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Gene expression profile in peripheral blood cells of patients with COVID-19

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Title of the Presentation

Abstract:

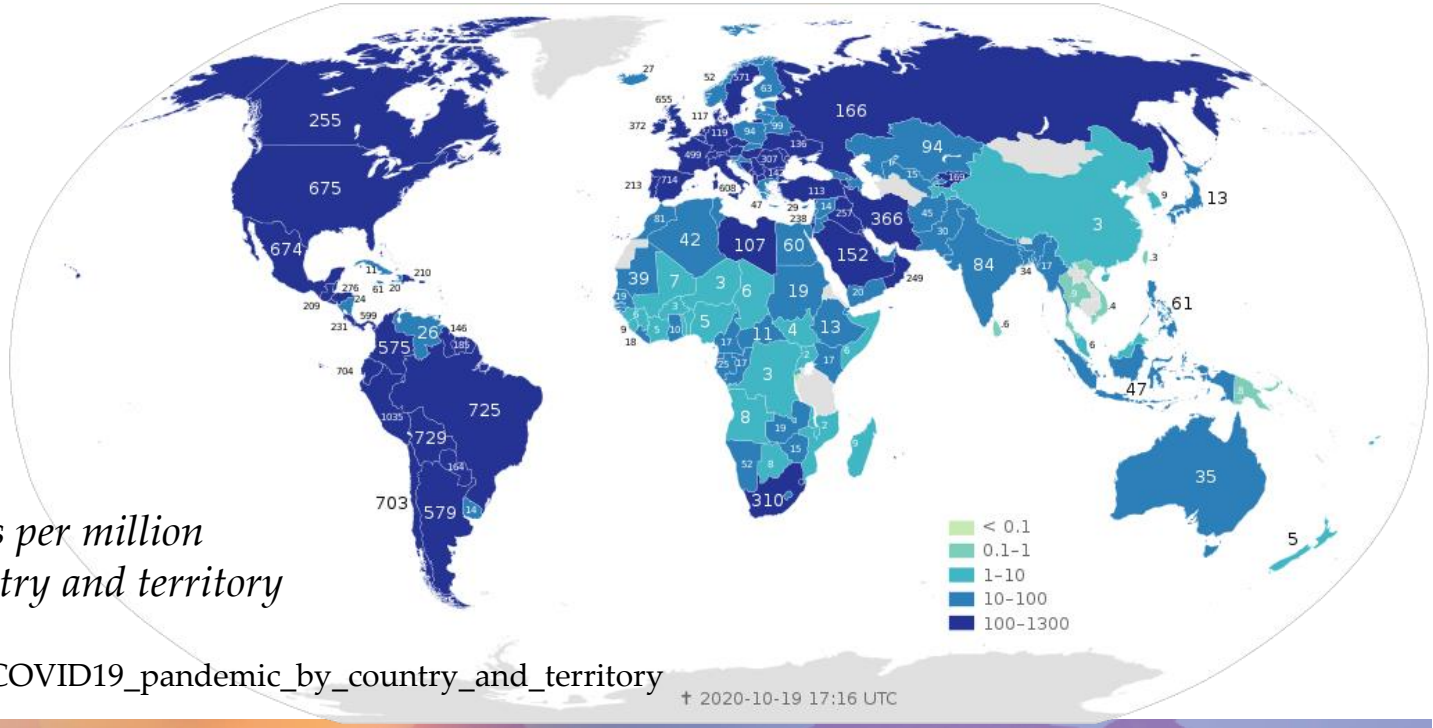
The clinical course of coronavirus disease 2019 (COVID-19) varies from mild symptoms to acute respiratory distress syndrome, hyperinflammation, and coagulation disorder. The hematopoietic system plays a critical role in the observed hyperinflammation, particularly in severely ill patients. Using peripheral blood cells (PBCs) for gene expression analysis is valuable to evaluate disease-associated and drug-response related genes. In this study, we aimed to explore the gene expression profile of PBCs in patients with COVID-19. Whole blood samples were collected from 19 patients with acute COVID-19 infection and 20 healthy volunteers. The gene expression of PBCs was determined by RT-qPCR. We investigated the expression of cytokines, chemokines, interferon-stimulated, pro-oxidation, and coagulation genes in PBCs of the infected and healthy samples. Up-regulated expression of some genes was found out in the blood of COVID-19-infected patients compared to the healthy sample. We have identified some genes in whole blood that classifies COVID-19-infected and healthy patients with good accuracy. These results suggested that the expression of cytokines, coagulation, and interferon-stimulated genes in PBCs can be used for early detection of hyperinflammation, coagulation disorders, and evaluation of efficiency treatment of this disease.

