Essential proteins in the immune response against viral pathogens are present in vaccinated patients infected with the Ômicron variant

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Introduction: Since its emergence on December 30, 2019, in Wuhan, China, COVID-19 has recorded 775 million cases and 7 million deaths, approximately. Besides the vaccination campaign's significant drop in new registrations, the SARS-CoV-2 virus still represents a challenge to health systems. In Brazil, in the year 2024, 560 thousand cases and 3,012 deaths were confirmed; in addition, the so-called long-COVID -19 affect the health and quality of life of millions of people. Because of its molecular nature and lack of an efficient repair mechanism, the SARS-CoV-2 virus has a high rate of mutations, which can establish themselves in circulating lineages and result in variants of concern (VOCs). Some examples of VOCs are: Alpha or B.1.1.7; Beta or B.1.351; Gamma or P.1.; Delta or B.1.617.2 and Ômicron or B.1.1.529 and subvariant X.B.B.1.5 (kraken). Therefore, it is essential to understand the mechanisms associated with viral replication processes and the host\'s immune response to SARS-CoV-2 infection. Thus, this study aimed to characterize the proteomic profile in nasal swabs from patients infected by the Ômicron variant and analyze the possible mechanisms involved in this viral infection. **Methods:** This study was approved by the Human Research Ethics Committee (CEP) with CAAE number 37311020.0.0000.0005. We selected 20 patients, infected by the Ômicron variant, with an average age of 45 years, divided into four groups: **Group 1-** Vaccinated symptomatic without comorbidities, **Group 2-** Vaccinated symptomatic with comorbidities, **Group 3-** Vaccinated asymptomatic without comorbidities; **Group 4-** Vaccinated asymptomatic with comorbidities. Nasopharyngeal swab samples had their protein content extracted and digested with trypsin. Then, the peptide mixture was subjected to reversed-phase chromatography/tandem mass spectrometry using the Fusion Lumos Orbitrap mass spectrometer (Thermo Fisher®). The analysis of shotgun data was performed with the PatternLab software for V and Diagnomass 2.1. The Metascape pathway database was subsequently used to identify molecular processes important for the manifestation of COVID-19. **Results:** A total of 1929 proteins were identified for the groups studied. When compared the Group1 *versus* Group 2, we identified 239 proteins shared between them; Group 3 *versus* Group 4, 267 proteins shared; Group 3 *versus* Group 1, 250; Group 4 *versus* Group 2, 257. This number of shared proteins indicates the similarity of molecular processes among the groups. In a more detailed, we found 8 significantly abundant proteins in Group 2 and 15 in the Group 4. Of these, we highlight the

Guanylate-binding protein 1, essential for protective immunity against microbial and viral pathogens; and the Interferon-induced GTP-binding protein Mx1, which perform antiviral activity against a wide range of RNA viruses and some DNA viruses; in addition to of acting in the process of cell death mediated by stress. Additionally, the enrichment analysis between these groups revealed action pathways especially related to the processes of response to chemical stress, platelet degranulation, neutrophil degranulation, cellular detoxification and glycolysis/gluconeogenesis. **Conclusion:** We characterized the protein profile of patients infected by the Ômicron variant, where the proteins presented are involved in the immune response and cellular stress. These data can contribute to understanding the response of vaccinated patients infected with SARS-CoV-2 variants.

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