



OpenMedicine
Foundation

Linda Tannenbaum, Founder & CEO/President

Accelerating ME Collaborative Research- An OMF Update

June 2019

ME

Myalgic Encephalomyelitis

**A Major Public Health Crisis
That Most People
Know Nothing About**

ME could strike anyone at anytime...

No diagnostic test

No FDA-approved treatments

No cure

YET!

Centers for Disease Control and Prevention (CDC) 2006

“Level of disability for ME/CFS is comparable to MS, AIDS, end-stage renal failure and other well-known very severe medical conditions.”

Dr. W. Reeves, Former Chief Viral Diseases

National Academy of Medicine (Institute of Medicine) 2015

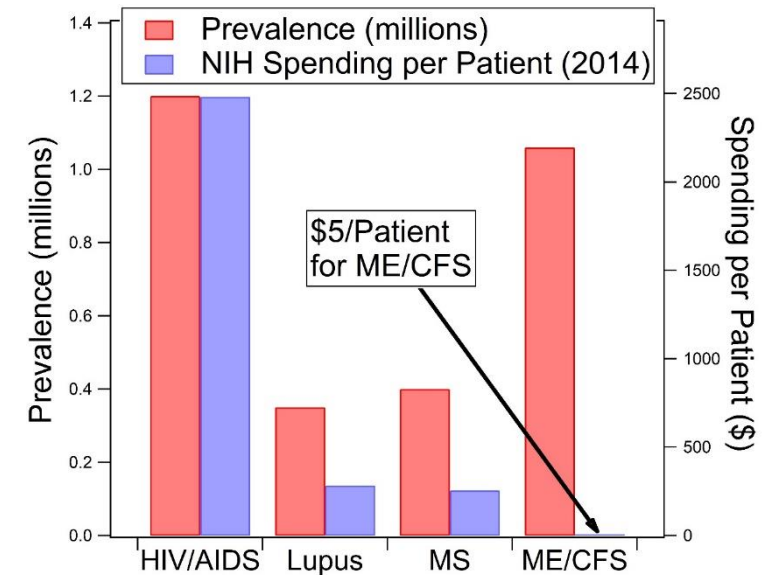
“ME/CFS is a serious, chronic, complex and multisystem disease that frequently and dramatically limits the activities of patients and in its severe form can consume the lives of those whom it afflicts.”

What Does ME Really Feel Like?

- **Debilitating pathological fatigue**
- **Post-exertional malaise (worsening of symptoms after physical, cognitive or emotional effort, ie “crash”)**
- **Unrefreshing sleep**
- **Cognitive impairment/brain fog**
- **Incapacitating migraines & dizziness**
- **POTS: Orthostatic intolerance**
- **Widespread pains & chronic infections**
- **Multi-systemic: Immunological, Gastrointestinal, Urological**

Key Facts About ME

- **An estimated 20 million suffer worldwide**
- **75% of patients are women**
- **NIH research funding is extremely low**
- **25% are home- or bed-bound at some point**
- **80–90% are not diagnosed or misdiagnosed**
- **Only a few medical specialists**
- **No diagnostic test, no FDA-approved treatment, no cure**
- **Symptoms typically persist for years; recovery is rare**



Coalition of ME Clinicians confer: GET and CBT Harm Patients

“In our expert opinion, it is inappropriate and potentially harmful for medical providers to recommend Graded Exercise Therapy (GET) or Cognitive Behavioural Therapy (CBT) as a treatment as studied in the PACE trial and similar trials. These trials are based on the premise that ME is not a physical illness, and that the illness can be cured by correct attitude and graded aerobic exercise. This view is not supported by the evidence of neurological, immunological, and energy metabolism impairment.”



