ORT_12 - High CLEC5A expression on monocytes is related with severe COVID-19

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Introduction: Clec5a, is a lectin superfamily receptor expressed abundantly in myeloid lineage cells. Its has been know that macrophages infected with Dengue virus and anti-Clec5a have produced decrease pro-inflammatory cytokines. Clec5a also appears as a contributor increase in cytokine production by monocytes in cases of infection with Zika Virus and immunomodulation after Yellow Fever vaccination. Cytokines storms are related in severe COVID-19 cases and Clec5a could be an important signaling pathway for the worsening clinical evolution and thus be a strategic therapeutic target.

Objective: Evaluate the expression of Clec5a in monocytes in Covid-19.

Methodology: To evaluate the possibility of interaction between proteins and to investigate sites of protein binding, molecular docking modeling was performed through the Cluspro 2.0 and Pymol 2.5 software. These data were essential for predictive analysis of potential receptor-ligand interactions. PBMC were subjected to assays ex vivo immunophenotyping with commercial antibodies to characterize the monocyte subpopulations and Clec5a expression. PBMC were isolated by Ficoll-Paque®, PBMC samples were analyzed by flow cytometry and subsequently evaluated by the software FlowJo Tree Star. The samples were divided into three groups: unexposed, mild COVID19 and severe COVID-19.

Results: Our finding showed that Clec5a is capable of interact with regions of the S1 subunit spike protein of SARS-CoV-2. Immunophenotyping shows that Clec5a is overexpressed on intermediate and non-classical monocytes. To establish a cut-off for Clec5A expression on non-classical monocytes related to severity, ROC curve was performed showing that 20,9% ($p = 0.007$) is the limit to define mild (20.9%). Our data also revealed an association of Clec5a expression with severe COVID-19 (OD=58.5;95%CI: 5.75-594.53, $p = 0.0006$).

Conclusion: These results indicated that exists interaction between Clec5a and spike protein of SARS-CoV-2. The expression of Clec5a was elevated in severe COVID-19 cases, which may explain the inflammatory status in this syndrome. In addiction, findings shows that Clec5a may be a good therapeutic target for new treatments for viral infections, including cases of COVID-19.

Keywords: Clec5a; SARS-CoV-2; Monocytes