



DEPARTMENT OF HEALTH & HUMAN SERVICES

National Institutes of Health
National Institute of Neurological
Disorders and Stroke

NINDS

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June 25, 2018

Laurie Jones
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Dear Ms. Jones:

Thank you for your thoughtful and detailed letter to National Institutes of Health (NIH) Director Dr. Francis S. Collins concerning myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Dr. Collins requested that I respond to you on his behalf.

Your letter, with 7,253 signatures, outlined your goals for ME/CFS research. We at NIH understand the devastating effects of ME/CFS and the necessity of improving diagnostics and finding effective therapies as quickly as possible. The Trans-NIH ME/CFS Working Group is reviewing your suggestions and will continue to discuss next steps to attract more researchers to this field and expand research on this disease.

You requested a meeting with Dr. Collins. Please provide the name and contact information of a representative or representatives who would participate in the meeting, and we will forward that information to Dr. Collins for consideration.

Below are responses to the other specific requests in your letter.

1. RFAs: Provide substantial funding for multiple, multi-year RFAs for biomarkers, treatment trials, and validation and further refinement of the data collection instruments recommended as part of the Common Data Elements initiative. Such dedicated funding is needed to encourage researchers to enter the field and to rapidly address key issues that are impeding progress.

As you know, NIH has released and funded two RFAs for the ME/CFS Collaborative Research Centers (CRCs) and the Data Management and Coordinating Center (DMCC). These centers will help to build a strong foundation for expanding research on ME/CFS. The CRCs will each conduct independent research but will also collaborate on several projects, forming a network to advance knowledge on ME/CFS. We hope that the new centers and other NIH efforts will attract researchers from other areas to propose research on ME/CFS and increase the number of young investigators entering the field. We believe that the steps NIH has taken over the past two years will lead to a significant increase in high-quality grant applications in the future.

NIH has also funded seven supplements to existing awards focused on understanding the causes and mechanisms of ME/CFS. Awarded supplements will enable existing projects to expand the collection and analysis of ME/CFS patient samples to aid in biomarker identification and help identify potential therapeutic targets. More details about the awarded supplements are available at <https://www.nih.gov/mecfs/funding> under “Funded Projects.”

Finally, NIH has released several RFAs and Program Announcements (PAs) that apply to topics related to ME/CFS even though they are not specifically focused on that disease. A list of these funding announcements can be found on the NIH website at <https://www.nih.gov/mecfs/funding>. We will, of course, monitor the scientific direction of the research and respond appropriately to support impactful science.

2. Case definition: Create a collaborative initiative that leverages existing expertise to rapidly reach consensus on the research case definition and case ascertainment methods. Until this is completed, patient selection in NIH-funded research must use CCC and/or ICC-ME and must use the NIH CDE approved DSQ to assess symptom profiles.

The ME/CFS Common Data Elements (CDEs) have been completed by a consensus of clinicians, researchers, individuals with ME/CFS, and caregivers working together. The CDEs should be validated in clinical studies going forward, including the funded Consortium, and each study will clearly define the case definition that is used for case ascertainment. Most clinical studies now utilize the CCC and/or ICC-ME case definitions, and investigators will be encouraged to use the instruments identified through the CDE initiative.

3. Program announcements: Create additional ME-specific Program Announcements, supported by multiple NIH Institutes, for investigator-initiated studies.

Our long-term goal is to build a pipeline of researchers who are regularly submitting grant applications to NIH. Alas, currently the NIH receives far too few applications for ME/CFS research as compared to the burden of illness. In the short term, the Trans-NIH ME/CFS Working Group will continue to assess the needs of the community and issue new funding opportunities as needed. NIH will work in partnership with MEAction and other patient advocacy groups whose mission includes motivating and supporting new investigators to work on scientific questions that may advance our understanding of ME/CFS. We deeply appreciate the work of the patient advocacy groups in engaging new, as well as seasoned, scientists to stimulate research in all areas of ME/CFS.

Funding opportunities with relevance to ME/CFS research can be viewed at the following Trans-NIH ME/CFS Working Group website: <https://www.nih.gov/mecfs/funding>. In addition, scientists can learn about available NIH funding opportunities by searching the “NIH Guide to Grants and Contracts” at this site: <http://grants.nih.gov/grants/guide/index.html>.

