NATIONAL ME/FM ACTION NETWORK

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Dr. Alain Beaudet
President
Canadian Institutes of Health Research

Dr. Jane Aubin
Chief Scientific Officer and Vice-President,
Research, Knowledge Translation and Ethics
Canadian Institutes of Health Research

Dear Dr. Beaudet and Dr Aubin,

Re: Research into ME/CFS and FM - US Developments

For several years, the National ME/FM Action Network has been asking CIHR to reconsider its approach to ME/CFS and FM research. The Network has

- asked that these diseases be taken much more seriously,
- asked that appropriate funding be made available, and
- suggested that a new institute be established.

While there has been a bit of movement, notably the designation of a fellowship, CIHR's overall response to date tells us that CIHR does not share our perspective on the seriousness of the diseases, the barriers in the funding process or even the scientific importance of the medical issues.

The ME/CFS patient community in the United States has been asking NIH to reconsider its approach. The US discussions have now moved to a new level. Government appointed committees and serious researchers are joining the discussions and are siding with patients. We would like to ensure that you are aware of these developments.

The US Chronic Fatigue Syndrome Advisory Committee (CFSAC) makes recommendations to the US Secretary of Health and Human Services (HHS). The committee met on August 18-19, 2015. At the meeting, CFSAC considered two recent reports on ME/CFS: the

Institute of Medicine (IOM)[1] and the Pathways to Prevention (P2P)[2] reports. The IOM report was commissioned directly by HHS and the P2P report was commissioned through the National Institutes of Health. In the background were two additional, recent reports on ME/CFS done through two other HHS agencies: the Agency for Healthcare Research and Quality (AHRQ)[3] and the Federal Drug Administration (FDA).[4] **The reports consider ME/CFS to be very serious. They identify lack of research as a roadblock to their being able to answer thoroughly the questions they were assigned and they call for more research.** See Appendix 1 for some quotes from those reports.

At the CFSAC meeting, a NIH official (Dr. Cheryl Kitt, Deputy Director of the Center for Scientific Review) suggested that **the reason for low NH funding was poor submissions**.[5] This comment raised the hackles of patients because the community knows that proposals for some very good research has been rejected. **This comment also raised hackles in the research community, including among some very prominent US researchers.**

Dr. Ron Davis, a member of the National Academy of Sciences and winner of the 2011 Gruber prize in Genetics, is one of the greatest scientists in the US today. He has developed many of the technologies used for modern diagnostic testing.[6] Dr. Davis was a

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[1] IOM (Institute of Medicine). 2015. *Beyond myalgic encephalomyelitis/chronic fatigue syndrome: Redefining an Illness.* Washington, DC: The National Academies Press. http://iom.nationalacademies.org/reports/2015/me-cfs.aspx

[2] National Institutes of Health, Pathways to Prevention Workshop: Advancing the Research on Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome , Executive Summary, December 9-10, 2014. https://prevention.nih.gov/programs-events/pathways-to-prevention/workshops/me-cfs/workshop-resources [Accessed September 5, 2015]

[3] Smith MEB, Nelson HD, Haney E, Pappas M, Daeges M, Wasson N, McDonagh M. Diagnosis and Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Evidence Report/Technology Assessment No. 219. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2012-00014-I.) AHRQ Publication No. 15-E001-EF. Rockville, MD: Agency for Healthcare Research and Quality; December 2014.. http://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-150505.pdf [Accessed September 5, 2015] Also published as two separate reports in the Annals of Internal Medicine in June 2015

[4] FDA (Food and Drug Administration). 2013. *The voice of the patient: Chronic fatigue syndrome and myalgic encephalomyelitis.* Bethesda, MD: Center for Drug Evaluation and Research (CDER), FDA. See Appendix 1 for a short extract on the need for research. A similar report was done on Fibromyalgia – FDA. 2014. *The voice of the patient: Fibromyalgia.* Bethesda, MD: Center for Drug Evaluation and Research (CDER), FDA. One of the themes of the Fibromyalgia report (p. 5) was the need, expressed by patients, to find the underlying cause.