Keywords

coagulation, COVID-19, gene expression, hyperinflammation, peripheral blood cells

Introduction

Coronavirus SARS-CoV-2 is the etiologic agent for COVID-19, a disease from which over 1180,000 persons have died in the past 10 months. The clinical course of COVID-19 varies from mild symptoms to acute respiratory distress syndrome, hyperinflammation, and coagulation disorder. Patients with COVID19 have a higher risk of developing blood clots (thrombosis) mainly in their lungs which is associated with higher death. In ~70% of COVID-19 patients, who died had disseminated intravascular coagulation. The blood clots can be in both venous and arterial circulations, clots in small blood vessels.

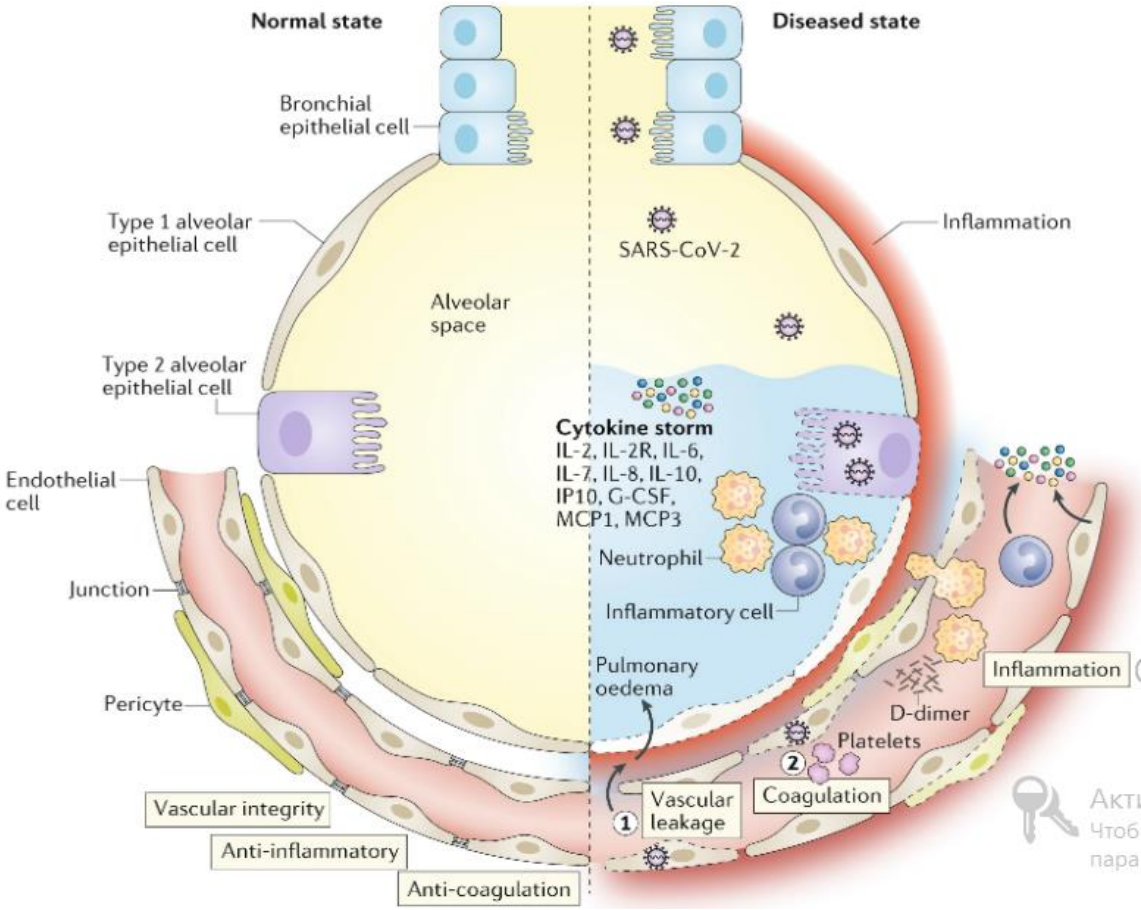


Total confirmed deaths per million of COVID-19 by country and territory

https://en.wikipedia.org/wiki/COVID19_pandemic_by_country_and_territory

Introduction

Endothelium plays a key role in the pathogenesis of coagulation disorders in infectious diseases and is important for the initiation and regulation of haemostatic. Although direct interactions between the infectious agent and the endothelial cells occur, cytokines—also endothelial-derived—are believed to be important mediators in this process.



