Review of: "Candida and Long Covid"

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Potential competing interests: No potential competing interests to declare.

Very interesting manuscript.

I attach brief comments as follows:

Abstract:

1. Please define what you mean by long haulers. Do you mean those having long COVID or PASC? Also there is one other missing there alongside ME/CFS
2. Can you provide specific examples or studies that support the need for defining 'long haulers' and 'IDO' as you suggested in the abstract?
3. Define IDO at first mention in abstract and ATM, also IFN is type II IFN-γ a common assay of T cell function.
4. Please spell out GPCR as G protein coupled receptor at first mention.
5. The bottom part of abstract please restructure or reduce slightly as abstracts should be 250-350 words, maybe some could go in introduction or similarly a brief overall statement that Candida has species and may affect the adaptive immune cell response through type II IFN-γ upregulation in concert with IDO and zonulin.
6. The phrase type II IFN-γ as a marker for LC requires re-defining as it is a T cell assay scale used in conjunction with cluster of differentiation proteins to define immune cell phenotypes and re wording., isn't there a type I IFN involved as well? (4) (PDF) Dr Jekyll and Mr Hyde: From Two Branches of Immune Response to Three Types of Interferon Response (researchgate.net) https://doi.org/10.1038/ncomms2343
7. Vaccines | Free Full-Text | Innate and Adaptive Immunity during SARS-CoV-2 Infection: Biomolecular Cellular Markers and Mechanisms (mdpi.com)

Introduction:

Some more text above the graph to outline the diversity and errors that can occur in either autoimmune diseases or immunodeficiency would balance the article better or introduce the ICD-10 classification systems. Maybe a theory about the incomplete data on asthma on the graph? There are two types - eosinophil and neutrophilic asthmatics or more.

https://doi.org/10.1016/j.jaci.2022.05.023

The “Autoimmune Registry” is missing a citation at end of sentence

Hypothetical Model:

Please number section 2 as section 1.

In point 7 you mention binding to TLR4, would this not potentially apply to many other bacterial infections as well though stimulation of it?

Regarding the hypothetical model, could you elaborate on how binding to TLR4 might affect other bacterial infections, providing comparative analysis or references?

Figure MCP-II - do you mean mast cell protease MCP II homology? Also, could this be considered together with a hypothesis on the actions of anti-histamines during SARS-CoV-2 infection?

Section 2:

Section A, autoimmune disease, please abbreviate to AI throughout after first mention.

Interesting you mention IgA antibodies as we have a few hypotheses there.

Section B on dementia:

IL-17 has many forms, perhaps specify which here? IL-17A is the better researched.

Again - is IFN gamma a marker of LC?

Section 6:

You delve into IFN gamma and tryptophan. There is further detail on this that goes some way to justifying the hypothesis. IDO1/2 forms were also differential and can affect macrophage differentiation pathways.

Overall comments.

Very interesting read and CXCR3 autoantibodies. CXCR3 is a predominant receptor for its ligands CXCL9/10/11 on many immune cells, I think.

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