

Peer Review

Review of: "A Proposed Mechanism for ME/CFS Invoking Macrophage Fc γ RI and Interferon Gamma"

Caroline Struthers¹

1. University of Oxford, United Kingdom

I am grateful to Qeios for asking me to review this article

I am primarily a patient advocate and have no clinical training or expertise in ME/CFS or any other condition. I have been interested in the evidence for treatments for ME/CFS, or rather the lack of evidence, for nearly ten years. I have a good understanding of the methodological limitations of previous treatment trials, and systematic reviews of those trials, particularly those into treatments such as Graded Exercise Therapy and CBT, which are based on a biopsychosocial understanding of the condition. By proposing potential triggering events and mechanisms for ME/CFS, the paper clearly exposes why the prevailing rehabilitative approach to the condition, particularly encouraging patients to undertake physical exercise, has no valid theoretical basis. It explains why activity could trigger non-specific immune signals that fuel macrophage-T cell interactions, which in turn trigger symptoms and make patients more unwell. I can't pretend I could fully grasp all the technicalities of the suggested mechanisms causing and driving ME/CFS, but the fact that this review lays out the evidence and reasoning behind the theory so fully and clearly is, I hope, an example to other researchers to follow a similar review framework to posit alternatives. The paper demonstrates a much-needed commitment to finding a plausible cause and mechanism for ME/CFS to focus trials of potential treatments more effectively, which I very much welcome. I was particularly encouraged by the last sentence of the conclusion, "Anecdotal evidence of improvement in ME/CFS following the use of relevant therapeutic agents for other co-incidental conditions might also provide useful motivation for specific clinical trials". This echoes the findings of a James Lind Priority Setting Partnership where ME patients were involved in setting a top ten list of research priorities. Second on the list was to answer the question "Which existing

drugs used to treat other conditions might be useful for treating ME/CFS?”
[<https://www.jla.nihr.ac.uk/priority-setting-partnerships/ME-CFS#tab-27556>].

The paper suggests several specific testable treatment approaches that follow on from the authors' mechanism theory and would provide hope in the short to medium term of finding a way to relieve symptoms and help people with ME do more, even if prevention or a cure is not yet on the horizon.

It might be useful for the authors to write a plain English summary of the paper in addition to the abstract to bring this important paper to the widest possible audience, including those who are not familiar with the finer details of immunology.

Declarations

Potential competing interests: No potential competing interests to declare.