Solve ME/CFS Initiative

Leading the Fight to cure ME/CFS

Solve M.E. Response to the National Advisory Neurological Disorders and Stroke (NANDS) Council Working Group for ME/CFS Research

May 1, 2019

Thank you for the opportunity to provide information and guidance to The National Advisory Neurological Disorders and Stroke (NANDS) Council Working Group as it develops new strategies for National Institutes of Health (NIH) to advance ME/CFS research. The ME/CFS field is significantly lacking the research infrastructure needed to make progress on a prevalent and debilitating disease; a fact that was recently emphasized by experts in the field at the April 2019 "Accelerating Research on ME/CFS" gathering. Maureen Hanson (PhD), Director of the Enervating NeuroImmune Center and Principal Investigator of the NIH Collaborative Research Center at Cornell University, noted: "like 30 years ago, what we don't have is adequate funding. We still don't have adequate respect for the seriousness of this illness. We have repeatedly heard there aren't enough researchers interested in studying this illness."

In the years since the last Request for Information issued by NIH in 2016, there has been progress in ME/CFS research and clinical care. However, efforts are concentrated in too few labs and clinics, and substantial gaps in our knowledge of this complex disease persist. ME/CFS still sorely lacks support commensurate with the disease burden. NIH is in a position to address institutional neglect, funding shortfalls, and barriers to research that impede scientific progress in this disease.

Our comments and suggestions are outlined below:

1. **<u>The most compelling ME/CFS research needs.</u>**

    a. Develop a consensus, overarching strategy that will drive cross-disciplinary research
    b. Address institutional and process barriers that persist at NIH
    c. Create a global, openly-available, centralized resource of well characterized ME/CFS patient, healthy control and disease control data and bio specimens
    d. Establish rigorous, standardized research practices; including the application of case definitions, methodological approaches, utilization of data collection instruments, and expansion in replication and studies that interrogate or build on previous findings
    e. Develop an infrastructure for researchers to easily share data (positive and negative findings) and methodologies to allow them to build on each other's discovery
    f. Promote a massive increase in the number of researchers working on the disease; particularly, early-career stage investigators and skilled scientists from relevant

scientific domains or related disease fields who can newly apply their expertise to ME/CFS

g. Redouble existing efforts and expand approaches to educate clinicians, encouraging better clinical care, partnerships in research, and a pipeline of study participants

h. Increase opportunities for collaboration and tools for communication among scientists, clinicians, people living with ME/CFS, and other stakeholders

i. Ensure that people living with ME/CFS are more meaningfully incorporated into research discussions, acknowledged as experts in their own right, and elevated to the level of partner in research studies

2. Strategies for overcoming scientific challenges or barriers to progress in ME/CFS research

a. Develop a consensus, overarching strategy that will drive cross-disciplinary research

- Activate a diverse stakeholder group in a "moonshot" model for ME/CFS to reach an agreed upon disease model that reflects the best current scientific knowledge and how it fits together. The group should be charged to set ambitious, time bound goals to fill gaps in the research pipeline, and meet regularly to monitor progress. Their activities should be communicated regularly to the community.
- Establish "Dream Teams" that consist of researchers organized by area of focus headed by a leading researcher (like this analog model of Standup to Cancer). The Dream Teams communicate on a regular basis, share findings, identify collaborative projects and support each other's work. The heads of the Dream Teams meet regularly to share findings across areas of research.

b. Address institutional and process barriers that persist at NIH

- The decision to organizationally position ME/CFS in a trans-NIH Workgroup and not in an Institute can be detrimental to progress and accountability. House ME/CFS in an Institute (NINDS), but ensure other related institutes are connected.
- Engage in communications efforts that reinforce the validity of the disease and increase awareness of ME/CFS among NIH researchers, scientists external to the field, clinicians, students, and the broader public; including, listing ME/CFS on the NINDS website, authoring blog posts on the impact of the disease Directors blog, placing impactful content in the Director's album, and amplifying the message on NIH social media channels