Vessel–lung tissue interface in normal state and in COVID-19 disease

Te uwen, L. et al. Nat Rev Immunol, 2020. https://doi.org/10.1038/s41577-020-0343-0

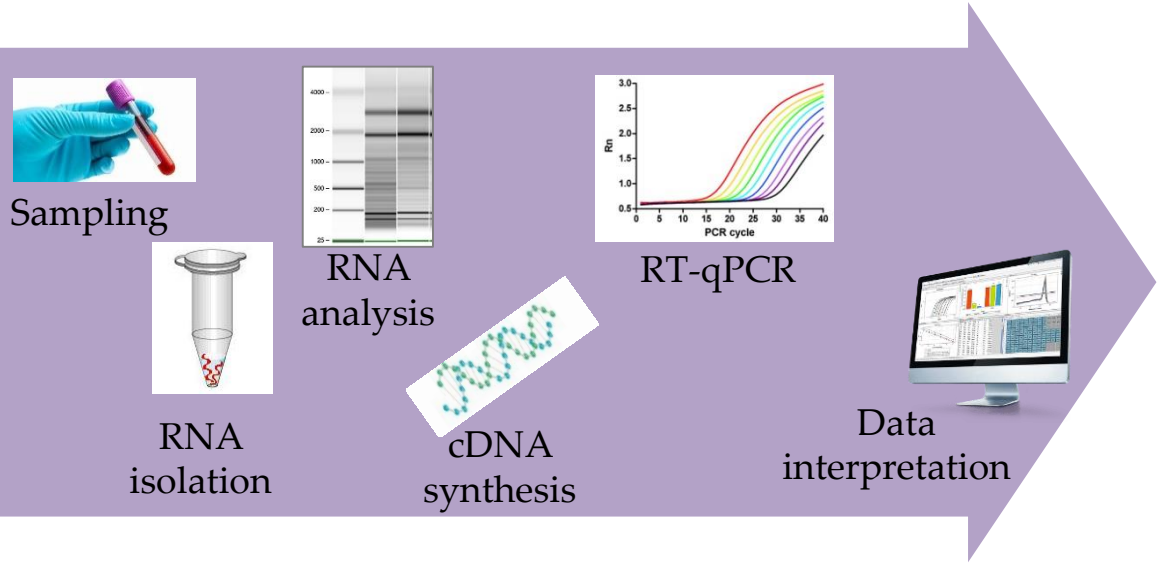
Introduction

· The hematopoietic system plays a critical role in the observed hyperinflammation, particularly in severely ill patients. Using peripheral blood cells (PBCs) for gene expression analysis is valuable to evaluate disease-associated and drug-response related genes. Early detection of inflammation and coagulation markers can indicate the onset of a cytokine storm, coagulation disorder and assist clinicians with timely interventions.

So the aim of our study was to explore the gene expression profile of PBCs in patients with COVID-19 and to find out genetic markers that indicate the onset of a cytokine storm, coagulation disorder.

Results and discussion

Whole blood samples were collected from patients with acute COVID-19 infection (*n*=19) and healthy volunteers (*n*=20). The gene expression of PBCs was determined by RT-qPCR.



