

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

Thiago Vinicius Defelippo Felipe<sup>1</sup>, Pedro Nobre Azevedo<sup>1,2</sup>, Diana Mota Toro<sup>3</sup>, Adriana Ferreira Lopes Vilela<sup>1</sup>, Carlos Arterio Sorgi<sup>1,2,3</sup>

<sup>1</sup>. FFCLRP-USP, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Avenida Bandeirantes, 1500, Ribeirão Preto, SP;

<sup>2</sup>. FMRP-USP, Faculdade de Medicina de Ribeirão Preto, Avenida Bandeirantes, 1500, Ribeirão Preto, SP;

<sup>3</sup>. FCFRP-USP, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Avenida Bandeirantes, 1500, Ribeirão Preto, SP;

COVID-19 is a viral disease characterised by degenerative respiratory system manifestations. Current studies implicate matrix metalloproteinases (MMPs) as the primary cause of pulmonary function loss due to tissue fibrosis. As proteases, MMPs directly degrade proteins, impacting specific enzymes in various metabolic pathways. Certain enzymes involved in sphingolipid metabolism can be affected by MMP species, resulting in an imbalance in this crucial class of membrane and signalling lipids. Understanding the interplay between MMPs and sphingolipid metabolism is vital for elucidating the mechanisms underlying SARS-CoV-2 pathogenesis and potential therapeutic interventions. This study aimed to evaluate the relationship between MMP3 and sphingolipid species in patients infected with SARS-CoV-2. By investigating this relationship, we sought to uncover potential targets for therapeutic intervention and gain insights into the metabolic dysregulation associated with COVID-19. Plasma samples were collected from both SARS-CoV-2-infected patients and control subjects. A portion of these samples underwent lipid analysis, involving liquid-liquid extraction to isolate lipid fractions. Subsequently, liquid chromatography coupled with high-resolution mass spectrometry (LC-MS/MS) was employed for sphingolipid profiling. Additionally, another portion of the samples underwent immunoassay analysis specific to MMP3 levels. Analysis of the data revealed a positive correlation between MMP3 levels and sphingolipid 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 during SARS-CoV-2 infection. This study underscores the importance of sphingolipid metabolism dysregulation in the context of SARS-CoV-2 infection and its potential association with MMPs activity. Further investigation into the mechanistic links between MMP3 and sphingolipid species may provide valuable insights into disease progression and identify novel therapeutic targets for mitigating COVID-19-associated pathology.

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