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Chronic Fatigue Syndrome Research

Research in our lab has led us to the conclusion that CFS is not a problem with energy "deficiency". It is a problem with cellular energy "distribution".

Commonly used clinical diagnostic criteria for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) include the Fukuda[1], Canadian[2], and Institute of Medicine, now known as the National Academy of Medicine (NAM)[3] criteria (Box 1). These clinical criteria are essential for accurately identifying possible cases ME/CFS. However, the accuracy of clinical diagnosis is

improved when additional objective testing is available. In our studies of genetic forms of mitochondrial disease we developed a novel mass spectrometry-based method that allows us to measure over 500 molecules in the blood. Some people have likened these NextGen metabolomics methods to a new lens, like the Hubble telescope, that allow us to see deeper and with greater clarity into the universe of the cell than has been possible before.

Box 1

Diagnostic Criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)

All 3 of the following core symptoms must be present:

1. Life altering fatigue lasting for more than 6 months
2. Post-exertional malaise
3. Unrefreshing sleep

One of the following two symptoms must be present:

1. Episodes of cognitive impairment (sometimes called “brain fog”)
2. Postural orthostatic tachycardia syndrome (POTS)

In our first studies of CFS[4] we answered 3 basic questions:

1. Can NextGen Metabolomics be used to assist with the diagnosis of CFS? A: Yes.
2. Can the chemical information provided by metabolomics be used to help with the development of treatment plans that are tailored to the individual? A: Not yet. A new method of dynamic metabolomic analysis (DMA) is needed. See below.
3. Does a systems analysis of the metabolic abnormalities found in CFS lead us to a better understanding of the root biology underlying the disease? A: Yes. ME/CFS is a chronic physiologic reaction to a perfect storm of severe environmental threats. It is a dauer-like metabolic syndrome that can be caused by at least 50 different triggers. ME/CFS prevents the orderly progression of the normal steps of healing[5], and causes life-long pain and disability[4]. If ME/CFS is truly like dauer[6], then the biological clock of aging is slowed during illness[7], but in a perverse twist of medical fate, without relief from long-term disabling symptoms.

(Open Access link) (PDF) (UC San Diego Press Release).

In our next studies of ME/CFS[8] we showed:

1. The serum of patients with ME/CFS contains an activity that fragments mitochondria and depletes cellular ATP, causing energy depletion. This activity can be detected in a new assay system that was developed in collaboration with Dr. Bhupesh Prusty in Würzburg, Germany.
2. The cell danger response (CDR) can be triggered in cultured cells in the lab by exposing them to environmental chemicals or metabolic stress.

When the CDR is triggered in cells that contain an integrated copy of human herpes virus 6 (iHHV-6), a small piece of the HHV-6 RNA can be reactivated. This causes cells in the laboratory to secrete an activity that is indistinguishable from the energy-depleting activity found in ME/CFS serum.

3. Although the secreted CDR-factors cause energy depletion and mitochondrial fragmentation, they also lead to a profound antiviral effect, protecting cells from many kinds of viral infection. This was measured in laboratory cells by challenging them with influenza virus and herpes simplex virus 1 (HSV1).

4. We think the CDR-activating factors that can be transferred to healthy cells in the lab from ME/CFS patient serum, and from the medium from iHHV-6 containing cells in the lab, are responsible for the post-exertional malaise (PEM) that is so devastating to patients with ME/CFS.

(Open Access link) (PDF) (UC San Diego Press Release).

Video Links
NIH ME/CFS Symposium, "Accelerating ME/CFS Research", April 4, 2019

Day 1: https://www.youtube.com/watch?v=1emsA2CcRK4

Day 2: https://www.youtube.com/watch?v=7bEuwoo3s3s

Dr. Naviaux's Talk on ME/CFS, Book 2 of Medicine, and the healing cycle is time stamped: 55:00 to 1:28:15 on Day 1.

Dr. Komaroff's ME/CFS research summary is time stamped: 6:02:43 to 6:51:15 on Day 2

New Research

In new research funded by the Steven and Alexandra Cohen Foundation and private donors, we will be using advanced methods in targeted metabolomics and exposomics to answer the following questions:

1. Can metabolomics and exposomics be used to diagnose acute Lyme disease?
2. Can these methods predict who is at increased risk to develop PTLDS?
3. Is there an overlapping chemical signature in PTLDS and ME/CFS?
4. Can a new test called "Dynamic Metabolomic Analysis" (DMA) be used to personalize metabolomic results, identify subtypes, and predict outcomes in Lyme or ME/CFS?

+ **References**

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