OPEN MEDICINE FOUNDATION

THE GAME CHANGING SOLUTION

THE **OMF** SCIENTIFIC ADVISORY BOARD

2 Nobel Laureates & 5 National Academy of Sciences Members



Ronald W. Davis



David Bell



Paul Berg



Jonas Bergquist



Mario Capecchi



Mark M. Davis



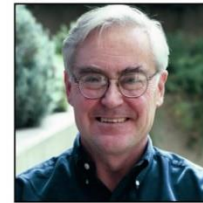
Øystein Fluge



Jennifer Frankovich



Maureen Hanson



H. Craig Heller



Olav Mella



Robert K. Naviaux



Baldomero Olivera



Daniel Peterson



Michael Snyder



Ronald G. Tompkins



Wenzhong Xiao

*Leading research.
Delivering hope.*

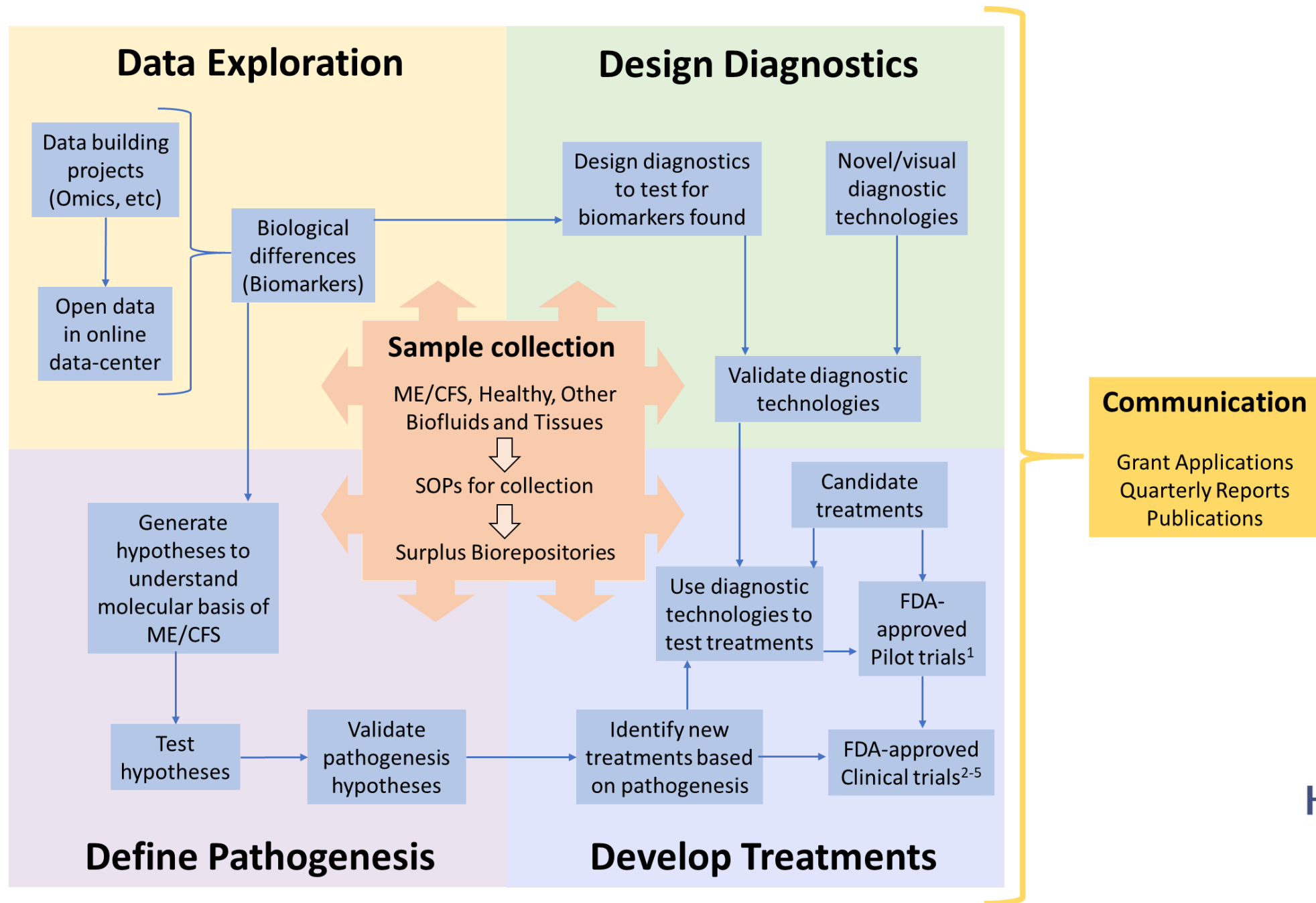
Biochemistry
Bioinformatics
Biophysics
Cellular Metabolism
Clinical Care
Data Analytics
Drug Development
Exercise Physiology
Genetics
Immunology
Microbiology
Neurobiology
Public Health Policy
Oncology
Pediatrics
Rheumatology
Surgery
Zoology



