ME/CFS NEWSLETTER

INTRODUCTION

This newsletter provides updates on the ME/CFS Research Network (MECFSnet), including recent Network publications, investigator meeting highlights, mapMECFS and searchMECFS resource updates, and NIH-related activities that support ME/CFS research.

Do you have suggestions for our newsletter? Please send them to info@mecfsnet.org.

MECFSnet PUBLICATIONS

MECFSnet researchers continue to publish findings that advance understanding of ME/CFS biology, diagnosis, and potential treatment targets. Featured recent publications include the papers below. For the full and most up-to-date list of MECFSnet publications, please visit the publications page on the MECFSnet website.

- Systematic Examination of Gene Expression and Proteomic Evidence Across Tissues Supports the Role of Mitochondrial Dysregulation in ME/CFS
  Keele GR, Enger M, Barnette Q, Ruiz-Esparza R, Alvarado M, Mathur R, Stratford JK, Giamberardino SN, Brown LM, Webb BT, Carnes MU

- Temporal Dynamics of the Plasma Proteomic Landscape Reveals Maladaptation in ME/CFS
  Germain A, Glass KA, Eckert MA, Giloteaux L, Hanson MR

NETWORK NEWS

2026 ME/CFS Investigator Meeting

The ME/CFS Research Network held the 2026 ME/CFS Investigator Meeting from March 30 to March 31, bringing together 83 participants attending in person and virtually. Attendees included Network researchers, NIH representatives, collaborators from Columbia's Center for Solutions for ME/CFS, Cornell's ME/CFS Collaborative Research Center, the Interdisciplinary Canadian Collaborative ME Research Network (ICanCME), and RTI International's Data Management and Coordinating Center, as well as advocacy groups and people with lived experience with ME/CFS.

Dr. Amy Adams, NINDS Acting Director, provided updates on the NIH funding strategy and the ME/CFS Research Roadmap. Dr. Adams also acknowledged Dr. Walter Koroshetz's legacy in cross-agency collaboration and impact. Dr. Jeffrey Taubenberger, the now former NIAID Acting Director, highlighted the Institute's commitment to ME/CFS research and other post-infectious and non-infectious inflammatory syndromes. More than 21 speakers shared updates across six research tracks, showcasing advances in ME/CFS research through scientific innovation. Presentation highlights are organized below by track so readers can explore sections of interest.

Multi-Omics and Systems Biology Updates

The Systems Biology of ME/CFS – Columbia, Dr. Oliver Fiehn

Dr. Oliver Fiehn presented a systems-level approach to ME/CFS research that integrates metabolomics with cytokine, immune, microbiome, proteomic, transcriptomic, and antibody data. He emphasized the use of chemical classes rather than exact compound identifiers for cross-study integration and noted that plasmalogens were associated with pain in large studies. Dr. Fiehn also addressed compound identification scores and functional assignments, suggesting that combining chemical and literature data and using Application Programming Interfaces (APIs) based on large language models may improve interpretation beyond current ontology-based approaches.

Plasma Multi-Omics in ME/CFS Patients and Sedentary Controls – Cornell, Dr. Katie Glass

Dr. Katie Glass presented an integrative analysis on the plasma proteome and metabolome in ME/CFS patients and healthy sedentary controls to identify biomarkers and investigate mechanisms underlying post-exertional malaise (PEM). Longitudinal analyses using gene set enrichment analysis (GSEA) showed broad dysfunction in ME/CFS patients at baseline, immediately post-exercise, and especially during recovery when PEM symptoms were more severe. The results suggest that PEM severity is reflected in both the metabolome and proteome and supported further study of protein–metabolite interactions and potential PEM biomarkers for clinical trials.

Multi-Omic Analysis of Post-Exertional Malaise – Columbia, Amit Ranjan

Dr. Amit Ranjan presented a multi-omic meta-analysis of ME/CFS integrating metabolomics, proteomics, and metagenomics to assess consistency across studies and identify disease mechanisms. Findings included altered immune, energy, lipid, and extracellular matrix pathways, along with persistent gut dysbiosis and reduced key metabolites. Integration of datasets identified four interaction modules spanning immune, metabolic, stress, and microbiome systems. These results were used to suggest potential therapeutic targets including immune dysregulation, oxidative stress, microclotting, and gut microbiome imbalance.

