy" Said by neurologist 2016 After 29+ yrs of ME

I have great life, great job, boyfriend, I just don't feel well; "Cause of her CFS is depression"

"I'm not sure how to help you.... Why don't we try antidepressants??"
- But I'm not depressed

"Oh I don't like to refer people with ME or fibro for wheelchairs as I believe it makes them lazy"

"Having ME might be "inconvenient" but there is really nothing I can do"
"No, no children get ME" ...suggesting it's a psychosomatic adult illness..
"go home and do some exercise."



A UK specialist told me to "Get a boyfriend and an active sex life, if you want a cure"

- NHS have left me to rot for 12 yrs!

'You have the right attitude to get over M.E'

I've still got the same 'attitude' years later, I'm still ill

"I don't "do" fatigue, I hope you grow out of it" - consultant immunologist

"you're listening to your body too much"

" you've had glandular fever but you're well over it now "

I was seeing a specialist for something else and I mentioned it and he said " oh come on don't give me that"

"Why don't you try actually going to the gym."

"When are you going to pull yourself together get off antidepressants and get back to work"

"Come back and see me when your head is spinning and you're spitting blood like in operas"

"There's no such thing as me/cfs it's just another fancy word for tiredness an that's what u have go"

'If blood tests don't show anything we'll assume you have ME'

"I'm old school. I don't believe in these new mumbo jumbo illnesses, you're lazy and want time off work"

"When you feel a bit tired you mustn't give in to it. GP after I'd had ME for years and had to give up work"

Very recently: "No one at the Surgery is experienced with dealing with it (CFS) because it's a rare condition"

"None of the GPs in this practice are interested in taking you on as a patient because you say you have ME"

"Have you tried any exercise?" (The stairs?? And once a week a bath I nearly die after)

"You have a high heart rate but we don't know why"

One GP I saw said to me get a full time job and a husband and you will be fine!!!! So in my head I leapt across the table and bitch slapped her!

"It's all stress related work, on your inner issues" (only stress was no answer or help being seriously ill)"It's anxiety" (No it's really NOT)

"You have caused your condition of CFS by choosing to lie in bed for years"

'all teenagers get tired and you're probably lazy too, there's nothing wrong with you'

"At age 16, "have a baby, a good shake up of your hormones should sort it." I had a baby in my late 20's guess what - it didn't sort it."

"6 years ago, (10 years into having M.E.), I had a bad relapse, bedridden. Doctor was called for a home visit; it was the doctor who had given me my initial diagnosis. He said "oh, I thought you were better, M.E. usually goes away by itself after 2 years"It took almost 2 years before I received the diagnosis, did he think once he'd told me what it was it'd go away? Doh!! Needless to say, I've since changed doctors."

"Probably just an adolescent pre occupation with health"

"What do you expect, you ARE middle aged?" I was 38

DWP Doctor in 1994

"Were you attending church when you developed ME?"



IIMEC11 PRESENTERS

Dr Ian Gibson – Conference Chair



Dr Ian Gibson, former Labour MP for Norwich North, worked at University of East Anglia for 32 years, became Dean of the school of biological sciences in 1991 and was head of a cancer research team and set up the Francesca Gunn Leukaemia Laboratory at UEA.

In 2011 Dr Gibson received an honorary doctorate of civil law from UEA.

Dr Vicky Whittemore

Program Director in the National Institute of Neurological Disorders and Stroke at the National Institutes of Health in the United States.



Dr. Whittemore is a Program Director in the Synapses, Channels and Neural Circuits Cluster. Her interest is in understanding the underlying mechanisms of the epilepsies including the study of genetic and animal models of the epilepsies.

The major goal is to identify effective treatments for the epilepsies and to develop preventions. Dr. Whittemore received a Ph.D. in anatomy from the University of Minnesota, followed by post-doctoral

work at the University of California, Irvine, and a Fogarty Fellowship at the Karolinska Institute in Stockholm, Sweden.

