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CD169 EXPRESSION ON MONOCYTES WAS INVOLVED IN SARS-CoV-2 INFECTION AND WAS ASSOCIATED TO CLINICAL FEATURES OF COVID-19.

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Aim: The COVID-19 is an acute infectious disease caused by the SARS-CoV-2 virus. To date, a standard therapeutic approach for COVID-19 patients (COV) has not been established and the identification of early biomarkers to predict disease progression is needed. Recently, was suggest that SARS-CoV-2 infects CD169 macrophages in the spleen and lympho-nodes playing a central role in mediating SARS-CoV-2 translocation. Moreover, CD169 was strongly overexpressed in the blood of confirmed COV. We analysed CD169 in blood cells of COV admitted to the hospital during the COVID-19 outbreak and correlated its expression with clinical characteristics.
Methods: The ratio of the Median Fluorescence Intensity (MFI) of CD169 between monocytes and lymphocytes (CD169 RMFI) was used to screening blood samples of COV and Healthy Donors (HDs) by flow cytometry, and its correlation with clinical signs, inflammatory markers, cytokines mRNA expression, and disease progression was evaluated. To clarify whether CD169 was directly activated by SARS-CoV-2 stimulation, Peripheral Blood Mononuclear Cells (PBMCs) from HDs were stimulated in vitro with SARS-CoV-2 Spike protein for 24 hours and CD169 RMFI and mRNA expression were analysed.
Results: CD169 RMFI was highly expressed in the macrophages of COV but not in those of HDs especially in untreated patients at sampling. In $CD4^+$ T cells of untreated patients, CD169 RMFI inversely correlates with the expression of central memory ($CD45RA^- CCR7^+$) and effector memory ($CD45RA^- CCR7^-$) cells and directly correlated with exhaustion markers ($CD57^+$ $PD1^+$). In $CD8^+$ T cells, its expression was associated with the decrease of naive ($CD45RA^+$ $CCR7^+$) and increase in EM ($CD45RA^-$ $CCR7^-$) cells. Finally, CD169 RMFI positively correlated with the senescence marker $CD57^+$. Moreover, the CD169 RMFI correlated with inflammatory markers, blood cytokine levels, and pneumonia severity in the untreated group of COV at sampling. Notably, in this group, CD169 reflects the respiratory outcome of patients during hospitalization. *In vitro* stimulation of PBMCs from HDs with SARS-CoV-2 Spike protein induced an elevated expression of the activation marker HLA-DR in monocytes and a significant increase in CD169 RMFI in a dose-dependent manner with a significantly increase of IL-6 and IL-10 gene expression.
Discussion: Considering the central role of CD169 macrophages in SARS-CoV-2 infection and subsequent cytokine storm, our data highlighted the association between CD169 expression and clinical status, inflammatory markers, and respiratory outcome. **Conclusion:** Considering the immunological role of CD169 and its involvement during the infection and the progression of COVID-19, it could be considered as an early biomarker of disease progression.