Immune Dysfunction and Viral Response Updates

High Dimensional Profiling of PBMCs in ME/CFS with Cytometry by Time-of-Flight Cornell, Claire McNally

Claire McNally, a PhD candidate, presented findings from a cytometry by time-of-flight analysis of peripheral blood mononuclear cells (PBMCs) in ME/CFS, using samples collected before and 24 hours after a maximal exercise challenge designed to induce post-exertional malaise. The study found no major differences in overall immune cell population proportions. However, sex- and subset-specific T cell dysregulation was observed. Women showed a chronically stimulated T cell phenotype, while men showed increased exhaustion and altered activation markers.

Virus Reactivation and Immune Response in ME/CFS – Columbia, Dr. Nischay Mishra

Dr. Nischay Mishra provided an update on ongoing research that examines virus reactivation and infection patterns in ME/CFS. The research team collected samples during peak symptoms, shortly after symptom resolution, and from pre- and post-diagnosis cohorts. High-resolution serology and sequencing indicate reactivation of herpesviruses (EBV, HHV-6/7) and HERV-K activity, suggesting disrupted viral latency control. This viral reactivation may occur in tissue reservoirs and contribute to ongoing immune activation, inflammation, and downstream effects such as mitochondrial dysfunction and autoimmunity. These findings may help improve diagnosis, monitoring, and understanding of treatment responses.

Monocyte Dysregulation in ME/CFS – Cornell, Ananya Kohli

Ananya Kohli, a PhD candidate, presented research on epigenetic changes in monocytes and how these changes may contribute to chronic inflammation in ME/CFS. The research team compared epigenomic profiles (chromatin accessibility, DNA methylation) of monocytes in females with ME/CFS and healthy sedentary controls at baseline. The study found increased expression of multiple inflammatory genes in monocytes in ME/CFS. They additionally found evidence of epigenetic predisposition for the dysregulation of these genes. This research also linked chronic monocyte dysfunction to abnormalities involved in cellular maintenance that may help chronically activate inflammation in monocytes. The results provided a model for monocyte dysregulation with therapeutic implications.

Dysregulation and Cytotoxic T Cells in ME/CFS – Cornell, Dr. Erin Wissink

Dr. Erin Wissink presented on the role of T cells in ME/CFS and how T-cell receptor patterns may provide insight into immune and infection history. The research team compared females with ME/CFS and female healthy sedentary controls using multimodal immune profiling. They found evidence that T cells in ME/CFS may be predisposed to exhaustion due to chronic inflammatory conditions. These T cells may also contribute to post-exertional malaise. Gene dysregulation was identified in both CD4 and CD8 cells. Findings from CD8 T cells suggest an ongoing balance between chronic immune activation and regulatory mechanisms that attempt to limit tissue damage and autoimmunity.

Data Resources and Program Updates

DMCC and searchMECFS Updates – RTI International, Quinn Barnette

Quinn Barnette, DMCC Center Manager, provided an update on recent improvements to the searchMECFS and mapMECFS websites aimed at enhancing user interface and site navigation. mapMECFS now also includes secure login options through NIH Researcher Auth Service using Login.gov or ID.me.

mapMECFS Policy Updates – NINDS, Dr. Vicky Whittemore

Dr. Vicky Whittemore provided an overview of new NIH data security standards that ensure NIH controlled-access data are appropriately safeguarded. These standards apply to the controlled access datasets on mapMECFS. Other access requirements include the use of an institutional email address and a data use agreement (DUA) signed by the investigator with whom the user is working and their institutional official (forthcoming). DUAs must be renewed annually.

ME/CFS Common Data Elements – NINDS, Dr. Vicky Whittemore and RTI International, Dr. Megan Carnes

Dr. Vicky Whittemore presented an update on the Common Data Elements (CDE) Initiative, which aims to standardize data collection and reporting studies. CDEs provide common definitions, validated best practice instruments/assays, and reporting methods that enable researchers to collect and report data consistently. Standardized case report forms incorporate these CDEs, facilitating data harmonization and making it easier to compare and combine data from different studies.

The ME/CFS CDEs have been refined from 168 to approximately 60 core elements. Over the last year, three working groups (Cognitive Assessments, Functional Capacity/Overall Severity, and PEM) have continued to refine the CDEs. Each working group includes at least two people with lived experience. Collectively, the working groups convened 48 meetings last year. Several recommendations including FUNCAP 27, a supplemental CDE and multiple manuscripts are forthcoming.

