Dear editor

I attach to this letter my article entitled "Understanding the SARS-CoV-2-human liver interactome using a comprehensive analysis of the individual virus-host interactions ", which I ask you to submit for examination by the Livers referees. The article discusses the picture of infection at the level of cellular processes of the liver in COVID-19 patients. I describe the complete picture of the affected part of the human proteome and the viral proteins involved using an interatomic approach supported by a reverse engineering filtering process.

Let me explain. For several years, BioGRID has been collecting and curating all the one-to-one experimental interactions that the 31 proteins of the SARS-CoV-2 genome implement on the human proteome. Today we have a wealth of over 30,000 experimental interactions available online. Their characteristic is that, proven through experimentation, they represent a unique wealth of knowledge of the virus biology. I collected all their files and organized a database through which you can query to find out whether any human protein might be involved in an interaction with a viral protein. This information is unique because it assumes that researchers can check any observation by considering the biological data present on BioGRID. They allow us to tell what happens during the infection. Obviously, besides being experimental, the data also have their own precise statistical classification regarding their reliability. The next step was to collect experimental information from the literature on the genes/proteins profiled as Hubs during the disease. I employed them as functional seeds to generate an interactome that is abundant in hepatic biochemical functionality. I applied control filtering (functional and experimental) to the collected data using the database. I performed numerical reduction on them and used the resulting data to calculate an interactome model using STRING and Cytoscape. His analysis revealed many surprises and showed that many hubs were not genuine hubs. I directed my attention to the large targets of the viral strategy (ribosomes). Since the breadth of results includes very different biochemical processes and molecular mechanisms, the system presents intrinsic heterogeneities that make it perplexing. One oddity was the discovery that many viral proteins (up to 20) attacked several single human proteins. I could disentangle this data using a biphasic power-law kinetic analysis that characterizes scale-free networks. This approach, which proved to be very current, allowed me to understand how to explain the distribution pattern of the many human proteins affected by the many viral proteins. In this model, I have made hypotheses I consider reliable to explain the general behavior of the proteins of the human proteome involved in the disease, at least for the liver. I also hypothesized a multiorgan viral strategy.

As my approach leans towards computational biochemistry rather than clinical, I have taken the liberty of including a list of referees. I've included all the database information in three Excel files and added the raw data management procedure in the Supplements. The article comes with an appendix, which is necessary so that the less experienced reader understands biological networks are informational objects that require certified significant experimental data. I have in fact highlighted in the article, where necessary, how the lack of knowledge of where, how and when viral and human proteins interact, makes many results present in the literature difficult to interpret at the very least. The evaluation process for scientific journals is becoming more challenging because of the multidisciplinary aspects of submission.

I confirm that neither the manuscript nor any parts of its content are currently under consideration or published in another journal.

I hope Livers' readers can read and consider this my article.

Regards

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