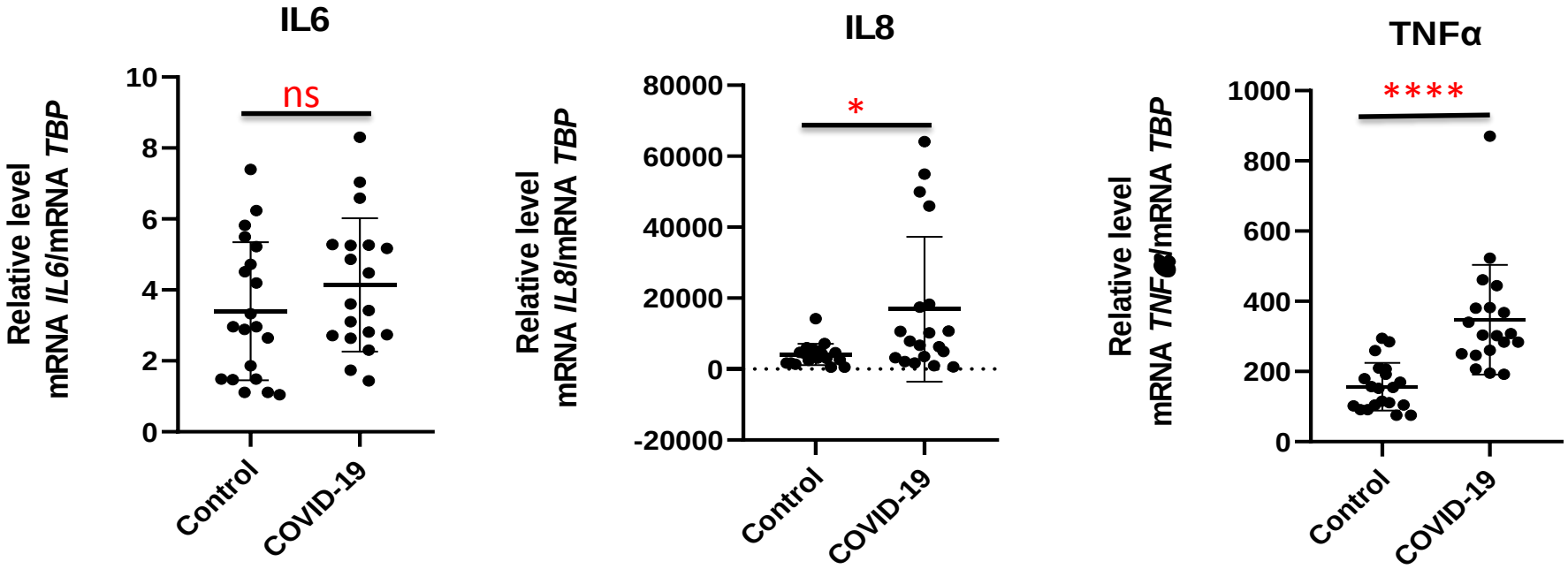
Schematic representation of the gene expression analysis

We investigated the expression of cytokines (*IL6, IL8, IL10, IL10R2, IL12, IL18, TNFα*), chemokines (*CCL, CXCL10*), coreceptors (*CD4, CD80*) interferon-stimulated (*OAS1, OAS3, RNASEL, MX1, EIF2AK2*), pro-oxidation (*ARG2, NOS2, XDH*), and coagulation (*F5, F10*) genes in PBCs of the infected and healthy samples.

Samples were normalized to *TBP* as a reference control. The Mann–Whitney U test was used to assess statistical differences in gene mRNA level values.

Results and discussion

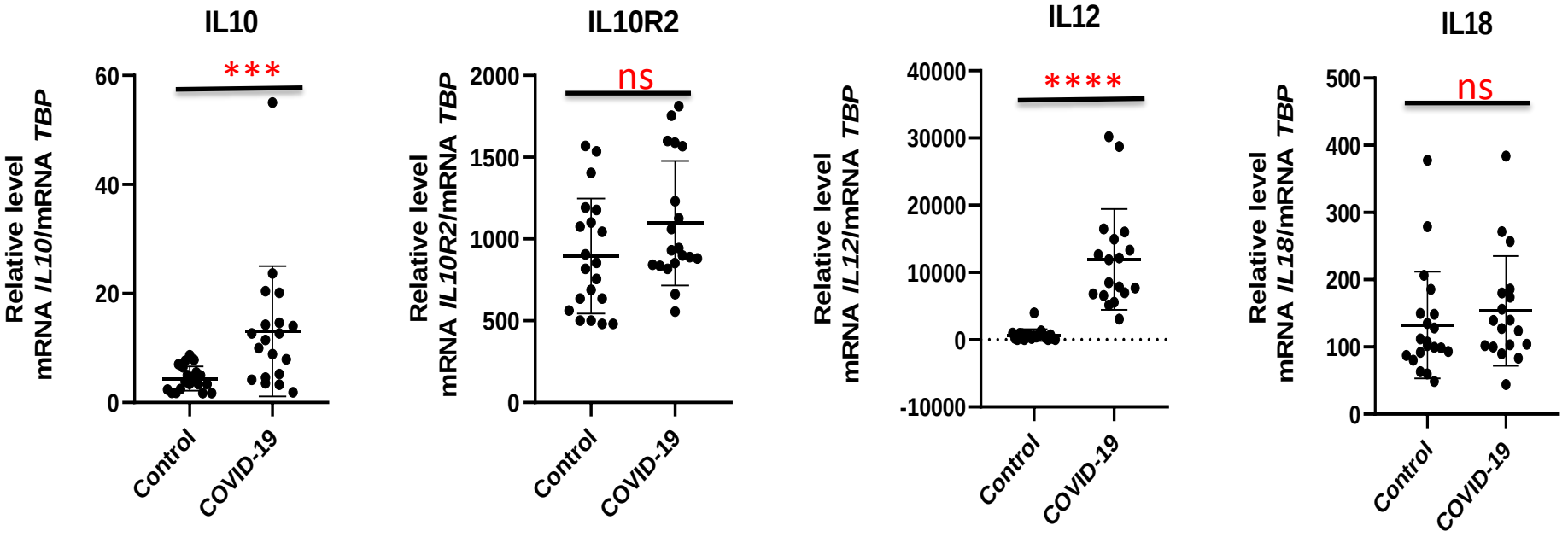
Up-expression of *IL8* and *TNFα* in PBCs of the COVID-19-infected patients