4. Intramural study: Accelerate the ongoing intramural study by identifying and addressing all barriers to achieving rapid results and dissemination of findings, for instance by providing additional funding, staff, and physical resources that would allow multiple study participants to be seen at the Clinical Center at one time.

Although several hundred patients have inquired about the NIH Intramural study, only a minority met the stringent criteria for this highly focused study. We appreciate the work of ME/CFS advocacy organizations to improve recruitment and speed the completion of the study by identifying appropriate candidates and assisting those candidates with the application process.

5. Administrative supplements: Fully fund the existing Collaborative Research Centers (CRCs) and the Data Management and Coordinating Center (DMCC) for the next four years and increase Center funding by issuing an RFA for Administrative Supplements.

It is our intent to fund the existing CRCs at the levels approved by the Advisory Councils. As for all grants, this will be dependent on funds being available in the overall NIH budget. Administrative supplements for the CRCs may be considered in the future depending on the needs and opportunities presented by the Consortium.

6. New collaborative research centers: Issue a new RFA for U54 grants to fully fund at least three additional Collaborative Research Centers.

NIH's current focus is to work with the new CRCs and DMCC, helping them to establish their work, coordinate their activities with the Coordinating and Data Management Center, and initiate the collaborative project. Future funding opportunity announcements will be guided by the results and progress of the CRCs and the needs of the research community.

7. Strategic plan: Establish an initiative to create a cross-agency, fully-funded strategic research plan that lays out activities and coordination necessary to understand, diagnose, treat, and prevent ME. This plan should include efforts to delineate possible disease subtypes, as well as be informed by input from key stakeholders including, but not limited to, people with ME, ME disease experts, caregivers, researchers, ME organizations, organizations for common comorbidities (i.e., POTS, MCAS, EDS, fibromyalgia, SFN, etc.), and representatives from government agencies including NIH, CDC, and the FDA.

Several agencies at various levels of government are focusing on ME/CFS. The Trans-NIH ME/CFS Working Group meets monthly to discuss current NIH-funded research in the area and identify strategies to move the science forward. In addition, this group conducted a detailed portfolio analysis to obtain a comprehensive picture of the ME/CFS research being supported by NIH. This analysis is helping us identify gaps in research and establish research priorities as we move forward in our efforts to better understand ME/CFS and eventually develop a treatment for this disease. At this point in time, it is important to focus on ME/CFS and work with the community to strengthen our ability to fund

high-quality applications, attract researchers from other areas to propose research on ME/CFS, and bring young investigators into the field. The Trans-NIH ME/CFS Working Group closely tracks discoveries from research in the related conditions mentioned above for relevance to ME/CFS.

In addition, the Department of Health and Human Services (HHS) CFS Advisory Committee brings together many agencies from HHS to discuss progress in research and a range of topics that directly affect patients, such as educational needs of children with ME/CFS.

Finally, a new Working Group of the National Institute of Neurological Disorders and Stroke (NINDS) Advisory Council is being formed to make recommendations for improving collaboration and communication between research agencies and stakeholders, including individuals with ME/CFS and researchers.

8. Outreach & engagement: Formulate and enact an aggressive outreach plan designed to increase engagement of researchers, major academic centers, the pharmaceutical industry, and major medical societies. This includes sponsoring scientific conferences targeted at clinicians and at researchers studying ME and comorbid conditions, NIH staff presenting at many more scientific and medical conferences not specifically focused on ME, and NIH working on the development of private-public partnerships with pharmaceutical companies.

NIH has been actively engaged in outreach with the patient and research communities. NIH representatives have presented at many ME/CFS-related conferences and meetings, including the annual Sleep Conference in 2017. NIH also sponsored an ME/CFS session at the [FOCiS \(Federation of Clinical Immunology Societies\) Conference](#) in 2017 in an effort to bring scientists from other fields into the area of ME/CFS. The Trans-NIH ME/CFS Working Group will host “Accelerating Research on ME/CFS,” a research conference, on April 4-5, 2019 at NIH. NIH representatives will continue to identify opportunities to make presentations about NIH efforts to support and advance ME/CFS research.

In addition, the Working Group continues to host regular telebriefings with the community, providing updates from NIH and answering questions from callers. Recordings and transcripts of each telebriefing are posted on the Trans-NIH ME/CFS Working Group website at <https://www.nih.gov/mecfs/events>. The next telebriefing is planned for July. Watch the Events page of the Trans-NIH ME/CFS Working Group website for updates.