ME/CFS Research Roadmap Implementation Plan – NINDS, Dr. Vicky Whittemore

Dr. Vicky Whittemore acknowledged progress made through the ME/CFS Research Roadmap and advances in ME/CFS research overall. She also provided an update on efforts to develop the ME/CFS Research Roadmap Implementation Plan, as directed by Congress.

Dr. Whittemore led an open discussion with meeting attendees to gather input on the implementation plan. The discussion focused on key questions that will inform the plan, including how to prioritize research activities, leverage existing clinical trial networks, promote biospecimen sharing and data sharing, and recruit early-career investigators, including basic scientists and clinician-scientists.

The Central Dogma – Transcriptomics, Proteomics, and Epigenetics Updates

Transcriptomic and Epigenomic Analysis of Skeletal Muscle in ME with Spatial and Cellular Precision – Cornell, Dr. Ben Cosgrove

> Dr. Ben Cosgrove provided an update on a collaborative project with the Hospital for Special Surgery in New York City examining transcriptomic and epigenomic differences in skeletal muscle between ME/CFS participants and healthy controls. The team will use high spatial and cellular resolution techniques to investigate cellular connections between muscle cells, vascular endothelial cells, and immune cells. About one-third of the planned 60 participants have been enrolled. Early results show reduced maximum hand grip strength and increased fatigability in ME/CFS, along with evidence of microvascular dysfunction.

Plasma Cell-Free RNA Following Exercise – Cornell, Anne Gardella

> Anne Gardella, a PhD candidate, presented research on cell-free RNA as a potential biomarker for ME/CFS. The research team analyzed over 450 plasma samples from 93 ME/CFS patients and 75 controls. They identified over 700 RNA molecules that differed significantly at baseline and developed a machine learning model using 21 genes that classified cases and controls with 77% accuracy. The research also revealed dysregulation in several immune cell types, including plasmacytoid dendritic cells, monocytes, and T cells, with notable changes in neutrophil degranulation pathways following exercise challenges.

SMPDL3B Dysregulation in ME/CFS: Linking Immune, Metabolic, and Physiologic Pathways – ICanCME, Bita Rostami-Afshari

> Bita Rostami-Afshari, a PhD candidate, presented findings on Sphingomyelin Phosphodiesterase Acid-Like 3B (SMPD3B), a lipid enzyme that links immune, metabolic, and physiological pathways. The study found that soluble SMPD3B levels vary significantly among patients, with higher levels (above 30 ng/mL) associated with more severe symptoms. Increased Phosphatidylinositol-specific phospholipase C (PI-PLC) activity was associated with reduced membrane-bound SMPD3B and elevated soluble forms, correlating with disease severity. Preliminary findings also suggest that vildagliptin and saxagliptin may help restore SMPD3B balance by inhibiting PI-PLC, indicating these drugs could potentially be repurposed to treat ME/CFS.

Distinct Circulating MicroRNA Signatures Stratify POTS from Comorbid Myalgic Encephalomyelitis and Identify miR-181a-5p as a Driver of Cardiac Calcium Dysregulation – ICanCME, Dr. Wesam Elremaly

> Dr. Wesam Elremaly presented findings from an ICanCME study on postural orthostatic tachycardia syndrome (POTS) and its comorbidity with ME/CFS, highlighting a microRNA signature that distinguishes patient subtypes with high accuracy. The research team identified miR-181a-5p as a potential biomarker for cardiac instability, linking

elevated levels to calcium dysregulation in cardiomyocytes, arrhythmias, tachycardia, and symptoms of orthostatic intolerance. Levels of miR-181a-5p were particularly elevated in ME/CFS patients with POTS compared to POTS alone and ME alone subgroups.

Clinical Implementation and Associations Updates

The Association Between Myalgic Encephalomyelitis, Obstructive Sleep Apnea, and Oral Health: The EMSOMDENT Study – ICanCME, Dr. Robert Durand

Dr. Robert Durand presented preliminary findings from the EMSOMDENT study on the relationship between ME/CFS, obstructive sleep apnea (OSA), and oral health. The study of 18 ME/CFS patients and 71 controls found no significant association between ME/CFS and OSA, although ME/CFS patients reported more insomnia and snoring. Despite poorer oral hygiene among controls, ME/CFS patients exhibited greater gingival inflammation. Future work will examine genetic factors and oral pathogens.