COLLABORATION



"It is the long history of humankind (and animal kind, too) that those who learned to collaborate and improvise most effectively have prevailed." *Charles Darwin, biologist*



RESEARCH OVERVIEW



Stanford
University

STANFORD COLLABORATIVE RESEARCH CENTER

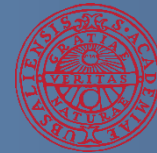
- ME Severely Ill Big Data Study
- Extended big data study in families
- T cells and the molecular immunology of ME
- Metabolic trap hypothesis
- Nanoneedle blood-based diagnostic
- Red blood cell deformability in ME



HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

HARVARD COLLABORATIVE RESEARCH CENTER

- ME Muscle biopsies for multi-omics study
- Repository of controls for ME studies



UPPSALA COLLABORATIVE RESEARCH CENTER

- Steroids, Autoantibodies and Proteomics



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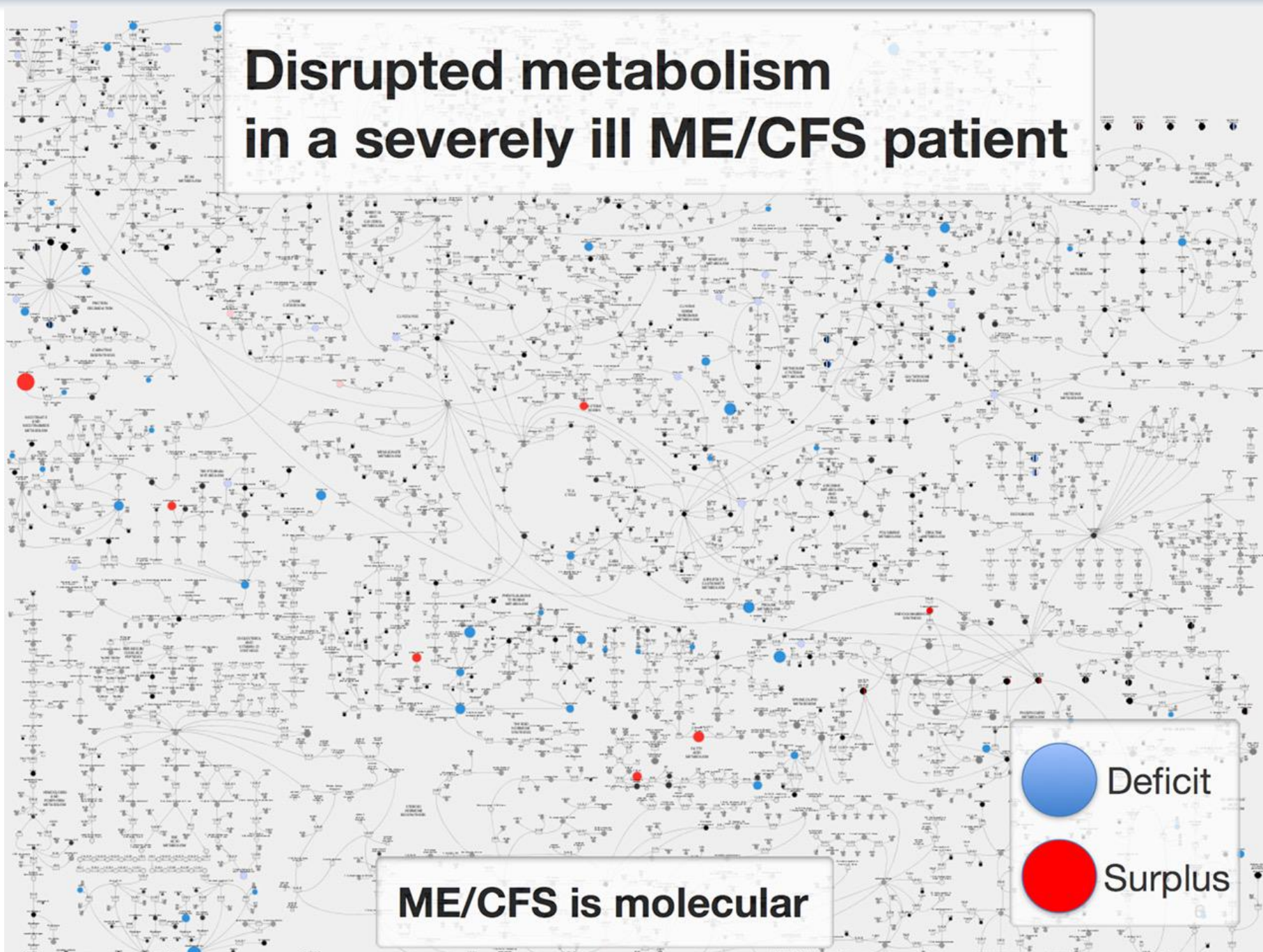
> 1000 tests per patient, 20 patients.