9. Data repository & biobank: Finalize a clearly articulated plan to establish and maintain NIH-funded centralized data and biospecimen repositories, which can store anonymized clinical and research data, including imaging data; and biospecimens collected from well-characterized patients in past, current, and future research studies. These repositories should be fully operational within two years and accessible by outside researchers. The repositories can be extensions of existing repositories that are storing ME/CFS data and biospecimens or built from scratch.

NIH is currently working with several resources, including the Collaborative Research Centers, international groups, and private organizations, to help increase the availability of ME/CFS biospecimens for research. We hope that researchers will take advantage of the recent Common Data Elements for ME/CFS Research to collect and analyze samples in a standard manner, thereby allowing for comparison between studies.

10. NINDS home & funding policy: Formally house NIH's ME/CFS program in the National Institute of Neurological Disorders and Stroke while also including ME/CFS in the strategic goals of the National Institute of Allergy and Infectious Diseases. Maintain the Trans-NIH working group to coordinate across all relevant institutes. Exclude all ME/CFS-related FOA's from any policy that limits funds or limits pay lines for grants to well-funded investigators.

Because the root cause and the driving pathology behind ME/CFS are unknown and the symptoms are so wide-ranging (including orthostatic tachycardia and hypotension, pain, immune system impairment, and neuroendocrine abnormalities), a trans-NIH approach that involves multiple Institutes is needed. The Trans-NIH ME/CFS Working Group includes representatives from many NIH Institutes, Centers, and Offices and provides a forum for coordination of ME/CFS research across NIH. It also facilitates discussion of scientific opportunities and gaps in the research that can be addressed by working together to further research on this disease. This is the best way to advance research in ME/CFS. We do not yet know where the answers will come from, so casting a wide net may help identify targets for future study.

Each Institute at NIH determines their funding pay lines and selection of grants for funding. It is a longstanding NIH-wide policy to specifically discuss at Advisory Council meetings any grants to investigators with over \$1 million in NIH funding. Advisory Council approval is required for any and all funding.

11. Clinical Care: To accomplish the NIH mission of doing research in this disease, the agency must tackle a problem that would ordinarily be outside its domain: the crisis in clinical care. So few physicians have expertise in ME that it is difficult for studies to enroll sufficient numbers of accurately diagnosed patients that reflect the diverse community affected by the disease. As research accelerates, this problem will become more acute. The NIH, in partnership with other federal agencies, must work with the medical community to address this as an urgent priority, before any more expert clinicians retire.

NIH recognizes the importance of effective clinical care for ME/CFS and impactful NIH-funded clinical and basic research usually occurs in the context of a robust clinical care program. In this regard the CRC sites are attached to centers of clinical care for ME/CFS. Improvements in physician education and medical practice are outside of the NIH mission, but the goal of NIH research is to inform medical practice through research findings. In addition, the HHS CFS Advisory Committee has a working group that is specifically looking for ways to improve physician education about ME/CFS and increase

dissemination of information to health care providers. For more information about this working group, please visit <https://www.hhs.gov/ash/advisory-committees/cfsac/index.html>.

As the CRCs and other research groups yield new insights about ME/CFS, clinicians will be able to use that information to improve diagnosis and treatment. NIH will work to distribute new study results as widely as possible in order to advance medical care for this disease.

NIH bases its funding decisions on a variety of factors, including the scientific quality of the proposed research, scientific opportunity, and disease burden. Funding decisions are also dependent on the amount of funding that NIH is appropriated each year by Congress. More funding alone does not solve the problems presented by a disease, and history has shown that research aimed at one target often ends up being relevant in other areas. Since it is impossible to know with certainty which area will produce the next important discovery for ME/CFS, it would be unwise to restrict research to specific topics. No one field has all the answers, but investigators in many different fields can ask questions that will provide more knowledge about disease and health. Advocacy organizations are critically important in encouraging scientists to bring real solutions to persons who suffer with ME/CFS and to grow a powerful cohort of new investigators to apply for ME/CFS grants.

Thank you again for your comprehensive letter. I hope that this information is helpful.

Sincerely yours,

A handwritten signature in blue ink that reads "Walter J. Koroshetz". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Walter J. Koroshetz, M.D. }

Director, National Institute of
Neurological Disorders and Stroke