[5] An extract from a transcript of her remarks follows: "We need many more people interested in the problem and applying for research dollars. As Vicky [NIH representative to CFSAC] said, we fund the best science. If applications come in… in fact ME/CFS is a very high priority for us. If there were meritorious applications to fund we would fund them. If Nancy were here she will tell you the challenge in peer review of these applications— I have to tell you they're all not that great. You wouldn't want us to fund those applications. We want to fund the best that will benefit you. And so that's the challenge for us. We get very few per year. Just throwing money out there will not get people to …sometimes they suddenly get interested, but they have to be poised and ready to go with a good idea and a good methodology to do it. It's not that we won't fund it, we would if there were applications there — and meritorious, that pass peer review..."

[6] gruber.yale.edu/genetics/2011/ronald-davis

member of the IOM ME/CFS panel and is the parent of a young adult with very severe ME/CFS. Dr. Davis has put together a medical team of prominent researchers and a medical advisory board that includes three Nobel Laureates[7] to study ME/CFS in a project they call "The End ME/CFS Project." They submitted proposals aimed at finding biomarkers for diagnosing ME/CFS using biochemical tests. Both their submissions were rejected at the pre-proposal stage. Following Dr. Kitt's comment, Dr. Davis released a short but powerful statement listing the reasons NIH gave for rejecting the proposals and his rebuttal to the rejections.[8] One reason for rejection was the lack of a hypothesis; Dr Davis responded that ME/CFS is in the observation stage which comes before the hypothesis stage. Another reason for rejection was that the proposal did not fit within the neurological institute's mandate; Dr Davis argued that it certainly did.

Dr. Ian Lipkin is a very respected scientist popularly known as 'the Virus hunter'[9]. He has, until very recently,[10] had his ME/CFS proposals rejected. Here is a quote from Dr. Lipkin:

> *"I have been in competition now twice to get funded, and the people there who reviewed me gave me abysmal scores. And the critiques of my work were unfair, and one of the people who critiqued my work said, in fact, that this is a psychosomatic illness. I was floored."* [11]

Just before the CFSAC meeting, a group of researchers released a letter stating that ME/CFS research was massively underfunded and **asking for designated funding** using a Request for Applications process[12]. A Canadian researcher was one of the signatories.

An issue that came up in this letter, in the statement prepared by Dr. Davis, at the CFSAC meeting[13] and in general discussions is the question of which institute of NIH is or should be responsible for ME/CFS. ME/CFS has been acknowledged as a multi-systemic acquired chronic condition with a hallmark symptom post-exertional malaise (also known as post-

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[7] Paul Berg (Chemistry) and Mario Capecchi and James Watson (Physiology or Medicine)

[8] http://www.meaction.net/wp-content/uploads/2015/08/ResponseToNIHRejectionsRonDavis.pdf

[9] Discover Interview: The World's most celebrated virus hunter, Ian Lipkin
http://discovermagazine.com/2012/apr/15-most-celebrated-virus-hunter-ian-lipkin
[accessed September 5, 2015]

[10] Award date - 14 August, 2015, Microbial discovery and immunity in ME/CFS
http://projectreporter.nih.gov/project_info_details.cfm?aid=9102389&icde=25862560

[11] http://www.cfscentral.com/2014/05/candid-conversation-with-dr-ian-lipkin.html
[accessed September 5, 2015]

[12] http://news.sciencemag.org/sites/default/files/ScientistLetterAugust179am.pdf [accessed September 5, 2015]

[13] Draft recommendation presented at the August 18, 2015 CFSAC meeting was: CFSAC recommends that the disease be assigned to the National Institute of Neurological Disorders and Stroke (NINDS) and supports the continuing role of the Trans-NIH ME/CFS Working Group but recommends that leadership be held jointly by the National Institute of Neurological Disorders and Stroke (NINDS) and by the National Institute of Allergy and Infectious Diseases (NIAID) (Slide 102)

exertion collapse, post-exertional neuroimmune exhaustion or systemic exertion intolerance). The NIH grants which have been awarded to study the biological underpinnings of ME/CFS have come from a wide range of Institutes including NINDS, NIAID, Office of the Director and the Institute of Nursing Research. Dr. Davis found his proposals in the middle of a ping-pong match between two institutes.

