ASSOCIATION OF COVID-19 INFLAMMATION WITH ACTIVATION OF THE C5A-C5AR1 AXIS

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Background Coronavirus disease 2019 (COVID-19) is a new pandemic disease caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The C5a anaphylatoxin and its receptor C5aR1 (CD88) play a key role in the initiation and maintenance of several inflammatory responses, by recruiting and activating neutrophils and monocytes in the lungs.

Methods We provide a longitudinal analysis of immune responses, including immune cell phenotyping and assessments of the soluble factors present in the blood and broncho-alveolar lavage fluid (BALF) of patients at various stages of COVID-19 severity: paucisymptomatic, pneumonia and acute respiratory distress syndrome (ARDS).

Results We report an increase in soluble C5a levels proportional to COVID-19 severity and high levels of C5aR1 expression in blood and pulmonary myeloid cells, supporting a role for the C5a-C5aR1 axis in the pathophysiology of ARDS. Abothalimab, an anti-C5aR1 therapeutic monoclonal antibodies (mAbs) prevented C5a-mediated human myeloid cell recruitment and activation, and inhibited acute lung injury (ALI) in human C5aR1 knockin mice.

Conclusions These results support the evaluation of avdoralimab to block C5a-C5aR1 as a mean of limiting myeloid cell infiltration in damaged organs and preventing the excessive lung inflammation and endothelialitis associated with ARDS in COVID-19 patients.

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Ethics Approval Human study protocol was approved by the Committee for the Protection of Persons Ile-de-France III – France (#2020-A00757-32). