THE 2020 IACFS-ME CONFERENCE REPORT

by Charlotte Stephens
MEA Research Correndent

The International Association for Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (IACFS/ME) held a virtual scientific conference on August 21st 2020. Over 200 people attended, including researchers, clinicians, patients and carers. There were some interesting talks and plenty of opportunity for Q and A's and some great discussions. Here we provide a brief summary of each talk.

If you wish to watch the full conference personally, you can visit the IACFS/ME home page (**https://www.iacfsme.org**) to register and pay for access to an online video recording of the meeting. The video will be available until October 31, 2020.

WHO ARE IACFS/ME?

IACFS/ME is an international, non-profit organization of clinicians, scientists, professionals, patients, and advocates dedicated to the care and research of people affected by myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS), fibromyalgia, and other related conditions.

They publish a peer-reviewed medical journal (Fatigue: Biomedicine, Health, and Behavior), organize international conferences, educate professionals and the public about ME/CFS, and promote science-based care, research, and public health policies. To find out more, visit: **https://iacfsme.memberclicks.net**.

Fried Freidberg, President IACFS/ME, reflects on the first virtual conference: **https://tinyurl.com/y3ag5o4a**

A video of the virtual conference is available for USD$40: **https://tinyurl.com/y259cnrq**

1 Does Chronic Fatigue Syndrome Follow Acute SARS (severe acute respiratory syndrome) Disease? If so, why?

Dr Harvey Moldofsky (University of Toronto) *Picture: healthrising.org*

Dr. Moldfsky carried out a study of nurses who had contracted SARS Cov1 in the 2003 outbreak. One to three years later, the nurses still reported a variety of symptoms which prevented them from returning to work, such as disturbed/unrefreshing sleep, musculoskeletal pain, chronic fatigue, and depressive symptoms.

Because of the similarity of SARS Cov1 to the current SARS Cov2 disease, anecdotal reports suggest the possibility of similar chronic fatigue health problems occurring for many patients.

Dr Moldfsky warned that those chronically affected by SARS1 were never properly followed up or documented and the same may happen with this current outbreak. We need epidemiological studies to determine the incidence, prevalence and long-term effects of those chronically affected by SARS2.

2 What Do We Know About Risk Factors for Developing COVID-19 and the Aftermath of this Disease?

Professor Leonard Jason (DePaul University, Chicago) *Picture: me-pedia.org*

Professor Jason's team have been studying the development of ME/CFS following viral infections, particularly infectious mononucleosis (glandular fever). Between 2014-2018, they collected data, including biological samples, from 4,501 healthy college students and are now following them up, waiting for them to contract a viral infection in order to then continue to monitor them to see if they later develop ME/CFS. They will then use this data to identify risk factors that may predispose someone to develop ME/CFS following a viral infection.

This IACFS-ME conference report was written by Charlotte Stephens, (pictured above), Research Correnspondent at the ME Association.

5% of the students they studied were diagnosed with infectious mononucleosis and 8% of those students went on to develop severe symptoms at 6 months. The findings of this study so far (including differences in some immune markers at baseline) have recently been submitted to a journal.

The research team are now also including COVID-19 data in the study, to see if they can identify risk factors predisposing patients to develop COVID-19. Furthermore, they hope to identify factors that separate those that go on to develop chronic symptoms following COVID-19 infection from those that don't. So far, about 5% of the sample has been infected with COVID-19 and the researchers will follow up these patients to see if they go on to develop ME/CFS.

Anecdotal evidence already suggests that some of those that had COVID-19 are developing symptoms of ME/CFS and there may be a link with variations in cytokine production. Professor Leonard highlighted that there is currently a unique opportunity to track how various factors may lead to post-infections fatigue.

DePaul University have also recently launched an online study to compare the symptoms of COVID-19 versus other chronic illnesses (such as MS, Post-Polio syndrome).

Studying COVID-19 will help us better understand predisposing factors in the development of COVID-19 and the maintenance of symptoms. This may lead to a better understanding of the development of other chronic illness following viral infection.

3 Understanding Susceptibility or Resilience to Chronic Effects of COVID-19 and Deepening Our Understanding of ME/CFS

Dr. Sadie Whittaker (Solve ME Initiative) *Picture: me-pedia.org*

You + ME is an online clinical study of individuals committed to identifying a cure for ME/CFS. Participants collectively provide

the research community with critical insight into the experience and genetics of ME/CFS.

Dr. Whittaker aims to create the largest possible dataset of people with ME/CFS and controls. Data collection is currently carried out through symptom tracking software through a mobile app and they aim to also start taking biological samples later this year. They currently have 1230 people with ME/CFS and 156 controls enrolled to the registry.

Not only does this act as a useful database for researchers, it also gives patients a tool to track their own symptoms and monitor what affect various things have on them and also to share their experience with carers and their healthcare team.

The database also gives the opportunity to easily capture data on the impact of COVID-19 on individuals with ME/CFS and they are currently tracking 40 individuals who have been infected in order to see what impact COVID-19 has on ME/CFS symptoms. They can also look at the long-term impacts of COVID-19 in healthy controls and monitor the development of ME/CFS- like symptoms.

The aim is that the database will allow us to better characterize ME/CFS, define subtypes, and point the way to drug development. They aim to partner with researchers to characterize biomarkers underlying resilience vs. susceptibility to persistent symptoms and to use a multi-omics (genetic, epigenetic, transcriptomic) approach to identify a signature of early onset ME/CFS.

■ You can learn more about the 'You + ME' registry here: **https://youandmeregistry.com**

4 Conversion of COVID-19 Patients to People with ME/CFS

Dr. Ronald Tompkins (Open Medicine Foundation, Harvard University) *Picture: MEA*

The Open Medicine Foundation (OMF) have established collaborative research centres that will be carrying out a COVID-19 ME/CFS Research Project. The current pandemic presents an opportunity to track the long-term effects of COVID and identify physiological factors that lead to the development of ME/CFS. These studies will allow the identification of biomarkers and possible drug targets and treatments.

The first aim of the study is taking blood, urine and cerebrospinal fluid (CFS) samples from patients admitted to hospital with COVID-19, in order to analyse genomics, proteomics and metabolomics and compare these to a huge database. They will then follow up patients, taking more samples, and identify differences between those that fully recover within 6 months verses those whose fatigue persists or worsens 6 months post-discharge.

They then hope to follow those who remain symptomatic up to 24 months post-discharge, taking more samples and symptom questionnaires, and identifying any biomarkers that demonstrate what may have predisposed people to developing ME/CFS, which may enable them to identify drug targets and prevention strategies.

Of the patients leaving hospital following COVID-19, they are predicting around 60% of them to show persistent fatigue at 6 months and around 40% to still not be fully recovered after 18-24 months.

5 The Impact of COVID-19 on the Risk and Prognosis of ME/CFS

Dr. Luis Nacul (London School of Hygiene and Tropical Medicine) *Picture: MEA*

Dr Nacul's team presented a strategy for investigating the prevalence and markers of post-viral fatigue syndrome (PVFS) following COVID-19. They are looking into using NHS electronic health record data (including primary care records, as well as A and E and ICU data) from 15 million people in the UK in order to estimate the risk of ME/CFS and other chronic diseases following COVID-19.

They have developed protocols for the long-term investigation of the impact of COVID-19 infection on the incidence, duration and severity of post viral fatigue syndrome. They also hope to investigate disease biomarkers by comparing early cases of PVFS with those who fully recover from COVID-19. Using existing data records like this is a cost-effective research method and allows for rapid translation of results.

In addition, The UK biobank team have started a pilot study looking into the short-term and long-term effects of COVID-19 infection on ME/CFS patients. Patients are asked to complete a 21-day diary log of symptoms severity and events. Preliminary results suggest that ME/CFS symptoms are worse in those infected with COVID (increased fatigue and PEM).

6 Immune Dysregulation with Deviated B Cell Receptor Repertoire in ME/CFS

Dr. Wakiro Sato (National Centre of Neurology and Psychiatry, Japan) *Picture: fttsus.jp*

Dr Sato's research team are aiming to elucidate the immune-related pathogenesis of ME/CFS and hope to develop diagnostic biomarkers and discover therapeutic targets. He was investigating why some ME/CFS patients respond well to B cell depletion therapy (such as Rituximab) and what the mechanism is behind this.

They found immune abnormalities in ME/CFS patients compared to healthy controls, such as increased frequencies of B cells or decreased activated regulatory T cells. Furthermore, they found that several immunoglobulin genes were significantly increased in ME/CFS compared to controls. This was significant enough that it could be used as a biomarker to diagnose ME/CFS.

They then looked specifically at Plasmablasts (precursor cells for plasma cells; a type of immune cell) and found that plasmablast antibody-secreting cells were increased in some ME/CFS patients compared to controls and this also correlated with disease severity. They also found that some genes were upregulated in plasmablasts in ME/CFS patients compared to healthy controls (MX1 and IFI16).

Finally, Dr. Sato's team confirmed that some patients had increased levels of anti-adrenergic receptor antibodies (autoantibodies), as found by another research group from Germany (Loebel et al., 2016)

Dr Sato's working hypothesis is that infection triggers plasmablast activation, which triggers selection of specific IGHs, which trigger autoantibodies (such as anti-adrenergic receptor antibodies) that become dysregulated and go to the brain, leading to ME/CFS symptoms. He proposes that this pathway should be targeted for treatment.

7 Defective Energy Metabolism in ME/CFS

Dr. Ina Katrine Nitschke Pettersen (University of Bergen, Norway) *Picture: uib.no*

Dr. Pettersen's hypothesis is that there is impaired cellular energetics in ME/CFS (changes in cellular metabolism and disturbed energy homeostasis). Her research team are investigating how a defective energy metabolism might be involved in the disease mechanisms of ME/CFS.

They carried out metabolite analysis of 20 amino acids in the blood serum of 153 ME/CFS patients and 102 healthy controls. Metabolic profiling indicated impaired pyruvate dehydrogenase (PDH) function (an enzyme involved in converting food to energy).

They found upregulation of multiple genes involved in PDH inhibition (including PDK4). Overexpression of PDK4 is associated with a metabolic shift in energy fuel utilization, from glucose to fatty acid oxidation, resembling an energy-starved condition (a semi-fasted state). Increased fatty acid oxidation leads to increased lactate levels and less energy and this will also be more evident on exertion compared to at rest.

Next, the research team wanted to investigate if there is something in ME/CFS serum that can change cellular metabolism in healthy cells (as other studies have shown before). They exposed healthy muscle cells to healthy control serum and ME/CFS patient serum for 6 days to see if something in the serum could change the metabolism in normal cells. They found increased overall mitochondrial respiration in the healthy muscle cells exposed to ME/CFS

serum, compared to controls, with increased ATP production. They believe this represents some sort of overcompensation. Glycolytic function was unchanged at rest, however, there was significantly increased lactate production under conditions of energetic strain (representing exertion). This may indicate the presence of a factor in the serum which is causing these metabolic changes in patients and they are now exploring these findings further.

The metabolite profile the researchers observed in ME/CFS patients suggests metabolic stress and the research team think that the metabolism is locked in a sort of "starvation mode" that we need to try to reverse. They believe that this may be triggered by some sort of immune response and that the mechanisms behind ME/CFS involves immune-metabolic interactions.

8 Why Patients Improve. Why They Get Worse. Model vs. Data in Me/CFS

Dr. Fred Friedberg (Stony Brook University, USA) *Picture: me-pedia.org*

Dr. Friedberg's research team are looking into why a large proportion of ME/CFS patients do not improve. They are investigating if there are biological or behavioural differences in patients that improve compared to those that don't. They hope to use any differences found to lead to enhanced self-management and help improvement in all patients.

