Ramsay Award Program
Application Instructions and Scope

TUESDAY, MAY 1, 2018

Application Deadline: June 30, 2018

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I. Background

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a complex, multi-system disease that impacts as many as 2.5 million Americans, and an estimated 17-24 million people worldwide. ME/CFS lacks conclusive biomarkers or objective diagnostic tests. The National Academy of Medicine (NAM) (formerly called the Institute of Medicine) was commissioned by several federal agencies, including the NIH alongside AHRQ, CDC, FDA, SSA, and others to establish clear clinical diagnostic criteria for ME/CFS and evaluate the current state-of-the-science. In 2015, the NAM released its 300-page report sounding the alarm regarding the dearth of investment and investigations in ME/CFS, pointing to the severe gaps in knowledge when it comes to this debilitating disease. Notably, the report stated that the committee was “struck by the relative paucity of research on ME/CFS” and found that it “was unable to define subgroups of patients or even to clearly define the natural history of the disease.” They put forth a specific recommendation for further study “aimed at assessing the natural history of the disease and its temporal characteristics (onset, duration, severity, recovery, and functional deficits).” In a press release on October 29, 2015 NIH Director, Francis S. Collins, M.D., Ph.D., stated that “of the many mysterious human illnesses that science has yet to unravel, ME/CFS has proven to be one of the most challenging.” He went on to say, “I am hopeful that renewed research focus will lead us toward in identifying the cause of this perplexing and debilitating disease so that new prevention and treatment strategies can be developed.”

II. Scope of Solicited Research

This funding opportunity invites applications that address gaps in knowledge of energy system defects, biochemical processing of ATP-bound substrates, nutrient sensing mechanisms and pathways, neuroinflammation, endocrine biology, cellular and systemic immunity, host/pathogen interaction, gut/brain axis, microbiome research. Characteristics of ME/CFS like, Post Exertional Malaise (PEM), Orthostatic Intolerance (OI), sleep abnormalities, and environmental and biological risk factors are also encouraged. More specifically:

- **Bioenergetics-type projects** encompassing cellular and biophysical processes regulating energy production, the adaptation to metabolic and genotoxic stress conditions, mitochondrial dysfunction, aerobic and anaerobic bioenergetics, cellular signaling of substrate uptake, storage and processing (fat, glucose, amino acids and complex lipids), tissue oxygen delivery, REDOX biology, biochemical and free radicals toxicity, DNA damage response, reactive oxygen species (ROS), and other structures affecting ATP generation and utilization, including nutrient/gene interaction in the regulation of energy source acquisition transport, mobilization and expenditure are welcomed.

- **Neuroendocrine-focused investigations** addressing adrenergic and non-adrenergic pathways, the Hypothalamic-Pituitary-Adrenal axis (HPA), glucocorticoids regulation and signaling, catecholamines, energy ‘rheostats’ systems and energy balance like leptin, ghrelin, alongside regulatory components of nucleotides, metabolites, substrates and precursors synthesis directly associated with energy production (mitochondrial and otherwise), as well as enzymes regulating glucose and fatty acid oxidation, glycolysis, TCA cycle biology, nutrient shuttle and shunting mechanisms and the transcriptional regulation of cell metabolism, hormonal response, feed-forward and feed-back adaptive response and the role of regulatory complexes (transcriptional, enzymatic and otherwise) important for the regulation of homeostatic energy systems across multiple tissues and organs are solicited.
Immunity and Inflammation proposals addressing defined aspects of pathogen/host interaction, immune dysfunction, autoimmunity, immunotherapy and the pathologies of chronic inflammation in ME/CFS. The areas of immune surveillance and immune-senescence biology are also of interest.