She was on the faculty of the University of Miami School of Medicine in The Miami Project to Cure Paralysis prior to working with several non-profit organizations including the Tuberos Sclerosis Alliance, Genetic Alliance, Citizens United for Research in Epilepsy (CURE), and the National Coalition for Health Professional Education in Genetics (NCHPEG). She also just completed a four-year term on the National Advisory Neurological Disorders and Stroke Council.

IIMEC11 PRESENTERS

ABSTRACT:

Not available at time of going to press – to be added later.

Professor Olli Polo



Chief of the Department of Pulmonary Medicine, Tampere University Hospital, Finland

ABSTRACT:

Not available at time of going to press – to be added later.

Professor Carmen Scheibenbogen

Professor for Immunology and Deputy Chair Institute of Medical Immunology Berlin Charite, Germany

Head of the Outpatient Clinic for Adult Immunodeficiency. Clinical Training in Hematology and Oncology. Research interest in CFS/ME, Immunodeficiency, Cancer Immunology.

**ABSTRACT****Autoantibodies to adrenergic and acetylcholine receptors in CFS/ME**

Carmen Scheibenbogen, Institute of Medical Immunology, Charité, Berlin
Autoantibodies directed against neurotransmitter receptors are causing various types of autoimmune diseases. Recently we were able to demonstrate elevated antibodies against beta2 adrenergic receptors and muscarinic acetylcholine

IIMEC11 PRESENTERS

receptors in a subset of patients with CFS/ME. Patients with elevated autoantibodies frequently had increased IgG levels, ANA titers and/or T cell activation. We therefore suspect that the autoantibodies can activate immune cells carrying these receptors by imitating adrenaline/ acetylcholine stimulation. Various other symptoms of CFS/ME could be explained by an overstimulation of the sympathetic/parasympathetic nervous system. In patients who were treated with rituximab in the Norway trials elevated autoantibodies normalized.

Loebel M, Grabowski P, Heidecke H, Bauer S, Hanitsch LG, Wittke K, Meisel C, Reinke P, Volk HD, Fluge Ø, Mella O, Scheibenbogen C. Antibodies to β adrenergic and muscarinic cholinergic receptors in patients with Chronic Fatigue Syndrome. Brain Behav Immun. 52: 32-39, 2016.

Dr Geraldine (Jo) Cambridge

B cells, Rituximab and ME/CFS

Dr Jo Cambridge is Principal Research Fellow Inflammation, Div of Medicine Faculty of Medical Sciences, UCL

Her group focuses its interests on B cell depletion (an idea which they introduced (with the Professor Jo Edwards) approximately 10 years ago for the treatment of rheumatoid arthritis), exploring more precisely how the technique works and trying to explain the marked variation in response between different patients



ABSTRACT

B cell biology and Rituximab treatment in Patients with ME/CFS

G. Cambridge and F. Mensah

Centre of Rheumatology Research, Division of Medicine, University College of London



IIMEC11 PRESENTERS

Use of Rituximab: Before the use of rituximab, the strongest accepted evidence for an association between B-cells and systemic autoimmune diseases such as lupus and rheumatoid arthritis, was that clinical disease was associated with serum autoantibodies. The ability to remove B-cells with rituximab (given in 2 injections 1 week apart) has revealed factors that are important for both inducing remission and resumption of symptoms. Firstly, we found that our patients with high levels of autoantibodies had a significantly more pronounced and predictable clinical response to rituximab than patients with no autoantibodies. Secondly, B cells are killed very quickly by Rituximab – within a week of the infusions - but the kinetics of the clinical response (taking from 1- 5 months after depletion), suggest that it is a constantly generated B-cell product (?autoantibody) and not B-cells themselves that need to be reduced for remission to occur. Thirdly, a considerable proportion of B cells are not depleted, being resident in protective niches in lymphoid and inflamed tissues, and autoantibody levels can often remain raised, in the presence of considerable improvement of clinical symptoms. Taken together, this would suggest that only a proportion of parent B cells and autoantibodies are actually directly 'pathogenic'. However, as patients eventually do relapse, the autoimmune response underlying the pathogenesis of disease must be self-sustaining. Patients are thus not 'cured' by Rituximab and symptoms can worsen again when the peripheral B cell compartment begins regenerating (6-9 months after infusion of rituximab), although some patients can have extended remission even after B cell return. Side-effects are rare and although reductions in serum total antibody levels can occur, effects on protective immunity are mild and serious infections rare. We have therefore learned much about how rituximab works in autoimmune rheumatic diseases but in ME/CFS patients, we are just beginning. As ME/CFS is such a heterogenous disease, our research is focussed on investigating B cell biology in these patients in order to qualify differences from healthy individuals and thus to identify those patients most likely to respond to rituximab and related therapies.