They created a model of non-improvement and a model of improvement based on bio-behavioural patterns that they hypothesised contributed to this. They then tested their models against data taken from 137 ME/6. The model of non-improvement included factors they thought may contribute to patients not improving, including:

- Maladaptive activity patterns (such as the 'push-crash'/ 'boom and bust' cycle or severely limiting activity).
- Increased incidence of stressful events or major negative life events (loss of job, a death).
- Reduced heart rate variability (HRV), which reflects autonomic dysregulation.

The model of improvement included factors they thought may contribute to improvement, including:

- Healthy activity pacing.
- Uplifting pleasant events (such as positive social interactions or fun/joyful activities) or major positive life events (a marriage, a birth, a new job, a holiday).
- Increased HRV, reflecting improved autonomic regulation.

They collected data from a 6-month home-based observational study, including questionnaires, weekly diaries (looking at fatigue, pain, activity patterns, and negative or positive events), activity monitoring using an accelerometer (to measure steps) and HRV. They then conducted an interview at the end of the 6 months to see if patients reported improvement or non-improvement and looked at the factors that contributed towards this.

At the six-month follow up, 26% of patients reported improvement and 74% reported no improvement or worsening of symptoms.

The data they collected showed:

- Surprisingly, no significant differences were observed in the activity patterns (push-crashing or limiting) or the level of healthy pacing between the improved and non-improved groups.
- HRV was Increased in the improved compared to the non-improved group.
- The frequency and/or intensity of positive/ uplifting events was significantly higher in the improved vs non-improved group.

Dr Friedberg's team are still currently analysing the data, but the self-management implications so far are focusing on HRV biofeedback to increase HRV and also focusing on increasing uplifts (positive events).

9 Heart Rate Variability in Exercise-Induced Postural Tachycardia (START) and POTS

Dr. James Baraniuk (Georgetown University, USA) *Picture: MEA*

Dr Baraniuk's research team conducted submaximal exercise testing in patients with Gulf War Illness (GWI) and ME/CFS and sedentary controls. They took measures of postural tachycardia and heart rate variability (HRV).

Their results showed that submaximal exercise caused transient postural tachycardia in about 25% of CFS, GWI and sedentary control subjects. Heart rate variability was not significantly different between the three groups.

10 The Effect of Self-Management Group Program on Health Status, Fatigue Severity, and Self-Efficacy in Patients with ME/CFS

Dr. Violetta Renesca (Nova Southeastern Unviersity, USA) *Picture: nova.edu*

Dr Renesca's team set out to evaluate the effectiveness of an educational self-management program that teaches energy conservation, relaxation techniques, healthy eating, and effective communication on improving fatigue severity, physical functioning, and self-efficacy in patients with ME/CFS.

26 ME/CFS patients attended four weekly

face-to-face sessions that lasted up to two hours.

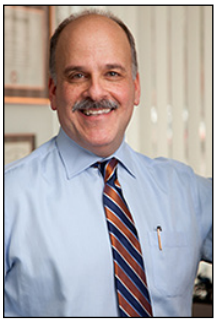
The primary outcomes of fatigue severity, physical functioning, and self-efficacy, were assessed at baseline, at the end of the intervention, and again one-month post-intervention, using questionnaires and activity logs.

At the end of the intervention, s statistically significant difference was seen concerning self-efficacy. At the one-month follow up, a statistically significant decrease in fatigue, anxiety, depression, pain interference, sleep disturbance, and an improvement in energy and ability to participate in social roles and activities were seen.

The results of this project suggest that educational intervention aimed at self-management has positive effects on patients and may improve their quality of life.

11 The Benefits of Oral Rehydration on Orthostatic Intolerance in Children with Postural Tachycardia

Dr Marvin Medow (New York Medical College, USA) *Picture: nymc.org*



Dr. Medow's team investigated whether equal volumes of oral rehydration solution (ORS) provide similar improvements in orthostatic intolerance (OI) in postural tachycardia syndrome (POTS) patients, compared to IV saline.

