NEW RESEARCH IN ME/CFS

INVEST IN ME

SPRING 2017
MAJOR CATEGORIES

• 1. TISSUE/BRAIN BANK

• 2. COMMON DATA ELEMENTS

• 3. MICROBIOME/METABOLOME

• 4. AUTOIMMUNITY
TISSUE/BRAIN BANK

• 1. NACAL & OTHERS, LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE & NIAID

• 2. ESTABLISH POST-MORTEM BRAIN AND TISSUE BANK FOR STUDY OF ME/CFS

• 3. ESTABLISH A SPECIFIC DONOR PROGRAM

• 4. RAPID COLLECTION AND PROCESSING
TISSUE/BRAIN BANK

• 5. SUPPLEMENTAL CLINICAL, LAB AND SELF-ASSESSMENT DATA COLLECTED FROM EACH POTENTIAL SUBJECT IN ADVANCE

• 6. INCORPORATE INTO AN EXISTING BIOBANK (CREUTZFELDT-JACOB DISEASE/ALZHEIMER’S)

• 7. POTENTIAL DONORS ACCESS A WEB PAGE AND FOLLOW INSTRUCTIONS
TISSUE/BRAIN BANK

• GOALS:

• 1. SEEK TO ESTABLISH A COHORT OF WELL CHARACTERIZED CONTROLS AND ME/CFS PATIENTS

• 2. IDENTIFY POTENTIAL BIOMARKERS AND RETRIEVE HIGH QUALITY PATHOLOGICAL SAMPLES

• 3. DISSEMINATE THIS RESOURCE GLOBALLY
COMMON DATA ELEMENTS


• ADDRESS PROBLEM OF VARIABILITY IN ME/CFS RESEARCH; CRITICAL ELEMENTS THAT SHOULD BE INCLUDED IN NEW RESEARCH
COMMON DATA ELEMENTS

1. STUDY DESIGN:
   a. type of study: case/control; longitudinal
   b. demographics: age, race, ethnicity, gender, duration of illness, disability status
   c. case definition: ?multiple vs one
   d. symptom inventory: frequency and severity of case defining symptoms; sleep, pain, include scoring methodology
COMMON DATA ELEMENTS

• e. use of self report scales: SF-36; sickness impact profile
• f. functional assesment: exercise testing
• g. allostatic loads: heart rate variability, body mass index; 24 hour urinary cortisol
• h. test HPA axis, i.e. cortisol, ACTH
• i. immune fx: nk studies, cytokines
COMMON DATA ELEMENTS

• j. sympathetic activity: salivary amylase
• k. imaging: MRI, functional MRI, SPECT scan
• l. genomic and transcriptomic studies:
  - Genome wide assessment studies; whole genome sequencing; transcriptomol analysis (mRNA); epigenetic studies
• m. proteomic studies: disease defining markers
• Professor Simon Carding, Institute of Food Research, Norwich Research Park, UK


• 1. Breaks in gut epithelial mucosa help transport elements of gut dysbyosis

• 2. Link to diminished cognitive function in ME/CFS patients
MICROBIOME

• 3. 77% of ME/CFS patients demonstrate small intestinal overgrowth
• 4. further examination of gut `virome’ which is unique to the individual and less subject to change that bacterial species; bacteriophages transport viral particles into the gut
METABOLOME


• 1. Diminished number of amino acids that fuel oxidative metabolism via the tricarboxylic acid cycle (TCA)

• 2. Amino acid pattern shows impairment of pyruvate dehydrogenase (PDH), key enzyme
• 3. inadequate generation of ATP by oxidative phosphorylation causes excessive lactate generation on exertion
• 4. diminished glucose oxidation and increased anaerobic metabolism with increased use of amino acids in the TCA cycle
• 5. PDH dysregulation and changes in amino acid metabolism provide one mechanism
• 6. Other studies have shown diminished sphingo-lipid and fatty acid metabolism

• 7. PDH dependent metabolism is important in exertional activity but may not be apparent when ME/CFS subjects are at rest
AUTOIMMUNITY


• 1. Infection triggered disease onset leads to chronic immune activation and autonomic dysregulation suggesting autoimmune antibodies directed against neurotransmitter
AUTOIMMUNITY

• Receptors in ME/CFS patients
• 2. in patients receiving Rituximab, B cell depletion therapy, those patients who are responders will have diminished antibody to these receptors at the end of treatment