B cell Research into ME/CFS: Fatigue is a major component of many systemic autoimmune rheumatic diseases where it is usually associated with the presence of inflammation and cytokine production. After rituximab, a marked reduction in fatigue indices has been reported, possibly due to reducing cytokine (usually interferon- α) production through removal of activating autoantibody containing immune complexes. The fatigue and other symptoms experienced by patients with ME/CFS differs in that no frank inflammatory site has been identified and the fatigue and other symptoms seems to be induced by both physical and mental stressors. We have hypothesized that dysregulation of metabolic re-programming in B cells may influence normal differentiation to appropriate (?Auto?) antibody secretion and memory B cell generation. Rituximab would therefore work by stopping the production of as yet only tentatively identified pathogenic antibodies. Following on from our already published data on B cells which showed that a certain marker,

IIMEC11 PRESENTERS



CD24 was up-regulated or retained by newly generated B cells, we have been using cells from patients and controls to follow B cell development patterns in response to certain stimuli. We have also established an *in vitro* system in which we can compare the metabolic function of B cells in ME/CFS patients with healthy controls. This system can also be used to examine the effect of soluble factors such as cytokines and antibodies and agonists/antagonists binding receptors shared between the immune and nervous systems.

G. Cambridge, PhD,
Principal Investigator.

Professor Tom Wileman

Professor of Infection and Immunity & Director at Biomedical Research Centre at University of East Anglia, Norfolk, UK

Professor Wileman is Professor of Infection and Immunity & Director and Director at Biomedical Research Centre at Univ. of East Anglia.

He was Head of Dep. Immunology and Pathology and Virus Cell Biology Group at Institute of Animal Health; Assistant Professor at Dep. Medicine at Harvard Medical School and Claudia Adam's Barr Investigator in Cancer Research, Dept. Molecular Immunology, Dana Farber Cancer Institute, Harvard Medical School; Fellow of the Parker Francis Pulmonary Research Foundation, Dept. Cell Biology, Washington Univ. Medical School.



ABSTRACT:

Tom Wileman

The human virome contains eukaryotic viruses that infect host cells and prokaryotic viruses that infect bacterial communities within the microbiota. The virome of healthy individuals interacts with the microbiota and the host immune system to set an inflammatory threshold that can influence susceptibility to many diseases

IIMEC11 PRESENTERS

including diabetes, cardiovascular disease and the metabolic syndrome. Modulation of the immune system can also stimulate bystander resistance to pathogens. Human prokaryotic viromes are relatively stable but they can be altered by diet and disease and this can influence the diversity of the microbiota. Changes in prokaryotic virus populations can lead to gene transfer able to influence microbial antibiotic resistance, virulence and metabolism. Recent work shows that the diversity of the enteric virome increases during inflammatory bowel disease and that this can reduce the diversity of microbial communities leading to dysbiosis and inflammation. We have developed methods to study the enteric virome of patients with chronic fatigue syndrome/ME to see if similar changes occur during the development of this debilitating disease.

Professor Don Staines

The National Centre for Neuroimmunology and Emerging Diseases (NCNED), Griffiths University, Australia



Dr Staines is a public health physician at Gold Coast Population Health Unit. He has worked in health services management and public health practice in Australia and overseas. His interests include collaborative health initiatives with other countries as well as cross-disciplinary initiatives within health. Communicable diseases as well as post infectious fatigue syndromes are his main research interests. A keen supporter of the Griffith University Medical School, he enjoys teaching and other opportunities to promote awareness of public health in the medical curriculum.

ABSTRACT:

Not available at time of going to press – will be added later.

IIMEC11 PRESENTERS

Professor Simon Carding

Leader, Gut Health and Food Safety Programme Institute of Food Research, Norwich Research Park, UK

Professor Simon Carding Professor of Mucosal Immunology at University of East Anglia and Institute of Food Research. Following his PhD at London he held postdoctoral positions at New York University School of Medicine, New York and at Yale University School of Medicine, New Haven, USA. He then moved to the University of Pennsylvania, Philadelphia, USA as Assistant and later Associate Professor. He joined University of Leeds as Professor of Molecular Immunology in the Institute of Molecular and Cellular Biology in 1999. His scientific interests are in understanding how the immune response in the gut functions and in particular, is able to distinguish between the commensal microbes that reside in the gut and environmental microbes that cause disease, and in the mechanisms by which the body's immune system no longer ignores or tolerates commensal gut bacteria and how this leads to immune system activation and inflammatory bowel disease.



ABSTRACT:

Despite excellent ME/CFS research being carried out in several centers and groups across Europe it remains fragmented and uncoordinated. With the support of the UK-based charity Invest in ME - Research EMERG has been established with the aim of developing a coordinated programme of European-based research to identify the underlying causes of ME/CFS and to develop more effective forms of treatment that can be supported by trans-national and national funders.

International ME Conference 2016

A New Decade of Research Begins

*#BRMEC6 - 6th Invest in ME - Research
International Biomedical Research into ME Colloquium*

IIMEC11 PRESENTERS

Professor Mady Horning

Markers of Immunity and Metabolism in ME

Mady Horning, MA, MD is a physician-scientist in the Center for Infection and Immunity (CII) at the Columbia University Mailman School of Public Health New York, USA where she serves as Director of Translational Research and is an associate professor of epidemiology.

Her research focuses on the role of microbial, immune, and toxic stimuli in the development of neuropsychiatric conditions, including autism, PANDAS (Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infection), mood disorders and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).



She is widely known both for establishing animal models that identify how genes and maturational factors interact with environmental agents to lead to brain disorders and for her work clarifying the role of viruses, intestinal microflora and xenobiotics in autism and other neuropsychiatric illnesses that may be mediated by immune mechanisms. Under her direction, proteomic analyses of umbilical cord samples are identifying potential birth biomarkers for autism in a prospective study in Norway, the Autism Birth Cohort (ABC).

She established that there was no association between intestinal measles virus transcripts and autism, and, with Brent Williams and W. Ian Lipkin at CII, has found altered expression of genes relating to carbohydrate metabolism and inflammatory pathways and differences in the bacteria harboured in the intestines of children with autism.

She also leads projects examining the influence of immune molecules on brain development and function and their role in the genesis of schizophrenia, major depression, and cardiovascular disease comorbidity in adults, and directs the Chronic Fatigue Initiative Pathogen Discovery and Pathogenesis Project at CII.

In 2004, Dr. Horning presented to the Institute of Medicine Immunization Safety Review Committee and testified twice before congressional subcommittees regarding the role of infections and toxins in autism pathogenesis.

Her work in ME/CFS is establishing immune profiles and helping to identify pathogens that may be linked to disease.

Her work on the MIND (Microbiology and Immunology of Neuropsychiatric Disorders) Project, one of the largest studies of immune factors in mood disorders

IIMEC11 PRESENTERS

and schizophrenia, examines the role of viruses and immune responses in the pathogenesis of these disorders.

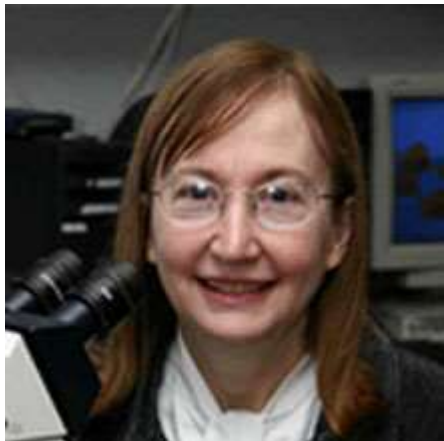
ABSTRACT:

Not available at time of going to press – will be added later.

Professor Maureen Hanson

Liberty Hyde Bailey Professor, Department of Molecular Biology and Genetics, Cornell University, New York, USA

Maureen Hanson is Liberty Hyde Bailey Professor in the Department of Molecular Biology and Genetics at Cornell University in Ithaca, NY. Previously she was on the



faculty of the Department of Biology at the University of Virginia in Charlottesville and an NIH NRSA postdoctoral fellow at Harvard, where she also completed her Ph.D. degree. While most of her prior research has concerned cell and molecular biology in plant cells, she began a research program on ME/CFS after noting at a 2007 IACFS meeting the paucity of molecular biologists studying the illness. Her lab was part of the 2012 multicenter study organized by Ian Lipkin's group at Columbia University to assess the actual role of XMRV in

ME/CFS. Dr. Hanson has a current project to examine the microbiome of ME/CFS patients and controls, in collaboration with Dr. Ruth Ley (Cornell Microbiology) and Susan Levine, M.D. (Manhattan, NY). Dr Levine is also collaborating with Dr. Hanson on an immune cell gene expression project that involves Dr. Fabien Campagne and Dr. Rita Shaknovich at Weill Cornell Medical School in New York City. Dr. Hanson's third project concerns analysis of blood samples from individuals performing a two-day cardiopulmonary exercise test at Ithaca College under the supervision of Dr. Betsy Keller

ABSTRACT:

The Search for Biomarkers in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

Maureen R. Hanson (presenter), Ludovic Giloteaux, Julia Goodrich, Anthony Walters, Susan Levine, Ruth Ley

IIMEC11 PRESENTERS

Biological markers (biomarkers) are objective measures of biological phenomena. Among possible biomarkers are the physical appearance of an organism or its components, amounts of molecules or cell types, responses of cells or tissue to a stimulus, enzyme activities, gene sequences, or level of interactions of one molecule with another. Many potential biomarkers for the identification of victims of ME/CFS have been measured in the past in the hope of understanding the pathophysiology of the disease. Such studies have revealed abnormalities in function, population and gene expression in immune cells, disturbances in brain morphology and operation, abnormal gas exchange parameters in exercise physiology, discordant levels of plasma signaling proteins, and atypical autonomic function.

While these abnormalities have provided some hints about the biological basis of the disease, much more information is needed to understand its underlying cause. Furthermore, the existing biomarkers are cumbersome to implement in a medical office setting, not available to be performed in typical medical testing labs, and are not able to identify all patients that can be diagnosed with the disease by an experienced ME/CFS physician.

We explored the possibility that levels of inflammatory proteins in the blood, in conjunction with bacterial species abundance in the gut microbiome, might serve as biomarkers for diagnosis if the intestinal microbiome is disturbed in ME/CFS. We examined the bacterial microbiome in 48 ME/CFS patients and 39 healthy controls by sequencing regions of DNA that allow identification of the different types of bacteria that are present. We found that ME/CFS patients had reduced diversity in bacterial types in comparison to healthy individuals, a finding that has also been reported in Crohn's disease and ulcerative colitis. While there is no set of species detected that is present in ME/CFS patients that is absent from healthy individuals, we identified a number of taxonomic groups that were represented in different abundance between ME/CFS patients and controls. By applying a statistical method to the blood analyses and the bacterial compositions, we were able to classify 83% of the subjects correctly as either patients or healthy individuals. Our results are consistent with an ongoing damage to the gut that leads to greater microbial translocation into the blood, which could then have adverse effects on the immune system.

The difference in population structure of the microbial community may be contributing to some ME/CFS symptoms and to their severity. However, there is no evidence that the disturbance in the gut microbiome is a cause of the disease rather than being one of its symptoms.

IIMEC11**PRESENTERS**

Professor Elisa Oltra

Professor Elisa Oltra is a professor of Cell and Molecular Biology at the Universidad Católica de Valencia “San Vicente Mártir” where she also works as a researcher in the area of stem-cell and cancer

Dr. Elisa Oltra is a professor of Cell and Molecular Biology at the Universidad Católica de Valencia “San Vicente Mártir” where she also works as a researcher in the area of stem-cell and cancer.