Patients received either 1L of ORS in 30 mins or 1L of IV saline in 30 mins, or no fluids in the control group. The results showed that saline and ORS resulted in the same improvement in the POTS patients. Furthermore, ORS was even slightly more effective at reverting orthostatic intolerance.

This study showed that ORS is a convenient, safe and effective therapy for short-term relief of orthostatic intolerance.

12 Low Dose Naltrexone in ME/CFS and FM – the Vancouver Experience

Dr. Rhonda Jane McKay (British Colombia Woman's Hospital and Health Centre, Canada) *Picture: gim.med.ubc.ca*

Low Dose Naltrexone (LDN) has been shown to have some beneficial effect in ME/CFS patients in some studies. It has been shown that the mechanisms of action for LDN could include modulating the immune system, supressing TNF (cytokine) production and enhancing the release of endorphins.

Dr. McKay works at 'The Complex Chronic Diseases Program (CCDP)', a multidisciplinary clinic in Vancouver that treats people with fibromyalgia, ME/CFS and Lyme disease and LDN is one of the treatment options used there. The clinic carried out a retrospective chart (medical record) review of 97 patients from their centre that were taking LDN, looking at the dosage used, side effects and benefits experienced.

Doses used were between 0.25mg and 4.5mg. They saw some beneficial effects of LDN, including increased energy, decreased pain, improved sleep, improved cognition and a reduction in crashes. Side effects included insomnia, skin rashes and gastrointestinal upset.

Dr. McKay concluded that LDN is safe and offers some benefits with minimal side effects and she believes a clinical placebo control trial is needed.

■ We created a summary review of LDN research here: **https://tinyurl.com/y3du98w9**

13 Health Care Responsibility and Compassion – Visiting the Housebound Patient Severely Affected by ME/CFS

Mrs. Caroline Kingdon (London School of Hygiene and Tropical Medicine) *Picture: lshtm.ac.uks*

Mrs. Kingdon's team were looking into ways to improve home visits for patients with severe ME/CFS and how to advise health practitioners on how to optimise these visits. They looked at data gathered from visiting nearly 100 severe ME/CFS patients.

Possible challenges were highlighted, such as how healthcare practitioners may sometimes feel vulnerable as the patient often knows more about the disease than they do, home visits may be cancelled last minute if the patient is having a bad day and the healthcare practitioner may also be greeted with hostility if the patient has had a previous bad experience.

They collected data from questionnaires and reported on the common symptoms that people with severe ME experience, as well as highlighting the symptoms that may affect them during a home visit, such as brain fog, PEM and noise sensitivity. Caroline emphasised the need for compassion and that home visits should be planned to minimise the risk of post exertional malaise (PEM) and must be thoughtfully undertaken She suggested some things that healthcare practitioners should be mindful of during visits, such as using a soft tone of voice, avoiding sensory overload, allowing enough time for the appointment and being patient, taking time to listen to and validate the patients experience.

Through improving home visits by focusing on compassion and validating the experience of the patient, health care practitioners can improve the quality of life of patients with severe ME/CFS, as well as gain a better understanding of the condition.

14 mapMECFS: A Myalgic Encephalomyelitis Focused Data Portal Supporting Data Discovery Across Multiple Biological Discipline

Mr. Mathew Schu, Ph.D. (RTI International, USA) *Picture: mecfs.rti.org*

mapMECFS is a secure online platform to help navigate the complex data landscape that researchers encounter when they are trying to study ME/CFS. It is a data sharing portal for the ME/CFS research network, which helps increase the discoverability of new data and allows data integration and sharing between researchers in different areas and across the multiple systems affected by ME/CFS.

There are smart search capabilities, to allow researchers to navigate the data as quickly and as easily as possible and to find the specific areas that they want data for. If a researcher has a specific thing they are interested in, such as a specific gene or a cell type, they can use the database to be able to look at all of the data that has previously been produced on that area within ME/CFS research.

mapMECFS was launched in January 2020 and over 30 datasets have been added to the network so far. The website currently hosts metabolomics, miRNA sequencing, gene expression, DNA methylation, and RNA sequencing data. It is currently only available to registered MECFSnet users, but they aim to develop a version of the data portal that is available to the broader research community.