Causes of Symptoms and Symptom Persistence in ME/CFS – Columbia, Dr. Anthony Komaroff

Dr. Anthony Komaroff presented a model suggesting that many biological abnormalities in ME/CFS and Long COVID may directly contribute to symptoms. He also proposed that neuroinflammation may trigger sickness behavior and mild torpor, leading to fatigue, cognitive dysfunction, and metabolic changes. He identified neuroinflammation as a potential therapeutic target and noted that self-reinforcing pathophysiological cycles may help explain the chronic persistence of ME/CFS.

What Canadian Physicians Need to Improve ME Diagnosis and Management – ICanCME, Sabrina Poirier and Dr. Todd Davenport

Sabrina Poirier and Dr. Todd Davenport presented findings from a recent survey on Canadian healthcare providers' knowledge and confidence in diagnosing ME. The survey found that while many healthcare providers reported diagnosing and treating patients with ME, they expressed low confidence in diagnosing ME and providing treatment and care coordination. It also found that many healthcare providers did not use established diagnostic criteria and had knowledge gaps regarding key clinical features, including PEM. Survey participants expressed a strong need for more ME education in both entry-level training and continuing professional development, with online asynchronous learning as the preferred format. Future analysis of the dataset may help identify specific healthcare provider groups in need of education, as well as the most appropriate delivery mode and level of training content.

Among the highlights of the two-day meeting were a presentation on ME/CFS genetics by Dr. Chris Ponting from the University of Edinburgh DecodeME project and a presentation on genetic and proteomic insights in ME/CFS by Dr. Jessica Maya.

ME/CFS Exchange Webinar Series Launches October 8

The National Institute of Neurological Disorders and Stroke (NINDS) in partnership with the ME/CFS Research Network (MECFSnet) is launching a new quarterly webinar series that will bring together researchers and experts from diverse disciplines to share insights, foster collaboration, and help advance ME/CFS research.

The first webinar will be held on **October 8 at 1:00 p.m. ET** via Zoom and will focus on post-acute infection symptoms, including their underlying causes and persistence in conditions such as ME/CFS. The session will be moderated by Anthony Komaroff, MD (Harvard Medical School) and feature presentations from leading experts in the field.

Additional details, including speaker and registration information, will be available soon. Please save the date!

RESEARCH NEWS

The following updates were previously shared with mapMECFS users and are included here for the broader MECFSnet community. These newly available datasets and biospecimens expand resources available to researchers studying ME/CFS.

Newly Released Data: MCAM Adult Longitudinal Cohort – Second Visit Data

Second-visit data from the MCAM Adult Longitudinal Study are now available for request on mapMECFS. The study, conducted from 2012-2020 across seven U.S. ME/CFS specialty clinics, includes data from 501 participants (346 ME/CFS cases and 155 healthy controls). The second visit took place approximately one year after the first (10-14 months).

The release includes repeated clinical and survey assessments from the first visit, along with additional instruments introduced at the second visit. These data complement the existing first-visit dataset from 802 participants (459 ME/CFS cases and 343 healthy controls).

Newly Released Data: MCAM Cognition & Exercise Sub-Study Data

Data from the MCAM Cognition and Exercise (CE) Sub-Study are now available on mapMECFS. Conducted from 2013-2019 across seven ME/CFS specialty clinics in the United States, the sub-study was designed to assess cognitive performance and symptom changes before and after CE testing to better characterize post-exertional malaise (PEM).

The dataset includes cognitive assessment data from 426 adults (261 ME/CFS cases and 165 healthy controls), with a subset of 342 participants (182 ME/CFS cases and 160 healthy controls) also completing exercise testing. Available data include:

- Cognitive assessments
- Exercise testing measures
- Symptom and survey data collection across multiple timepoints

Newly Released Biospecimens: MCAM Adult Longitudinal Cohort – Second Visit Data

Biospecimens from the second study visit of the MCAM Adult Longitudinal Cohort are now available on searchMECFS. Available biospecimen types include RNA, DNA, plasma, and saliva.

These newly released specimens expand the existing first-visit collection, providing researchers with valuable longitudinal sample sets to support studies of disease progression, biological changes over time, and biomarker discovery.

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