Results OPEN and available on our website for registered researchers.

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Disrupted metabolism in a severely ill ME/CFS patient



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Searching for a genetic predisposition for ME through patients and their direct families.

Using unaffected family members of patients as controls reduces variance in genetics, environment, and diet.



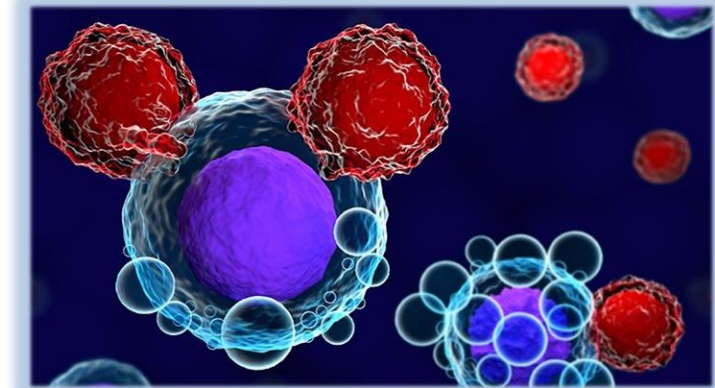
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Using single-cell RNA sequencing, T-cells have clonally expanded in ME patients.

Infection or an autoimmune disorder?



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Robert Phair, PhD: Studying computer modelling of enzyme kinetics and the results of the SIPs cohort, mutations have been seen in all of the severe patients in the IDO2 gene.

IDO2 synthesizes kynurenine from tryptophan.

The outcome of this is an increased conversion of tryptophan to serotonin and a reduced conversion of tryptophan to kynurenine. Additional patients are currently being examined.