15 Longitudinal Assessment of Clinical Severity Indicators and Determinants of Quality of Life in People with ME/CFS: A Prospective Cohort Study in the UK ME/CFS Biobank (UKMEB)

Dr. Eliana Lacerda (London School of Hygiene and Tropical Medicine) *Picture: lshtm.ac.uk*

Dr Lacerda presented the results of the UK ME/CFS Biobank's analyses of clinical data collected from 316 ME/CFS patients (249 mild/moderate and 57 severe), 90 MS patients and 143 controls. The data included multiple questionnaires, such as the UKMEB phenotyping participant questionnaire, short-form questionnaire, fatigue severity scale and pain analogue scale, as well as clinical assessments, including blood tests for creatine phosphokinase and hand grip strength testing.

Data from the participant phenotyping questionnaire can ascertain symptom severity and can differentiate between the different groups (mild/moderate ME/CFS, severe ME/CFS, MS and healthy controls). From the longitudinal follow-up (at 6-12 months), they saw a slight improvement in the physical component scores and fatigue severity scores in the mild/moderate group, but no changes in the severe group.

They found that hand grip strength is decreased in all ME/CFS patients, but is even more so in severe ME/CFS; there was a very significant difference seen between the severe and mild/moderate patients. This could serve as a very simple clinical diagnostic test. They also found decreased serum creatine phosphokinase in severe ME/CFS patients, which could be a potential biomarker. The Biobank team aim to further validate the use of CPK and hand grip strength testing as tools for diagnosis.

16 ME/CFS and Autoimmune Associated Small-Fiber Neuropathy

Mr. Ryan Whelan (Simmaron Research, USA) *Picture linkedin.com*

Many ME/CFS patients present symptoms of autonomic dysfunction, such as orthostatic intolerance and temperature dysregulation, and these are also reported in autoimmune associated small fibre poly neuropathy (aaSFPN). There is also evidence to support an autoimmune component to ME/CFS and so the research team felt it may be important to identify ME/CFS patients with comorbid small fibre neuropathy as it has been shown that immune modulatory agents, including intravenous gamma globulin (IVIG), reduces the autonomic symptom burden in aaSFPN patients.

A pilot study was carried out, looking into whether autoantibodies that were found to be increased in ME/CFS in previous studies are present in their patient population. (These include anti B1 and B2 adrenergic antibodies and anti-muscarinic cholinergic receptor 3 and 4 antibodies). They also set out to see if their ME/CFS patient population had comorbid aaSFPN. 364 patients with ME/CFS underwent extensive medical record analyses to identify the presence of aaSFPN comorbidity, based on symptom questionnaires as well as the presence of serum autoantibodies.

They found that 52% of patients tested positive for at least one of the autoantibodies, suggesting an autoimmune component to the condition. 38% of patients met the criteria for aaSFPN and these patients had significant dysregulation in the serum expression of the autoantibodies. Interestingly, they found that individuals with elevated anti-muscarinic cholinergic receptor 3 and 4 autoantibodies demonstrated a favourable response to IVIG therapy.

International Association for

IACFS/ME

Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis

Dedicated to the care and research of people affected by ME/CFS and related disorders

IACFS/ME is an international, non-profit organization of clinicians, scientists, professionals, patients, and advocates dedicated to the care and research of people affected by myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS), fibromyalgia, and other related conditions. We publish a peer-reviewed medical journal, organize international conferences, educate professionals and the public about ME/CFS, and promote science-based care, research, and public health policies.