In a video, Dr. Davis[14] noted that his son scores normal on usual tests, but scored an astonishing 16 standard deviations from the mean on a special test. The implication is that ME/CFS is very different from commonly-considered diseases and that new approaches are needed. Dr. Davis describes ME/CFS as perhaps the last major unexplored area of medicine. He mentions that there are other diseases like it. While he doesn't mention FM, that is an obvious candidate. **He suggests the establishment of a new institute at NIH to look into this area.**

In summary, the issue of ME/CFS research is being actively discussed in the US, there is increasing recognition of the seriousness of the disease, and the pressure for change is growing.

Many of the issues raised in the discussions apply equally to Fibromyalgia as to ME/CFS. Although the IOM, P2P and AHRQ reports were commissioned to deal with ME/CFS, they did acknowledge the often co-existing condition of Fibromyalgia and its clinical overlaps with ME/CFS. There were several presentations at the P2P Workshop dealing with overlapping conditions and the need for research studies that take these conditions into account. The IOM report (footnote 1 pp. 145-147) discusses some of the issues related to distinguishing ME/CFS and FM while the AHRQ report (footnote 3 page ES-10 and 89) specifically highlights the need for diagnostic instruments that would enable the conditions to be clinically distinguished.

As always, the National ME/FM Action Network is prepared to work with CIHR to more research into ME/CFS and FM forward.

Yours truly,

MParlor

Margaret Parlor
President

CC. Dr. Hani El-Gabalawy,
Director, Institute of Musculoskeletal Health and Arthritis
Canadian Institutes of Health Research

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[14] Dr. Ron Davis The Scientific Process and how ME/CFS can get NIH funding, August 17, 2015 -- Youtube video from the Open Medicine Foundation https://www.youtube.com/watch?v=lHhJmpHCORw accessed September 5, 2015.

APPENDIX 1 presentation to CFSAC on need for research

Presentation to CFSAC by their P2P/IOM Working Group August 18 2015 [Note: page numbers from the reports added]

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EVERY RECENT FEDERALLY-SPONSORED REPORT HAS UNDERSCORED THE NEED FOR SUBSTANTIAL RESEARCH

IOM: "… the committee was struck by the relative paucity of research on ME/CFS conducted to date.... More research is essential." (p 9)
NIH P2P: "Overall, there has been a failure to implement what we already know for ME/CFS patients while the disease steals their health and well-being. Scientifically rigorous research is needed to improve this situation..."(p. 8)
AHRQ: "More definitive studies are needed to fill the many research gaps in diagnosing and treating ME/CFS…" (p. vii Structured abstract)
FDA: "A significant unmet medical need exists for patients with CFS and ME… Patients are desperate for research and development of treatments that can: (a) better relieve their most significant symptoms and (b) address the underlying cause(s) of their disease." (p. 5)

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PRIORITY: RESEARCH FUNDING & RESOURCES
NIH P2P: ME/CFS is "**an unmet public health need**" (p. 1) with "tremendous impact at the individual, family, and societal level." (p. 3)
IOM: "Remarkably little research funding has been made available to study the etiology, pathophysiology, and effective treatment of this disease, especially given the number of people afflicted (p. 9)… The disease causes "significant impairment and disability that have negative economic consequences at both the individual and the societal level.(p. 16) .. and there is an "**urgent need for more research**."

A substantial commitment of resources by HHS agencies is needed in order to enable scientists to reproduce important research, address identified gaps, accelerate progress, and better understand this disease.