Time-resolved plasma proteomics predicts survival outcome of COVID-19 patients during hospitalization

Mauricio Quinones-Vega[1,2,3], Patricia Sosa-Acosta[1,2,3], Giovanna Câmara Giudicelli[4], Mariléa Furtado Feira[4], Nathan Araujo Cadore[4], Renan Cesar Sbruzzi[4], Fernanda Sales Luiz Vianna[4,5], Fábio C.S. Nogueira[1,2,3], Gilberto B. Domont[1,3]

[1.] IQ-UFRJ, Institute of Chemistry, Universidade Federal do Rio de Janeiro, Avenida Athos da Silveira Ramos, nº 149, Bloco A – 7º andar Centro de Tecnologia – Cidade Universitária – Rio de Janeiro – RJ, Rio de Janeiro - RJ, 21941-909;
[2.] LADETEC, Laboratory of Proteomics (LabProt), Laboratório de Apoio ao Desenvolvimento Tecnológico - UFRJ, Avenida Horácio Macedo, Polo de Química, bloco C, 1281 - Cidade Universitária, Rio de Janeiro - RJ, 21941-598;
[3.] CPMP, Centro de Pesquisa em Medicina de Precisão, esquina com Ilha do Fundão - Avenida Carlos Chagas Filho, Rua Maria Dolores Lins de Andrade - Cidade Universitária, Rio de Janeiro - RJ, 21941-902;
[4.] CPE-HCPA, Centro de Pesquisa Experimental, Hospital de Clínicas de Porto Alegre, Santa Cecília, Porto Alegre - State of Rio Grande do Sul, 90450-190;
[5.] UFRGS, Universidade Federal do Rio Grande do Sul, Farroupilha, Porto Alegre - Río Grande del Sur, 90010-150;

The need to understand the progression of COVID-19 and SARS-CoV-2 infection is essential to identifying potential biomarkers and therapeutic targets. Monitoring the progression of the disease is essential to predict the prognosis of patients from the initial times of hospitalization. The goals of this study are to comprehend the trajectory of the disease by characterizing changes in the plasma proteome over time and propose putative biomarkers proteins that can differentiate between non-survivor and survivor phenotypes. During hospital admission, plasma samples were collected weekly from 44 unvaccinated patients over a six-week period from Hospital de Clinicas de Porto Alegre Biobank (total = 198). Plasma was processed using S-TrapTM digestion protocol and acquired in 90 min gradient using a Vanquish™ Neo UHPLC System coupled to an Orbitrap Exploris™ 480 Mass Spectrometer. Proteins were identified using DIA-NN software. Proteomics analysis identified a total of 1600 proteins, of which 851 were selected for quantitative analysis. It was observed that the acute phase response and the inflammatory reaction was dysregulated over time returning to normal levels by the sixth week. Other processes such as antigen binding, endocytosis, and vesicle-mediated transport increased during hospital admission related to the first week. In the global correlation map was observed clusters associated with cytokine stimulation, insulin-like growth factor II binding, complement cascade and acute-phase response. Furthermore, the comparison between patients who survived and those who died revealed differentially abundant proteins even in the first weeks of hospitalization. In non-survivor patients were found more abundant proteins related to complement activation and the innate immune response, while the humoral response and antibody-related annotations decreased in these patients, especially in the first three weeks. From the fourth week onwards, patients who died related to survivors present increased acute inflammatory response, accompanied by a reversal of previously diminished processes, such as leukocyte chemotaxis and complement activation. To identify potential biomarkers that could predict survivor or non-survivor phenotypes a linear SVM model was trained with proteins with different statistical significance HPR, PF4, LPA, IGFALS, COLEC11 resulting in a ROC curve with AUC 0.916. In addition, the model correctly classifies 85% of the patients. This study provides insights into the pathophysiology and progression of COVID-19 and highlights proteomics as a powerful tool for understanding the host response during viral infection as well as correlating and validating the clinical information

Agradecimentos: This research is supported by Brazilian CNPq 404140/2020-3 (G.B.D.), CNPq

315167/2020-3 (F.C.S.N), 404134/2020-3 (M.Z), FAPERJ E-26/210.173/2018 (G.B.D.), FAPERJ E-26/201.249/2022 (F.C.S.N.). M.Q.V. and P.S.A. thank FAPERJ E-26/201.604/2021 and FAPERJ E-26/202.309/2022 for their Ph.D. scholarships. We thank all individuals in the cohort and the multidisciplinary team involved. The funders had no role in study design, data collection and analysis, publication decisions, or manuscript preparation