She obtained an M.S. degree in Biochemistry at the Universidad de Valencia (Spain) and later earned her PhD in Biochemistry, Cell and Molecular Biology at the University of Miami, FL (USA) where she stayed for her post-doctoral training and later, as Senior Scientist till 2006 when she moved back to Spain.

During her studies at the University of Miami she identified alternative 5´UTR sequences involved in regulating cell-cell communication through mechanisms of differential connexin43 expression in the heart.

She also isolated a novel essential protein (Ini) and demonstrated its participation in mechanisms of transcription and splicing.

In 2009 she started a project to investigate the molecular basis of Fibromyalgia having identified at present irregularities in RNaseL expression and miRNAs profile changes in the participating patients which could lead to a deeper understanding of the disease.

In 2012 she joined the IVP Valencian Institute of Pathology, also at the Universidad Católica de Valencia where she is currently studying a specific type of vesicles: the exosomes, as mediators of stem-cell based therapies.

She is also academic director of the first officially accredited Master degree in Biobanking in Europe in collaboration with the Spanish Network of Biobanking at

IIMEC11 PRESENTERS

the Instituto de Salud Carlos III, Madrid (Spain). From <https://publons.com/author/361418/elisa-oltra#profile>

ABSTRACT:

Molecular Biomarkers of Myalgic Encephalomyelitis

Elisa Oltra, Jaime Cuquerella, Armando V. Mena-Durán, Vicente Monsalve and Germán Cerdá-Olmedo

School of Medicine, Catholic University of Valencia (Spain)



Summary

At present no objective diagnostic method for ME or related diseases exists. A lack of reliable markers not only leads to misdiagnosis but limits the possibility of finding effective treatments and/or preventive actions as well. MicroRNAs, also called miRNAs or miRs, are a set of small molecules that work as important modulators of gene expression in tissue-specific physiologic pathways, in response to environmental cues and in disease. Their high stability in body fluids has already shown the use of these small nucleic acids in the diagnosis and prognosis of certain type of cancers and other diseases, appearing as attractive biomarker candidates for the development of precision medicine programs. Encouraged by the idea that miR profiling must be altered in ME patients and related diseases, we and other researchers have pursued the analysis of miRs in blood and other body fluids finding alterations that need to be understood. In our initial study, we performed a genome-wide expression profiling of these miRs in Peripheral Blood Mononuclear Cells (PBMCs) of patients with chronic fatigue and fibromyalgia comorbidities (N=11) and population-age-matched controls (N=10) using human v16-miRbase 3D-Gene microarrays (Toray Industries, Japan). This analysis led to the identification of a miRNA signature of 5 of these small nucleic acids that showed marked down-regulation (6-fold or higher). In addition, the low levels of the hsa-miR223-3p, hsa-miR451a, hsa-miR338-3p, hsa-miR143-3p and hsa-miR145-5p could be validated by real-time quantitative PCR amplification (qPCR), an alternative method for measuring the expression levels of these molecules. At present, we are extending this study to a larger cohort of participants presenting a more varied symptom profiling than those that participated in our pilot study with the aim of unveiling symptom and symptom-severity-associated miR profiles. We are including additional body fluids and sub-fractions in our analysis to determine the most appropriate sample to use for a liquid biopsy-based diagnostic method of ME and related diseases.

IIMEC11**PRESENTERS**

Professor James Baraniuk

Professor of Medicine at Georgetown University Medical Centre, Washington, USA



James N. Baraniuk was born in Alberta, Canada, south of Banff. He earned his honours degree in chemistry and microbiology, medical degree, and unique bachelor's degree in medicine (cardiology) at the University of Manitoba, Winnipeg, Canada. Thereafter, he moved to Akron, OH, USA, for his internship and internal medicine residency at St Thomas Hospital.

After another year of internal medicine residency at Duke University Medical Center, Durham, NC, he trained with Dr C.E. Buckley, III, in allergy and clinical immunology. He moved to the laboratory of Dr Michael Kaliner at the National Institute of Allergy and Infectious Diseases, Bethesda, MD, and there began his long-standing collaboration with Dr Kimihiro Ohkubo. After 2 years studying neuropeptides, he joined Dr Peter Barnes' laboratory at the National Heart and Lung Institute, Brompton Hospital, London, UK. Dr Baraniuk returned to Washington, DC, and Georgetown University, where he is currently Associate Professor with Tenure in the Department of Medicine.