The mRNA level of cytokines in PBCs of the COVID-19-infected patients.
****P<0.0001 vs. Control; *P<0.05 vs. Control; ns, non significant vs. Control.

Results and discussion

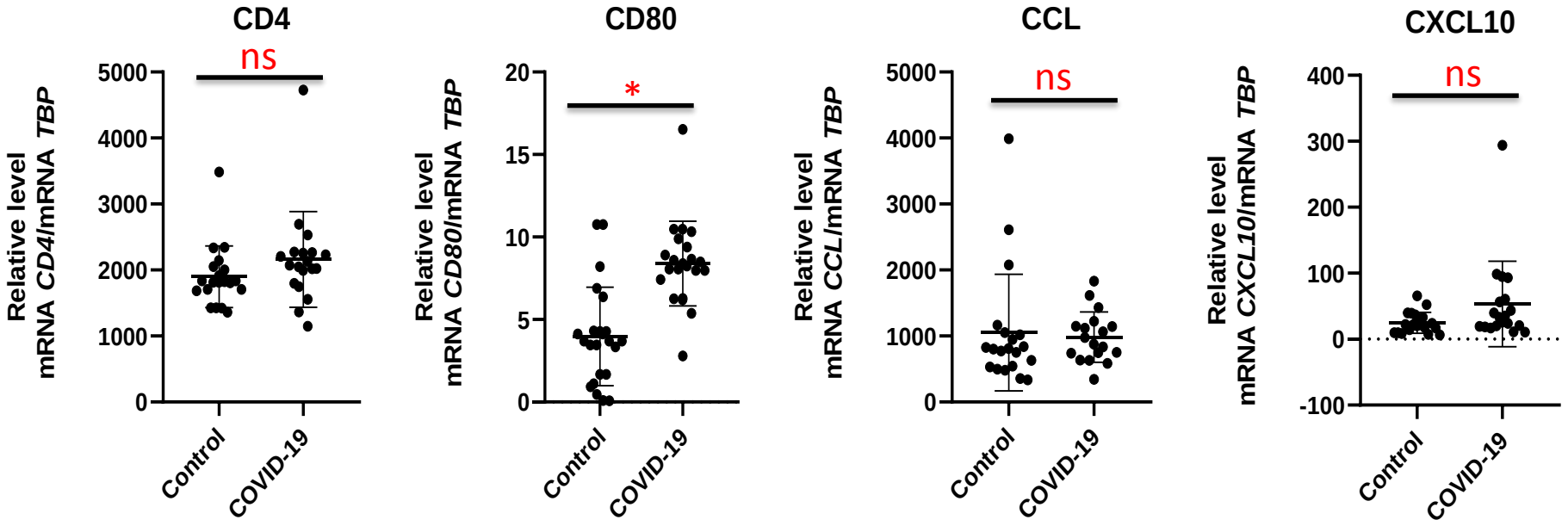
Hyperexpression of *IL10* and *IL12* in PBCs of the COVID-19-infected patients



The mRNA level of cytokine genes in PBCs of the COVID-19-infected patients.
****P<0.0001 vs. Control; ***P<0.001 vs. Control; ns, non significant vs. Control.