- Expedite the impact of the consortium approach adopted by NIH's creation of Collaborative Research Centers by marshaling the funds to aggressively expand the number of Centers. Although the three centers are advancing great work, high-quality proposals were left on the table; the centers are too few, too small and too narrow. NIH needs to fund more centers in more diverse domains (e.g. in autonomic nervous system dysfunction)
- Initiate an investigator-initiated research funding stream aimed at hypothesis generation to amplify existing community-driven and privately-funded seed funding mechanisms, like Solve M.E.'s Ramsay Award Program – with the aim to build a robust bench of researchers and pilot data that can be used to apply for R-01 level funding based on defined hypotheses
- Increase the amount of funding available for researchers wishing to better understand this disease

c. **Create a global, openly-available, centralized resource of well characterized ME/CFS patient, healthy control and disease control data and bio specimens.**
    - Provide directed funding opportunities to support the establishment of a global registry and biobank for ME/CFS that integrates data from existing, disparate sources (e.g. SolveCFS Biobank/You + ME registry, UK's ME/CFS Biobank at London School of Hygiene and Tropical Medicine, Simmaron Research, and other research groups)
    - Support methods for longitudinal data collection, including biosample collection at multiple time points and ongoing capture of symptoms and outcomes
    - Ensure house- and bed-bound people with ME/CFS are reflected in the global biobank and registry by requiring methods to complete at-home blood draws or facilitate travel to blood draw centers or clinics

d. **Establish rigorous, standardized research practices; including the application of case definitions, methodological approaches, utilization of data collection instruments, and expansion in replication and studies that interrogate or build on previous findings**
    - The lack of a consensus research case definition is a fundamental barrier to progress and quality research and replication. Until a consensus can be agreed upon, or a new research criteria is universally-adopted, NIH should issue guidance that researchers require the presence of post-exertional malaise (PEM) in determining a case of ME/CFS.
    - The field lacks the studies and instrumentation to back up a standard for disease severity.
    - Utilize open science framework mechanisms to increase transparency and share data (positive and negative findings) and methodologies to ensure researchers are building on and synergizing each other's findings.

- Package up the state of ME/CFS scientific knowledge and most promising areas research, best data collection practices, and optimal research methods (including how to define an ME/CFS case, the use of Common Data Elements and other validated or recommended questionnaires) into a NIH sanctioned toolkit for researchers new to the field. Update it yearly and make it readily available on the NIH website, making a concerted effort to publicize it to potential new researchers (analog from Solve ME's Ramsay Program here).

e. **Promote a massive increase in the number of researchers working on the disease; particularly, early-career stage investigators and skilled scientists from relevant scientific domains or related disease fields who can newly apply their expertise to ME/CFS**
    - Create NIH-sponsored career growth resources, mentorship opportunities, and retention mechanisms that encourage young researchers into the field and reinforces the field of study is a valid, viable career path.
    - Repeat the 2019 US-based "Thinking the Future" young investigators conference every year.
    - Make use of existing networks of researchers, for example Solve ME's Ramsay Award Program Investigators, as a vertical structure for mentorship and a resource for idea generation, proposal validation and career advice in the field of ME/CFS
    - Issue directed funding to support the development of tools for a ME/CFS researcher network that brings new actors into the field
    - Make a research toolkit that readily orients new researchers to the field and reduces the learning curve for best practices

f. **Redouble existing efforts and expand approaches to educate clinicians, encouraging better clinical care, partnerships in research, and a pipeline of study participants**
    - Support and expand the efforts of the Clinical Education Working Group (Bateman Horne)
    - Leverage opportunities to educate clinicians about the disease by making them aware of clinical research opportunities (e.g. at NIH, or in the creation of a disease registry/biobank)

g. **Increase opportunities for collaboration and tools for communication among scientists, clinicians, people living with ME/CFS, and other stakeholders**
    - Host a yearly conference on the NIH campus
    - Fund non-NIH sponsored conferences aimed at building an integrated network of researchers. There is an existing network of researchers funded through Solve ME's Ramsay Program, consisting of established ME/CFS researchers, young investigators, and scientists new to the field, that can be

capitalized on to build out a robust agenda for a conference that is generative and collaborative
- Open up research by establishing a central data sharing platform to allow researchers to share data (both positive and negative findings) and methodologies
- Establish an ME/CFS research communication channel (e.g. Slack) to allow for real-time communication between researchers
- Encourage young researchers to come into and stay in the field through mentorship programs with established ME/CFS researchers

h. **Ensure that people living with ME/CFS are more meaningfully incorporated into research discussions, acknowledged as experts in their own right, and elevated to the level of partner in research studies**
    - Provide opportunities for people living with ME/CFS to weigh in before decisions are made on priorities, strategy, study design and research approaches
    - Promote community-based participatory research approaches in ME/CFS