Quantitative plasma proteome profiling of COVID-19 patients with mild and moderate symptoms

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The COVID-19 pandemic has caused more than 5 million of deaths around the world in less than two years, and it is still unfolding (https://coronavirus.jhu.edu/map.html). Because of the high complexity of COVID-19 pathogenesis, it is of great interest to understand the host responses to SARS-CoV-2 infection at protein level. These responses include two layers, one of which is the immune responses to viral proteins, especially the antibody responses. Another is the change of the human protein level upon SARS-CoV-2 infection.

To profile the antibody responses, a serial of studies has been carried out. For example, Tao *et al.*, developed a SARS-CoV-2 proteome microarray and a peptide microarray that fully covers the Spike protein.[1–3] Based on these arrays, ~2,000 COVID-19 sera of varied severity were analyzed. Bead-based systems were also applied to determine the SARS-CoV-2 specific antibody responses.[4] Alternatively, Yu *et al.*, developed a peptide microarray that fully covers all the SARS-CoV-2 proteins and allows us to construct an overall picture of epitopes for SARS-CoV-2 antibodies COVID-19 infection.[5]

To monitor the SARS-CoV-2 specific human protein change, several proteomics bases studies have been performed. Guo *et al.*,[6] accomplished a proteomic analysis of 144 autopsy samples from seven organs in 19 COVID-19 patients. In comparison to the controls, they found that more than 5,000 proteins were altered in the COVID-19 patients. By applying O-link technology, Filbin *et al.*, (from the same group of this study) have analyzed COVID-19 samples of severe symptoms.[7]

In this paper of EBioMedicine, Zhong *et al* capitalized on the O-link technology and quantitatively analyzed the plasma protein profile (~1,500 proteins) of 50 COVID-19 patients with mild and moderate symptoms.[8] They found the levels of 200 proteins were significantly higher when diagnosed than that of 14 days after diagnosis, and many of these proteins are related to cytokines and immune responses.

In this study, Zhong *et al.*, have made interesting findings. Some are consistent to previous studies while some are new. A few of these findings are worth further exploration. Firstly, upon SARS-CoV-2 infection, the levels of many proteins are increased, while there is no statistical difference among patients of mild, moderate and severe symptoms. This indicate profiles of these proteins are independent of symptoms, which have potential to be used as biomarkers for the diagnosis of COVID-19. Secondly, the authors identified the protein scavenger receptor class B member 2 (SCARB2) as the most significantly elevated protein upon infection. After comprehensive validation, the connection between SCARB2 and COVID-19 may warrant further in-depth functional exploration to reveal the underlying mechanistic role. Thirdly, authors found that many of the older patients, although free of symptom, have a plasma profile similar to that of patients with the active infection even after 14 days of diagnosis. It is well known that COVID-19 is more dangerous to old people. Thus this observation is worth of further study. It is known that old COVID-19 patients usually have high SARS-CoV-2 specific antibody level.[2] So, is it possible that there are some correlations between high protein level and the high antibody level?

The key platform used in this study is the O-link technology. The beauty of O-link resides in its power of quantitative and simultaneous analysis of many proteins, that even of low abundance. However, it has limitations. First, the number of proteins that could be analyzed is still far fewer than mass spectrometry. However, these two technologies could be complementary to each other. Another limitation is the difficulty for pairing of antibodies for each target protein. This could be overcome by a highly efficient epitope mapping technology.[9]

The study has its merit that ~1,500 proteins were quantitatively analyzed. However, the findings lack further independent validation. To strengthen these findings, it is anticipated that some validations will be carried out use an independent assay with an independent cohort of samples. The protein profiles were nicely compared between the two time points. If more longitudinal samples could be analyzed, we could then obtain a more detailed picture of the changes of the protein levels over time. Finally, to combat the COVID-19 pandemic in a more efficient way, it is urgent to generate a comprehensive knowledge map by integrating varies of proteomics data, including the data of this study, from both antibody level and protein level.[10]

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Declaration of interest

No disclosure relevant to this topic.

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