Transcriptomic clustering of critically ill COVID-19 patients

Cecilia López-Martínez[1,2,3], Paula Martín-Vicente[1,2,3], Juan Gómez de Oña[1,4,5], Inés López-Alonso[1,2,3,6], Helena Gil-Peña[1,7], Elías Cuesta-Llavona[1,4], Margarita Fernández-Rodríguez[1,3], Irene Crespo[1,2,8], Estefanía Salgado del Riego[1,9], Raquel Rodríguez-García[1,2,10], Diego Parra[1,10], Javier Fernández[1,11], Javier Rodríguez-Carrio[1,8], Francisco José Jimeno-Demuth[12], Alberto Dávalos[13], Luis A. Chapado[13], Eliecer Coto[1,4,5,14], Guillermo M. Albaiceta[1,2,3,8,10,15] and Laura Amado-Rodríguez[1,2,3,10,14,15]

[1]Instituto de Investigación Sanitaria del Principado de Asturias, Oviedo, Spain. [2]Centro de Investigación Biomédica en Red (CIBER)-Enfermedades Respiratorias, Madrid, Spain. [3]Instituto Universitario de Oncología del Principado de Asturias, Oviedo, Spain. [4]Servicio de Genética Molecular, Hospital Universitario Central de Asturias, Oviedo, Spain. [5]Red de Investigación Renal (REDINREN), Madrid, Spain. [6]Departamento de Morfología y Biología Celular, Universidad de Oviedo, Oviedo, Spain. [7]Servicio de Pediatría, Hospital Universitario Central de Asturias, Oviedo, Spain. [8]Departamento de Biología Funcional, Universidad de Oviedo, Oviedo, Spain. [9]Unidad de Cuidados Intensivos Polivalente, Hospital Universitario Central de Asturias, Oviedo, Spain. [10]Unidad de Cuidados Intensivos Cardiológicos, Hospital Universitario Central de Asturias, Oviedo, Spain. [11]Servicio de Microbiología, Hospital Universitario Central de Asturias, Oviedo, Spain. [12]Servicio de Informática, Hospital Universitario Central de Asturias, Oviedo, Spain. [13]Instituto Madrileño de Estudios Avanzados (IMDEA) Alimentación, CEI UAM+CSIC, Madrid, Spain. [14]Departamento de Medicina, Universidad de Oviedo, Oviedo, Spain. [15]G.M. Albaiceta and L. Amado-Rodríguez share last authorship.

Corresponding author: Guillermo M. Albaiceta (gma@crit-lab.org)

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Abstract

Background Infections caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may cause a severe disease, termed coronavirus disease 2019 (COVID-19), with significant mortality. Host responses to this infection, mainly in terms of systemic inflammation, have emerged as key pathogenetic mechanisms and their modulation has shown a mortality benefit.

Methods In a cohort of 56 critically ill COVID-19 patients, peripheral blood transcriptomes were obtained at admission to an intensive care unit (ICU) and clustered using an unsupervised algorithm. Differences in gene expression, circulating microRNAs (c-miRNAs) and clinical data between clusters were assessed, and circulating cell populations estimated from sequencing data. A transcriptomic signature was defined and applied to an external cohort to validate the findings.

Results We identified two transcriptomic clusters characterised by expression of either interferon-related or immune checkpoint genes, respectively. Steroids have cluster-specific effects, decreasing lymphocyte activation in the former but promoting B-cell activation in the latter. These profiles have different ICU outcomes, despite no major clinical differences at ICU admission. A transcriptomic signature was used to identify these clusters in two external validation cohorts (with 50 and 60 patients), yielding similar results.

Conclusions These results reveal different underlying pathogenetic mechanisms and illustrate the potential of transcriptomics to identify patient endotypes in severe COVID-19 with the aim to ultimately personalise their therapies.