Results and discussion

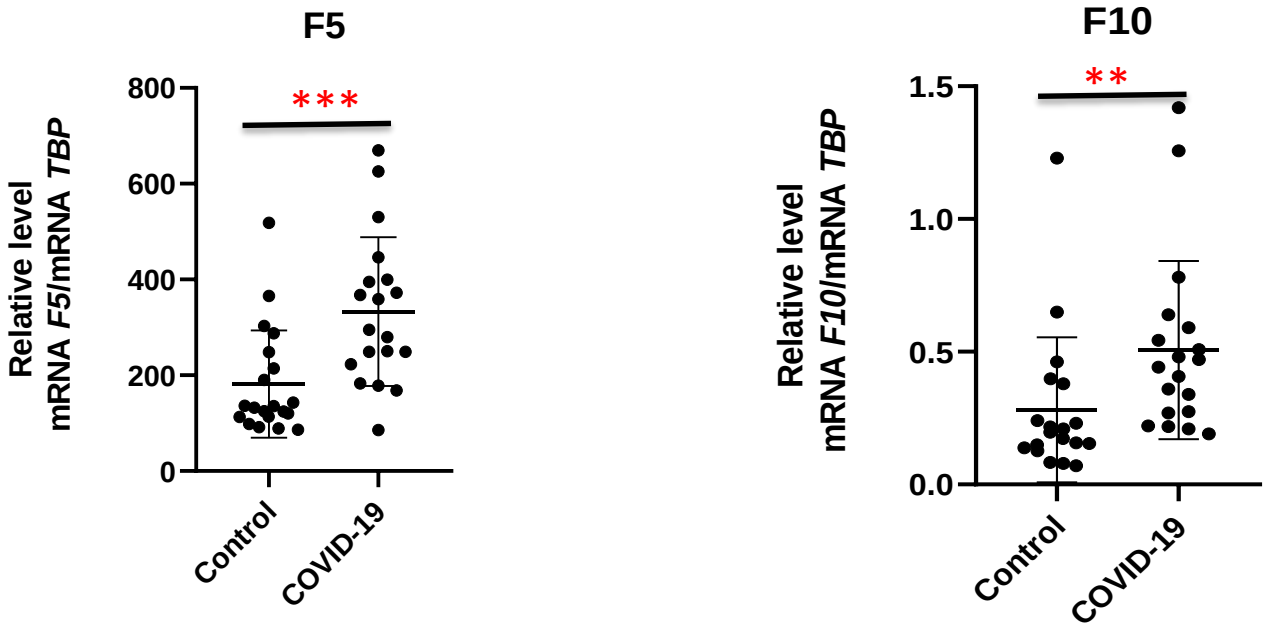
Increased expression of *CD80* in PBCs of the COVID-19-infected patients



The mRNA level of chemokines and coreceptors in PBCs of the COVID-19-infected patients. ****P<0.0001 vs. Control; ns, non significant vs. Control.

Results and discussion

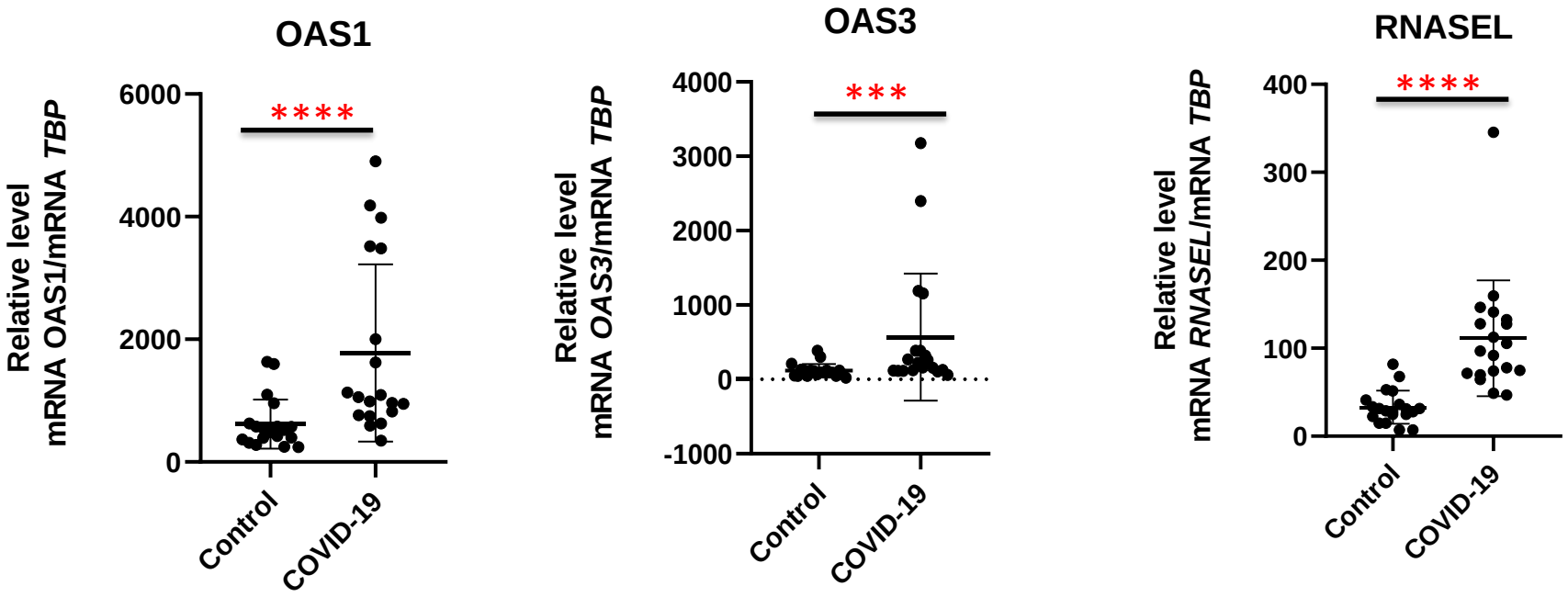
High expression of *F5* and *F10* in PBCs of the COVID-19-infected patients