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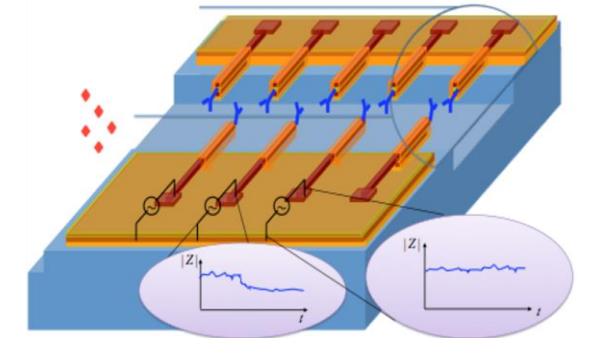
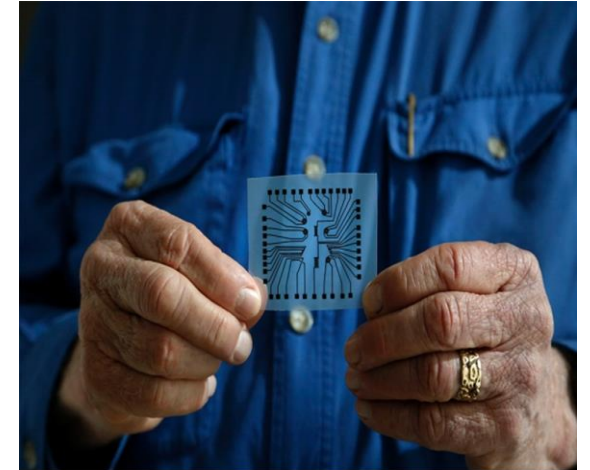
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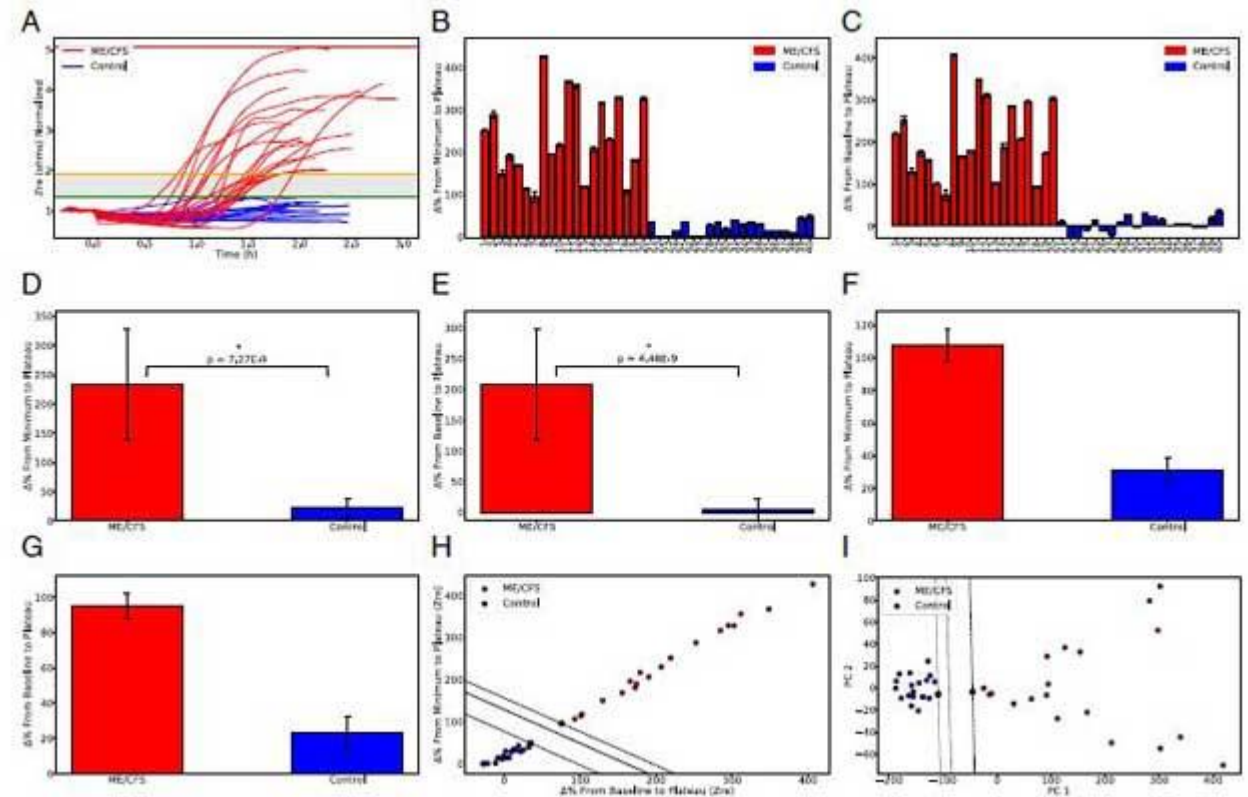
Nanoneedle

Nanofabricated device that creates an electrical current and measures the impedance of that current by cells.

Changes in the cell will create a change in the current. Under salt stress ME patient cells had a big change of current compared to healthy cells.



