Review of: "In Silico Investigation of Potential COVID-19-Associated MicroRNA Signatures"

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Potential competing interests: No potential competing interests to declare.

The manuscript uses bioinformatics tools to analyze the role of microRNAs in SARS-CoV-2 infection.
The analysis is interesting but very "basic" and limited to the miRNA target which is certainly important, but it is not the host targets that determine the susceptibility/resistance to infection.

Below are my specific comments:
1. It is now widely demonstrated that rare variants in genes associated with congenital defects of immunity are the main genetic determinants of the disease with ORs sometimes exceeding 50! (see and quote: PMID: 32972995; PMID: 35090163 ; PMID: 36538032; PMID: 37020259).
2. In the introduction they should include a paragraph on miRNA expression studies in COVID-19 that are not limited to plasma but also in other tissues (see and quote PMID: 36073344);
3. At the beginning of the results the authors report 149 COVID-19-relevant genes. I tried to repeat the same search on GeneCards and found 471 with scores >9. I therefore ask for further details on the search and selection of these genes and to also indicate in the supplementary table (S1) the score of each individual gene, an accession number or ID. Also list them by score and not in alphabetical order. The aim of the work is in fact to identify genes relevant to COVID on which to then identify regulatory miRNAs;
4. It is not clear to me how the authors analyzed: “the differential expression profiles of several COVID19-related top-25 genes (Table S1) between SARS-CoV-2-infected patients and healthy controls were further investigated through the “differential expression ” module of COVID19db (Zhang et al., 2022). Among those, the cytokines IL10, IL18 and CXC10 are up-regulated in the COVID-19 group (Figure 4), consistent with their pro-inflammatory effects (Callahan et al., 2021; Dinarello, 2000; Lauw et al., 2000)”. What does “differential expression” mean? In theory they should have described the method in section 2.6. Independent Validation, but there is nothing.
5. In figure 3 the authors report the 24 top-ranking genes…..but weren't there 25??????? (see Table S1). Furthermore, however, I did not understand by what criteria these top-genes are defined;
6. Please report the results of figure 3 first and then those of figure 4 and not vice versa.