The mRNA level of coagulation genes in PBCs of the COVID-19-infected patients. ***P<0.001 vs. Control; **P<0.01 vs. Control.

Results and discussion

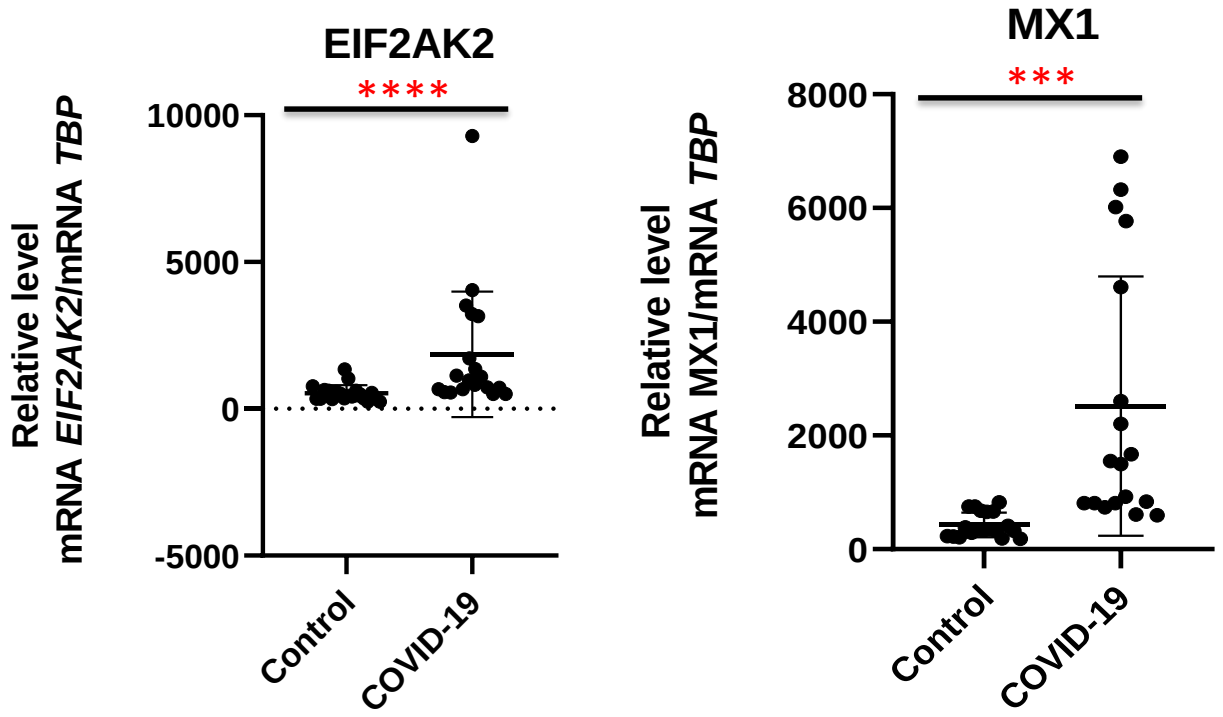
Up-expression of *OAS1*, *OAS3*, and *RNASEL* in PBCs of the COVID-19-infected patients



The mRNA level of interferon-stimulated genes in PBCs of the COVID-19-infected patients. ****P<0.0001 vs. Control; ***P<0.001 vs. Control.