IACFS/ME Mission Statement:

The mission of the IACFS/ME is to promote, stimulate and coordinate the exchange of ideas related to CFS, ME and fibromyalgia (FM) research, patient care and treatment. In addition, the IACFS/ME periodically reviews the current research and treatment literature and media reports for the benefit of scientists, clinicians and patients. The IACFS/ME also conducts and/or participates in local, national, and international scientific conferences in order to promote and evaluate new research and to encourage future research ventures and cooperative activities to advance scientific and clinical knowledge of these illnesses.

The IACFS/ME shall at all times be organized and operated exclusively for charitable, scientific, literary or educational purposes as a qualified exempt organization described under section 501 (c) (3) of the Internal Revenue code of 1986 and the regulations promulgated thereunder as they may now exist or as they may be hereafter amended.

17 Dyregulation of Mitochondrial Function and Fuel Preference in ME/CFS Lymphoblasts

Mr. Daniel Missailidis (La Trobe University, Australia)

Mr/ Missailidis's team have been studying energy supply and energy sensing pathways in ME/CFS patient cells. AMPK and TORC1 pathways are the two master regulators of mitochondrial respiration and regulate cellular energy supply. The research team wanted to see if there were any alterations in these pathways in ME/CFS cells.

They took blood samples from 65 ME/CFS patients and 37 healthy controls and made lymphoblast cell lines, to give them actively respiring cells to study. They used the 'seahorse' machine to measure the oxygen consumption rates of these cells, as well as other biochemical assays and gene and protein expression through proteomic and transcriptomic analyses.

They found no differences in the basal (resting) rate of respiration or the levels of ATP between ME/CFS patients and healthy controls. However, they found that ATP synthesis is inefficient in ME/CFS cells, despite the overall ATP content being normal. This suggests that ME/CFS lymphoblasts appear to maintain normal ATP levels and respiration rates at rest by compensatory up-regulation of respiratory complexes.

Next, they looked to see if there were any dysregulations in the TORC1 or AMPK pathways, as these can both upregulate respiratory function. They found that TORC1 activity is chronically upregulated in ME/CFS cells, suggesting a persistent stress response, which would be driving the compensatory upregulation of respiration. They also found elevated non-mitochondrial metabolism.

There also found increased levels of enzymes involved in breaking down fatty acids and amino acids for use as fuel for energy production. This represents a shift

Above: Seahorse Analyser (Picture: me-pedia.org)

in metabolism towards fat and protein being used preferentially by ME/CFS cells, over glucose. This shift in metabolism (as a result of TORC1 activation) could compensate for the inefficient ATP synthesis at baseline, leading to the unchanged ATP levels. However, this would leave the cell inflexible in the face of additional energy demands, as it is already using the 'back up' route and fuel sources that would be ordinarily be used during exertion when the normal respiration routes aren't keeping up with energy demand. This means that under stress or exertion, the cells would be unable to keep up with the increased energy demand.

Their next aim is to see why there is inefficient ATP synthesis and what the root cause of the mitochondrial dysfunction is.

THE ME ASSOCIATION

The Ramsay Research Fund

The research arm of the ME Association

Please help us to further The Ramsay Fund's invaluable work in supporting biomedical research into M.E. (Myalgic Encephalopathy)/Chronic Fatigue Syndrome.

The Ramsay Research Fund was set up to find answers to:

- how and why M.E. starts.
- how we can develop a test. And better still...
- how we can cure more of the 250,000 people with M.E. in the UK today.

With your help, that day could be much sooner.

You can donate:

- By cheque (payable to The ME Association) and with a covering note explaining that you wish your donation to go to research
- Online through our JustGiving campaign page for Ramsay Research Fund: www.justgiving.com/campaigns/charity/meassociation/ramsayresearchfund
- Or if you would like to make a regular donation, please contact our office to set up a standing order or use this link and type RRF in the message www.justgiving.com/meassociation/Donate

The ME Association's Ramsay Research Fund

Striving to find ways to help those living with M.E. today

The ME Association,
7 Apollo Office Court, Radclive Road, Gawcott, Buckinghamshire MK18 4DF
Registered Charity no. 801279
www.meassociation.org.uk/research/
facebook.com/MEAssociation ■ Twitter @meassociation