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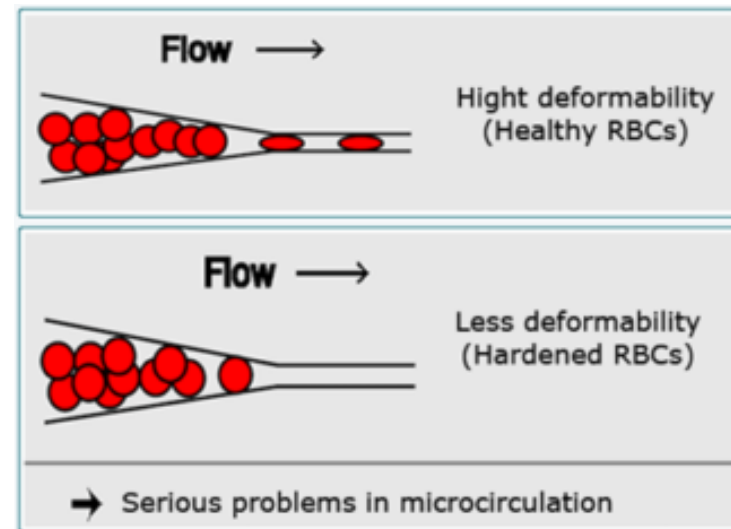
Red are ME cell impedance measures
Blue are Healthy cell impedance measures

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A microfluidic device in collaboration with San Jose State University that measures blood flow & deformability of red blood cells.



OMF-funded HARVARD COLLABORATIVE RESEARCH ACTIVITIES

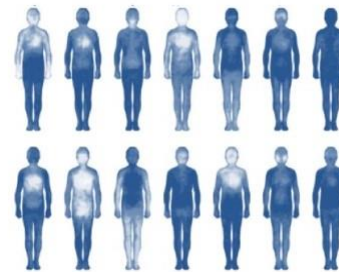
Massachusetts General Hospital and Harvard Affiliated Hospitals



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- **Repository of controls for ME studies**



Understand the multi-omics signature of muscle biopsies from ME patients before, during exercise and during their recovery from mild muscular stress.

Hypothesis is that the inflammation-related recovery mechanisms in ME patients are dysregulated, and that this delays recovery from post-muscular stress.

Will also run experiments to determine whether the metabolic trap is in skeletal muscle. **HOPE**

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Massachusetts General Hospital and Harvard Affiliated Hospitals

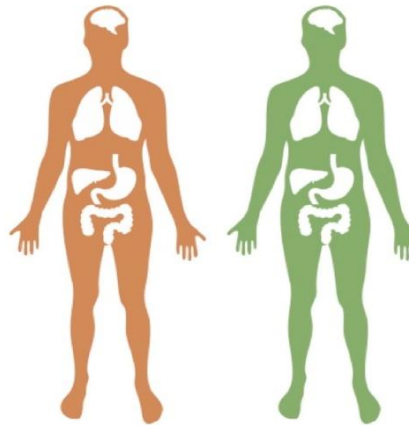


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Patients vs Controls



Creating access to sedentary controls for future research studies.

Muscle and blood samples.

Genomics of human skeletal muscle strongly depends upon the fitness and activity level of the donor.



OMF-funded UPPSALA COLLABORATIVE RESEARCH CENTER

(Director Jonas Bergquist, MD, PhD)

■ **Steroid, Autoantibodies, Proteomics**



Steroid hormonal dysregulation. Measuring 22 steroids in the plasma of patients and healthy controls to determine whether steroid hormones are part of the pathophysiology of ME

Autoantibodies. Validating preliminary data in plasma. Not seen in spinal fluid.

Proteomics. Measuring approximately 100 proteins related to pain and neuroinflammation

OMF's PATIENT ENGAGEMENT

- 170 active volunteers worldwide
- Outreach extends to 100+ countries
- Communications translated in 15 languages
- Openly communicate activities and funded research
- Host science and community symposiums
- Interact via email and social media
- OMF ME Worldwide Tour





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Delivering hope.*

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