

SARS-CoV-2-linoleic acid interaction

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I would like to congratulate the Authors of this very elegant and nice article, reporting the interaction dynamics occurring between the host cell receptor binding domain (RBD) within SARS-CoV-2 spike (S) protein and linoleic acid (LA) (1). Alongside the highly intriguing "dimension" of the article, the aforementioned viral-host interaction, resulting in a lower "affinity" of SARS-CoV-2 towards the ACE2 cell receptor (1), could have relevant implications for the therapy of severe CoViD-19 forms, thereby widening the spectrum and/or potentiating the activity of the currently available antiviral drugs (i.e. remdesivir, as reported by the Authors), as well as of those "counteracting" the remarkable (and often systemic) health effects caused by SARS-CoV-2 on infected patients.

As far as the latter drugs' "category" is specifically concerned, the work nicely carried out by the Authors provides large biological plausibility, in my opinion, to the favorable responses/outcomes which are frequently observed when corticosteroids (dexamethasone) are employed for the therapy of severe CoViD-19 disease phenotypes. It is well known, in fact, that corticosteroids - both natural and synthetic - act through selective inhibition of phospholipase-A2 enzyme, converting LA into linolenic acid, a critical reaction in the biosynthetic pathway leading to prostaglandins and leukotrienes, two groups of key mediators of acute inflammation and of its related modifications/signs, including fever, pain, and discomfort (2).

In conclusion, while this beautiful paper (1) may well contribute to explain why corticosteroid administration to patients with severe CoViD-19 often results in a substantial improvement of their clinical condition, it would be also desirable that more experimental work is carried out in this direction, thereby taking advantage from a number of SARS-CoV-2-susceptible animal models (3) with special emphasis on those sharing the highest levels of ACE-2 receptor homology/similarity with the human one.

References

- 1) Toelzer, C., et al. (2020) - Free fatty acid binding pocket in the locked structure of SARS-CoV-2 spike protein. *Science* (21 September 2020: eabd3255).
- 2) Robbins Pathologic Basis of Disease, 6th Edition (1999) - Inflammation (3rd Chapter).
- 3) Di Guardo G. (2020) - Animal models and pathogenetic insights to CoViD-19. *Journal of Comparative Pathology* 179 (Pathology Matters).