LETTER TO THE EDITOR



Response to Ribeiro da Silva et al, "Role of nonstructural proteins in the pathogenesis of SARS-CoV-2"

Dear Editor,

We are writing regarding the Letter entitled "Role of nonstructural proteins in the pathogenesis of SARSCoV-2" from Ribeiro da Silva et al, published in the *Journal of Medical Virology*.¹ We welcome the discussion on published article, which could improve the science and clarify any controversial issues.

We would like to thank you the authors for recognizing the significant value of our manuscript. The preliminary results we have shown in our manuscript pointed out that the genome of SARS-CoV-2 has so far undergone few mutations, which are not going to influence the general molecular structure of this novel virus, confirming the low variability of SARS-CoV-2 during the evaluated time.² Despite it will be difficult to prove the biological relevance of these mutations by pure bioinformatic approach, in the absence of any experimental study, we would feel that the authors would agree that the analysis of full-length genomes during outbreak it is useful and could help in the identification of specific mutation that could be related (or not) to any possible differential clinical outcomes.³ Despite the only use of bioinformatics-based analysis, which is unlike to explain the pathogenetic process underling the SARS-CoV-2 infection, we have been proposing hypotheses based on objective data analysis in our study. Whether the hypothesis is correct would require further experimental validation. No doubt, that the hypothesis may be wrong or maybe right and very likely experiments will be able to prove or disprove them. As the letter's authors says, experiments may be complex and time consuming while there is no a-priori guarantee that they will definitively clarify the phenomenon under study. The role of rigorous and state-of-the-art theoretical analyses, by means of bioinformatics and molecular epidemiology approaches, is to support rational design of experiments and help the interpretation of the results in the hope to speed up the process of knowledge acquisition.⁴ We do hope that the letter's authors will undertake all the experiments necessary to decipher the biology and pathogenesis of this dreadful virus also taking into account our hypotheses.

Collaborations among groups with different expertise are necessary to fight and win the battle against emerging pathogens. Massimo Ciccozzi¹ D Domenico Benvenuto¹ Marta Giovanetti^{2,3} Martina Bianchi⁴ Stefano Pascarella⁴ Silvia Angeletti⁵

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