Results and discussion

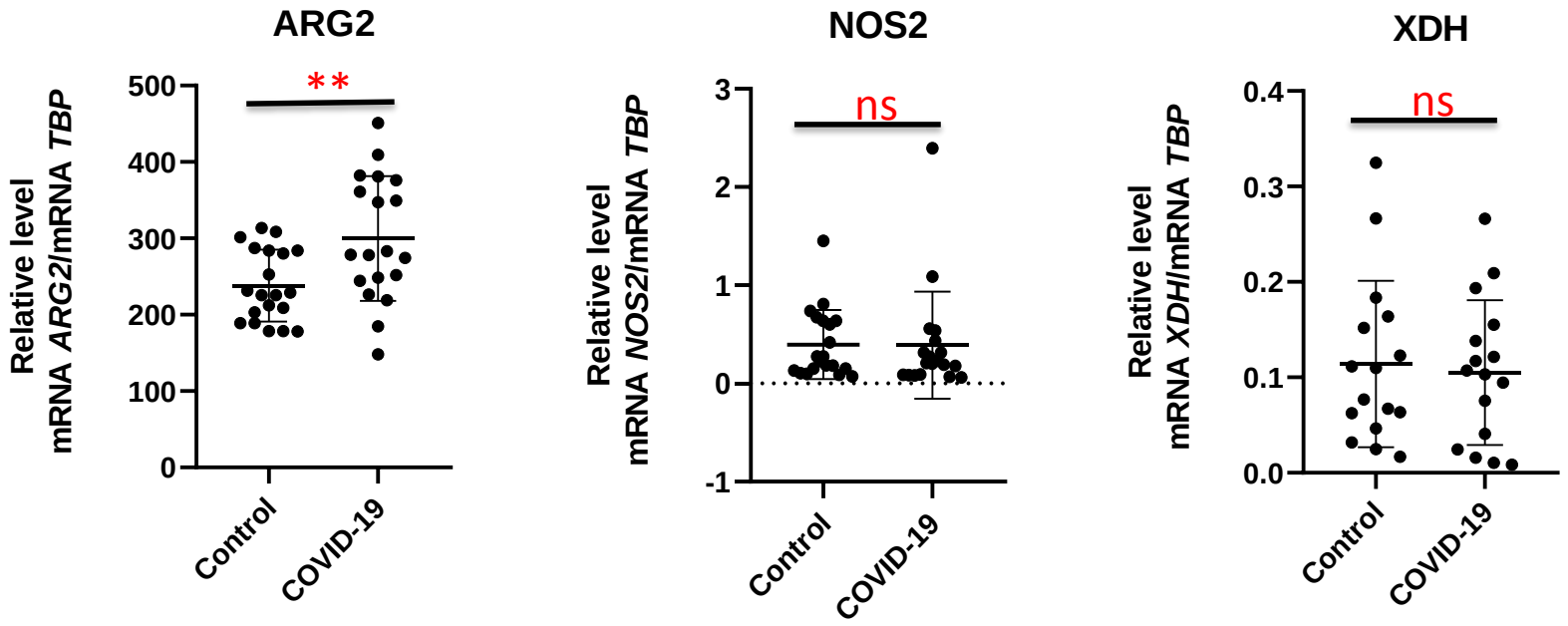
Hiperexpression of *MX1* and *EIF2AK2* in PBCs of the COVID-19-infected patients



The mRNA level of interferon-stimulated genes in PBCs of the COVID-19-infected patients. ****P<0.0001 vs. Control; ***P<0.001 vs. Control.

Results and discussion

Increased expression of *ARG2* in PBCs of the COVID-19-infected patients



The mRNA level of pro-oxidation genes in PBCs of the COVID-19-infected patients.
**P<0.01 vs. Control; ns, non significant vs. Control.

Results and discussion

Expression of the ***IL8, IL10, IL12, TNFα, CD80, OAS1, OAS3, RNASEL, MX1, EIF2AK2, F5, F10, ARG2*** was increased in the PBCs of COVID-19-infected patients compared to the healthy sample. These genes can be used as genetic markers for early detection of hyperinflammation and coagulation in patients with acute COVID-19 and evaluation of efficiency treatment of this disease.

Conclusions

- Up-regulated expression of *IL8, IL10, IL12, TNFα, CD80, OAS1, OAS3, RNASEL, MX1, EIF2AK2, F5, F10, ARG2* genes was found out in the blood of COVID-19-infected patients compared to the healthy sample;

- mRNA expression of *IL8, IL10, IL12, TNFα, CD80, OAS1, OAS3, RNASEL, MX1, EIF2AK2, F5, F10, ARG2* classifies COVID-19-infected and healthy patients with good accuracy in whole blood;

- Gene expression profile in PBCs can be used for early detection of hyperinflammation, coagulation disorders, and evaluation of efficiency treatment of this disease.

Acknowledgments