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DELIVERING OUTCOMES FOR M.E.

A GOAL-FOCUSED COMMITMENT

Prepared for

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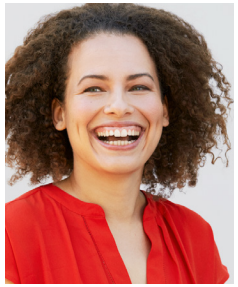
Who We Are



JENNIFER BREA

#MEAction Executive Director and filmmaker

MARY DIMMOCK

Retired from pharma; ME/CFS advocate since her son became ill

BEN HSUBORGER

#MEAction Campaigns Director

ROCHELLE JOSLYN, PH.D.

Immunologist, remitted & relapsed ME patient since 2004

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Former biochemistry professor at Williams College; ME patient since 2014

TERRI WILDER, MSW

Diagnosed with ME March 2016. Director of HIV/AIDS Education and Training at large hospital in NYC

Agenda

- What's missing
- What's needed
- Discussion

We are asking for

1. **Bold Leadership**
2. **ME/CFS-Specific Multi-Year RFAs & Investigator-Initiated Funding Opportunities**
3. **A Strategic Plan**
   Comprehensive, Fully Funded, Cross-Institute, & Outcomes-Driven

NIH is moving but...

Lack of Urgency

- Serial efforts and a 'wait and see' approach will take years to produce outcomes that matter to patients

Lack of Researchers & Lack of Research Diversity

- Too few researchers to investigate the breadth of research needed
- Current focus on basic disease mechanisms & early researchers will take years to pay out
- Patients cannot fix the lack of researchers - funding and NIH leadership will

Lack of Funding

- Amount far below what's commensurate with disease burden & needed to achieve key goals
- No ME-specific funding opportunities
- Insufficient institute support

Critical Barriers Remain Unaddressed and Unresolved

- Trans-NIH model not producing needed commitment and focus
- Case definition/patient selection methods
- Clinical care crisis - is impacting research

Continued stigma, hostility, and disbelief

Psychogenic theories and treatments fill the void

Underdiagnosis, misdiagnosis, and mistreatment

Key R&D players uninvolved, e.g. researchers, clinicians, industry

NIH Inaction Perpetuates Harm

Essential research and drug development not being done

Crisis in clinical care – few experts, no medical specialty

75% can't work, 25% bedbound or housebound for decades;

Limited disability and health insurance

Billions of dollars lost to the US economy

THIS MUST CHANGE

What's Needed

1

Bold Leadership

- Immediately and widely evangelize to researchers, clinicians and the public
- Seize scientific opportunity
- Address structural barriers

2

ME/CFS-Specific Multi-Year RFAs & Investigator-Initiated Funding Opportunities

- Broad scope - from methods development to basic research to biomarkers and treatment trials
- Consistent funding stream to demonstrate NIH is serious and it's safe to enter the field
- Researchers write grants when they know funds are available, not when sick patients email them

3

A Strategic Plan:

Comprehensive, Fully Funded, Cross-Institute, and Outcomes-Driven

- "Moonshot" approach - a plan to deliver diagnostic(s) and treatment(s) in 5 years
- Full weight of Director's Office to make this happen

Discussion & Next Steps

Supplemental Material

STRATEGIC PLAN

STARTS WITH THE GOALS

- **Outcomes-Driven**
  Designed to deliver biomarkers and treatments as quickly as possible
- **Sufficient Funding**
  To achieve defined goals and outcomes
- **Comprehensive**
  Covers the breadth of disease pathology, diagnosis, and treatment
- **Defined, Aggressive Milestones**
  To ensure rapid progress
- **Collaboratively Developed and Implemented**
  With key stakeholders
- **NIH-wide**
  Full, strategic commitment by Director's Office and key institutes - money, resources, and goals
- **Tackles all key barriers and needs**
  E.g. research methods, dearth of researchers and clinicians, inadequate Trans-NIH approach, lack of a biorepository

EXAMPLES OF RFAS

PROPOSED RFAS	EXAMPLES OF POTENTIAL RESEARCH AREAS
Clinical Trials and Interventions Consortium	• E.g. as Dr. Klimas is doing for Gulf War Illness
Biomarkers & Diagnostic tools	• Blood: cytokines, metabolomics, transcriptomic/methylation/exosome profiles, cellular integrity & function (e.g. NK cytotoxicity, RBC deformability, B cell maturity, etc.) • Imaging: neuroinflammation, functional connectivity in the brain • Functional: CPET alternatives, NASA lean • Diagnostic instrument development & validation (for clinical & research use)
Treatment trials	• Disease-modifying treatments: antivirals, Ampligen, IVIG, rituximab, immunoadsorption, isoprinosine, HPA axis treatments, plaquenil • Symptom relief: naltrexone, mestinon, IV saline, fludrocortisone, gabapentin, amitriptyline, trazodone, methylphenidate, modafinil, duloxetine, pacing • Comorbidity-specific therapies: POTS, FM, MCAS, SFN, SIBO, endocrine dysfunction, etc.
Cross-sectional studies to understand subgroups, range of severity	• Define spectrum & prevalence of symptoms, identify subgroups by symptom clusters & biologic measures • Define spectrum & prevalence of functional debility & disease severity • Define prevalence & subsets of comorbidities (e.g. POTS, EDS, FM, MCAS, SFN, endocrine dysfunction, SIBO, MCS, etc.)

EXAMPLES OF RFAS CONT.

PROPOSED RFAS	EXAMPLES OF POTENTIAL RESEARCH AREAS
Studies to understand onset, progression	• Cross-sectional studies to define spectrum & prevalence of onset types, triggers • Prospective longitudinal studies following triggering events (infectious and non-infectious) • Retro- & prospective longitudinal observational studies to define disease progression (develop a prognosis framework), incidence of progression to other diseases (e.g. autoimmune disease, cancer, cardiac disease), causes of premature death
Patient selection methods, outcome measures, and other needed instrumentation	• Reach consensus on core inclusion/exclusion criteria & methods used for all ME/CFS research cohort selection to facilitate cross-study comparability & reproducibility • Develop & validate standardized objective & subjective outcome measure methods & instrumentation - numerous recommendations for additional research in NIH's ME/CFS CDE initiative
Additional funding for existing and new CRCs	• Current levels for existing CRCs are insufficient and tenuous - important work is not being done because of lack of funds • Additional CRCs are needed to improve research diversity, accelerate progress
Expanded Pathophysiology Studies	• Characterize pathophysiology underlying PEM (e.g. metabolites, cytokines, cellular composition, cardiopulmonary and metabolic dysfunction, etc.) • Characterize neurological and neurocognitive dysfunction • Characterize autonomic, orthostatic and vascular dysfunction • Characterize immunologic dysfunction (e.g. autoreactivities, immunodeficiencies, chronic inflammation) • GWAS to identify predisposing & symptom-associated polymorphisms, subsets • Prospective study of impact hormonal change (e.g. pregnancy, menopause, HRT) on disease status