Review of: "The α7 Nicotinic Acetylcholine Receptor: a Key Molecule in Post-COVID Syndrome?"

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Potential competing interests: No potential competing interests to declare.

Global evaluation:

Interesting data are brought to our attention, but it is rather weird to read comments and interpretations on data that no one has seen, in this “pre-review paper” of unpublished data compared and interpreted with published others. Consequently, the implicit conclusion is that the author should wait for the submitted manuscripts with the experiments and results being argued here to be published, before making and submitting this manuscript as a good “review” on the subject.

Detailed comments and suggestions on the text:

- *suggests the ways of treatment;* better :“therapeutic avenues”.

- *COVID-19 neuropathology was shown to include Alzheimer-like features*; “features” is too vague, please specify (symptoms, neuropathology, ALZ-like memory impairment, but in which model? Not in humans of course. How relevant? Why this need to link ALZ disease here ?

-*more prone to developing Alzheimer disease and Alzheimer patients could be more susceptible to severe COVID-19* assertion presuming certainty, which is far from being the case. The cited paper is much more cautious and uses the conditional tense and a question mark in the subheading on AD after COVID-19.

- *in long COVID, and is associated with cognitive impairment (Cysique et al., 2022)* the cited paper is a non-peer reviewed pre-print. Being so affirmative is not appropriate and may reveal not to be confirmed. So, “may be” or “is suggested to be” would be better than “is”.

- *the data provided above clearly indicates*; why not “the published and previously cited data suggests that…..” ?

-repeatedly mentioned “*In our experiments*”; where are they presented? Have they been published? They should not be evoked like this without showing the complete studies with these experiments or without citing a peer-reviewed publication.

- *We have found that ACE-2 expressed in astrocytoma U373 cells interacts with α7*

nAChR because their complex was identified in U373 cell lysates by Sandwich ELISA (Lykhmus et al., submitted) if not published, should be provided to the reviewers of the present manuscript, otherwise the reasoning and the arguments

cannot be evaluated for its review. Alternatively, it may be posted on MedRxiv or BioRxiv, and be commented with more precaution in the terms to be used.

- *Therefore, affecting α7 nAChR can interfere with (prevent) virus penetration into the cell. However, this idea needs experimental confirmation*; if needing experimental confirmation, it “may” interfere…

- *appeared to be very efficient in treating patients with severe COVID*; no, please read carefully the case reports of the cited publication: it improved certain symptoms and prevented further issues in the presented cases and calls for further clinical evaluation. Like the rest of the text, too many interesting but uncertain notions are presented as definite and beyond their scope.

- *agonist/allosteric modulator can be beneficial for treatment of COVID patients. However,*

the situation with post-COVID syndrome (PASC) is not so clear, why “can be beneficial” when the disease pathogenesis itself is “not (so) clear” ?

- *is hardly to be explained by continuous virus persistence in the organism*; it was shown to be the case, at least in a subgroup of patients e.g., read “Natarajan, A. et al. 2022. Gastrointestinal symptoms and fecal shedding of SARS-CoV-2 RNA suggest prolonged gastrointestinal infection. Med 3:371-387 e379”. Long COVID rather represents heterogeneous groups of patients.

- *Analysis of these immunoglobulins demonstrated that they contain SARS(674-685)-specific antibodies (both IgM and IgG), as well as α7(179-190)-specific antibodies (mainly IgM) (Lykhmus et al., 2022 and submitted)*; This is very important if reliably supported by a dedicated study. But why comment on results before they have been properly published?