ABSTRACT:

Not available at time of going to press – will be added later.

Professor Ron Davis

Professor of Biochemistry and Genetics at the Stanford School of Medicine in Stanford, California, USA



Ronald W. Davis, Ph.D., is a Professor of Biochemistry and Genetics at the Stanford School of Medicine in Stanford, California.

He is a world leader in the development of biotechnology, especially the development of recombinant DNA and genomic methodologies and their application to biological systems.

At Stanford University, where he is Director of the Stanford Genome Technology Center, Dr. Davis focuses on the interface of nano-fabricated solid state devices and biological systems.

He and his research team also develop novel technologies for the genetic, genomic, and molecular analysis of a wide range of model organisms as well as humans.

The team's focus on practical application of these technologies is setting the standard for clinical genomics.

ABSTRACT:

Big Data Approach: Severely ill ME Patient Cohort

Our first major effort with multiple patients was to collect a large number of molecular observations on patients with ME/CFS. Once published these data could serve as the basis for a large number of hypotheses that NIH and other government agencies might fund. The cost of this type of study will be very expensive per patient. In order to reduce the overall cost it was recommended by the OMF Scientific Advisory committee to study severely ill patients because they should show the largest molecular signature. With a larger signal fewer patients can be used and still achieve statistical significance. This study has been called the Big Data Study of Severely Ill CFS Patients. These patients are bed bound so do not visit clinics and have not been studied. We send a medical team to each home in the San Francisco Bay Area to collect blood, urine, saliva, tears, and stool. We will be collecting more molecular data on each patient at one time point than has ever been collected in any study in history.

While we were seeking funding for the Big Data Study we tested some of the technologies on a few severe and not severe CFS and healthy control patients. We discovered that the metabolome (the small metabolites found in the blood and urine) of the serum gave clear indication of metabolic abnormalities. Preliminary results indicated that glycolysis may be impaired with glucose being routed to fatty acid synthesis. Possibly more important, the metabolites in the citric acid cycle in the mitochondria were lower than in healthy controls and some almost undetectable. This cycle generates most of the energy (ATP) for the body. It makes it clear that this is no psychosomatic disease. From preliminary analysis it would appear that not only ATP is low but also ADP, AMP, GTP and in some cases uracile. These cofactors are involved in hundreds of molecular reactions in the body including in the brain. Their decrease would cause a large number of body functions to be abnormal. We don't know which cells in the body are being affected (possible all cells) and are currently studying the various white and red cells with a variety of commercial and custom technologies.

Sufferers of M.E., carers, family and friends, all want to know what causes M.E. in order to determine how the condition can be prevented, treated and cured. With over 3000 scientists at the Norwich Research Park, consisting of 4 world leading research institutes, a university and a teaching hospital, it is one of Europe's largest single-site concentrations of research in Food and Health and Environmental sciences. Having academic excellence across a range of diverse, but related fields, in one location is a very powerful way to deliver a step-change in potential outcomes across a number of health issues. Importantly, the new centre for food and health, due to open at the end of 2017 at the Norwich Research Park, takes co-location to a new level as it uniquely integrates academic excellence with clinical expertise; by bringing together the Institute of Food Research with aspects of the University of East Anglia's medical school and science faculty with the Norfolk and Norwich University Hospitals' gastrointestinal endoscopy facility, working alongside industry. The new Institute will provide a novel holistic, systematic and integrated approach to deliver faster innovation as



