Correlation of Matrix Metalloproteinase-3 and the Sphingolipid Metabolism in Patients with COVID-19.

Thiago Vinicius Defelippo Felippe[1], Pedro Nobre Azevedo[1,2], Diana Mota Toro[3], Adriana Ferreira Lopes Vilela[1], Carlos Arterio Sorgi[1,2,3]

[1.] FFCLRP-USP, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Avenidada Bandeirantes, 1500, Ribeirão Preto, SP;
[2.] FMRP-USP, Faculdade de Medicina de Ribeirão Preto, Avenidada Bandeirantes, 1500, Ribeirão Preto, SP;
[3.] FCFRP-USP, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Avenidada Bandeirantes, 1500, Ribeirão Preto, SP;

COVID-19 is a viral disease characterised by degenerative respiratory systemmanifestations. Current studies implicate matrix metalloproteinases (MMPs) as the primarycause of pulmonary function loss due to tissue fibrosis. As proteases, MMPs directly degradeproteins, impacting specific enzymes in various metabolic pathways. Certain enzymesinvolved in sphingolipid metabolism can be affected by MMP species, resulting in animbalance in this crucial class of membrane and signalling lipids. Understanding the interplaybetween MMPs and sphingolipid metabolism is vital for elucidating the mechanismsunderlying SARS-CoV-2 pathogenesis and potential therapeutic interventions. This study aimed to evaluate the relationship between MMP3 and sphingolipidspecies in patients infected with SARS-CoV-2. By investigating this relationship, we soughtto uncover potential targets for therapeutic intervention and gain insights into the metabolicdysregulation associated with COVID-19.Plasma samples were collected from both SARS-CoV-2-infected patients and controlsubjects. A portion of these samples underwent lipid analysis, involving liquid-liquidextraction to isolate lipid fractions. Subsequently, liquid chromatography coupled withhigh-resolution mass spectrometry (LC-MS/MS) was employed for sphingolipid profiling.Additionally, another portion of the samples underwent immunoassay analysis specific toMMP3 levels. Analysis of the data revealed a positive correlation between MMP3 levels andsphingolipid concentrations in SARS-CoV-2-infected patients compared to controls.Specifically, elevated MMP3 levels were associated with increased sphingolipid species,suggesting a potential role for MMP3 in modulating these metabolism pathways duringSARS-CoV-2 infection. This study underscores the importance of sphingolipid metabolism dysregulation inthe context of SARS-CoV-2 infection and its potential association with MMPs activity.Further investigation into the mechanistic links between MMP3 and sphingolipid species mayprovide valuable insights into disease progression and identify novel therapeutic targets formitigating COVID-19-associated pathology.

Agradecimentos: The authors thank FAPESP, CNPq, and CAPES agencies for financial support.