In addition, gut microbiome research to identify and characterize microbes that contribute to ME/CFS, including via immunomodulation, pathogen resistance, maintenance of intestine structure/function and nutrition and host metabolism are encouraged. Investigations addressing hemodynamic changes (e.g., reduced blood volume in ME/CFS patients) and studies of organ system physiology nature particularly cardiovascular, cardiopulmonary, nephrology, exercise physiology, muscle contractility, neuromuscular and associated functions as well as the detoxifying roles of the kidney and immune surveillance are welcomed. A better understanding of signaling pathways, cross talk and integration between multiple organs functioning and organelles biology (e.g., ER, mitochondria) in ME/CFS using interdisciplinary studies will promote the knowledge of how cells sense and respond to genotoxic and environmental stresses or triggers. This will also identify system perturbation in the adaptive response to pathological insults that is likely deficient in ME/CFS. Furthermore, possible determinants of heterogeneity including endogenous and exogenous stressors such as toxic metals, pesticides and air pollution components as well as disease-associated genetic mutations (gain- or loss-of-functions), chromosomal deletions translocations, point mutations, polymorphism including Single Nucleotide Polymorphisms (SNPs) genetic variants, inherited traits and epidemiological studies that address the natural history of the disease using strong patients registries or large epidemiological studies are also invited. Studies that build on current knowledge in identifying biomarkers, innovative treatment modalities, and/or the modifiable risk and protective processes specifically targeted by preventive and/or treatment interventions are encouraged. Innovative platforms using modern investigative tools such as RNA interference, iPS, CRISPR, single-cell-analysis or large scale, high-throughput and deep-resolution profiling, identification and screening of metabolic, immune, genetic, pathogenic and phenotypic signatures in ME/CFS using imaging, NMR, mass spectrometry, calorimetric and other technologies are welcomed.

SMCI is interested in funding interdisciplinary research that will enhance our knowledge of the disease process and provide evidence-based solutions to improve the diagnosis, treatment, and quality of life of all persons with ME/CFS. Studies that will synergize, inform or complement existing national efforts at the NIH and the CDC (e.g., the intramural ME/CFS study at the National Institutes of Health and the multisite clinical assessment study at the CDC) are welcomed. Applications will be subject to a rigorous peer-review process and funding decisions will focus on applications most likely to make highly impactful contributions to ME/CFS research.

III. Award Information

Each grant award typically ranges between $35,000 and $55,000 for a one-year period, with the possibility of renewal for projects yielding promising results. Submitted proposals will be subject to a peer review process to ensure that only applications of the highest merit are selected.

Each grant application receives two independent reviews and proposals are ranked numerically on a defined scale based on the following:

- Relevance and significance of the work
- Quality and training of the investigators
• Innovation aspect of the proposal
• Feasibility and soundness of the approach(es)

IV. Application Preparation and Submission Details

Kindly email the full application, as one PDF, to research@solveCFS.org by June 30th, 2018. Include ALL of the following components with your application (please use Arial or similar sans-serif font, 11 pt. or higher):

Application Components

1- Cover Pages - includes signature page with assurances and certification, contact information of signing official, and general audience summary (form “Grant Application Signature Page” provided)

2- Structured Technical Abstract (1 page)

3- Budget and Justification (up to 2 pages)

4- Biographical Information of Applicant and Key Personnel (form “Biographical Sketch Template” provided)

5- Research Plan (up to 5 pages, excluding Facilities and References)
   A. Specific Aims
   B. Background and Significance
   C. Preliminary Studies (if available)
   D. Research Design and Methods
   E. Statement of ME/CFS Relevance
   F. Facilities
   G. References

Please include any applicable supporting documentation, such as subcontract documentation/consortium agreement or letters of collaboration, attached as an Appendix.

*SMCI will allow up to 10% institutional overhead for this Ramsay ‘18 application cycle*
V. Award Administration Information

Ramsay Award Application & Award Process Timeline

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<td>JUN</td>
<td>JUL</td>
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<tr>
<td>Application open</td>
<td>Application closed</td>
<td>Internal &amp; peer review</td>
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The Award notification is anticipated in October 2018. A Ramsay Award notice consists of the recommended funding level for the proposed project and the applicable award conditions, including the award policies and project reporting requirements. Applicants whose proposals are declined will be advised as promptly as possible.

VI. Organizational Contact

Questions and inquiries should be addressed to Allison Ramiller, Scientific Administrator, at research@solvecfs.org