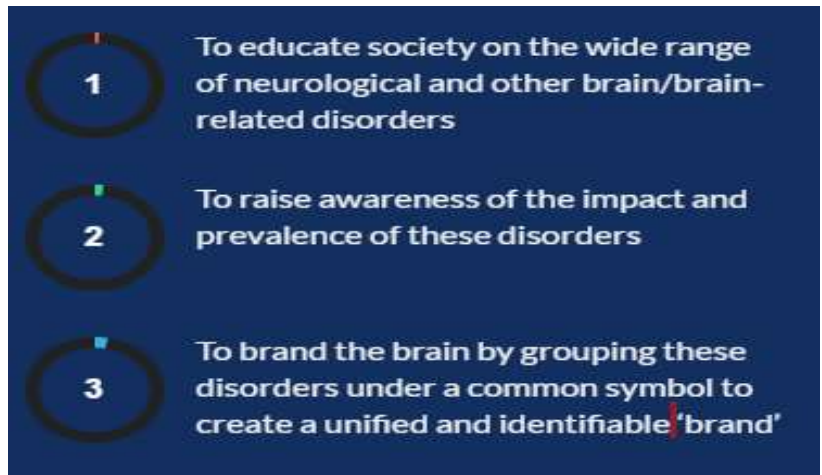
well as helping to inform government policy on a range of gut and diet related issues including M.E. **The development of this new centre, together with the other expertise and facilities located at the Norwich Research Park, puts it in a very good position to lead a UK and European Centre of Excellence for biomedical research for M.E. to provide possible prevention and solutions.**

- *Professor Ian Charles Director of Institute of Food Research
IMEC10 conference*

Together Under the Umbrella

Invest in ME are members of European ME Alliance (EMEA) – who are members of the European Federation of Neurological Alliances (EFNA). The Together Under the Umbrella campaign will lead to an increase in public, political and scientific support for all brain and brain-related disorders, resulting in reduced stigma.

<http://undertheumbrella.eu>





Conference Agenda

www.investinme.eu/IIMEC11.shtml

Start	Presenter	Presentation
07.45	<i>Registration</i>	
08.55	IIME	Welcome to IIMEC11
09:00	Dr Ian Gibson	10 years – Looking Back, Looking Forward
09:10	Dr Vicky Whittemore	Keynote Speech: NIH Research into ME
09:35	Professor Olli Polo	Clinical Diagnosis of Myalgic Encephalomyelitis
10:00	Professor Carmen Scheibenbogen	Autoantibodies to adrenergic and acetylcholine receptors in CFS/ME
10.30	<i>Coffee/Tea Break in the Great Hall</i>	
11:00	Dr Jo Cambridge	B cells, Rituximab and ME/CFS
11.25	Professor Tom Wileman	Gut Virome in ME
11:50	Dr Don Staines	Update from NCNED: Receptor identification and intracellular signalling
12.30	Professor Simon Carding	European ME Research Group
12.45	<i>Lunch in the Great Hall</i>	
13.45	Professor Mady Hornig	Pathogen Discovery in ME
14:25	Professor Maureen Hanson	The Search for Biomarkers in ME
14:55	Professor Elisa Oltra	Molecular Biomarkers of Myalgic Encephalomyelitis
15.25	<i>Coffee/Tea Break in the Great Hall</i>	
15:55	Professor James Baraniuk	Exercise testing and orthostatic tachycardia
16.20	Professor Ron Davis	Big Data Approach: Severely ill ME Patient Cohort
17.10	Dr Ian Gibson	Plenary Session Status of ME Research
17.30	<i>Adjourn (Note: the agenda, format and times are subject to change)</i>	

Invest in ME

Invest in ME Research

Invest in ME Research

Invest in ME Research

Invest in ME Research

Invest in ME Research

Invest in ME Research

Invest in ME Research



FAST TRACKING SOLUTIONS FOR ME



of Excellence for ME

investinmeresearch.org

Let's  research!

Myalgic Encephalomyelitis (ME) is a serious, chronic neurological disease. UK Charity Invest in ME - Research (IMER) are establishing a Centre of Excellence for ME - a hub for research activity in Europe - enabling a strategy of high-quality biomedical research projects to follow, coordinated and collaborating with other institutes. Please support our C of E for ME. Let's Do It for ME. Let's C research into ME. See <http://www.investinme.org/research#CofEforME> #LetsCresearch @LetsDolt4ME

Invest in ME - Research (UK charity nr. 1153730)

www.investinme.org

email: info@investinme.org