Review of: "Candida and Long Covid"

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Potential competing interests: No potential competing interests to declare.

Dear Patrick Chambers,

Your manuscript, "Candida and Long Covid," provides a comprehensive exploration of the interplay between microbial disturbances, particularly Candida overgrowth, and a variety of chronic and autoimmune diseases exacerbated by Covid-19. The hypothesis linking the gut microbiome, specifically Candida-related mechanisms, to long Covid and other autoimmune diseases is intriguing and opens up potential new avenues for understanding and treating these conditions. Here are some suggestions and comments aimed at enhancing the clarity and impact of your work:

Clarification of Mechanisms:
Section "Hypothetical Model": You propose that Candida overgrowth contributes to autoimmunity through the activation of zonulin. While the link between zonulin and increased permeability is well-established, the transition from Candida overgrowth to specific autoimmune conditions could be better detailed. How does this mechanism specifically differentiate or lead to the diseases mentioned (e.g., celiac vs. Crohn's disease)? Adding more direct evidence or proposing specific experiments could strengthen this hypothesis.
Strengthening Evidence:
Figure 1 and 2: These figures illustrate crucial aspects of your hypothesis but would benefit from updated data or a meta-analysis that directly links changes in Candida abundance with autoimmune disease rates over time.
References to experimental data: Some claims, such as the role of Candida in cognitive diseases (e.g., dementia), are quite strong. It would be beneficial to cite more direct studies or clinical trials that have observed these effects, rather than relying predominantly on associative studies.
Methodological Enhancements:
Experimental Design: Consider suggesting specific microbial or immunological markers that could be experimentally validated in clinical settings to test your hypothesis. For example, longitudinal studies tracking zonulin levels in Covid-19 patients could be insightful.
Discussion of Gender Disparities:
You mention gender disparities in autoimmune responses but do not fully integrate this discussion into your overall hypothesis. Could hormonal differences influence zonulin levels or Candida's pathogenicity? Addressing this could enrich the discussion and make the study more comprehensive.
Broader Implications and Preventative Strategies:
While the manuscript excellently outlines potential pathogenic mechanisms, it could also benefit from a section discussing

potential preventative measures or treatments based on your findings. For example, could dietary changes or specific probiotic strains reduce the risk of Candida-related complications in long Covid?

Language and Structure:

The manuscript occasionally uses highly technical language which, while precise, could be simplified for broader accessibility. Furthermore, some sections are quite dense; breaking them into sub-sections with clear subheadings might help maintain reader engagement.

Citing Sources:

Ensure all figures, hypotheses, and cited mechanisms are backed by the most recent and robust scientific evidence. This not only strengthens your argument but also aligns with academic standards of evidence-based discussion.

In conclusion, your manuscript provides a valuable contribution to the ongoing discussion about the long-term impacts of Covid-19 on human health, particularly through the lens of autoimmune diseases and the microbiome. With some additional data, clearer mechanistic descriptions, and more direct evidence, it could potentially make a significant impact on the field. Thank you for the opportunity to review this intriguing work.

Best regards, Julio Alberto Díaz Ramos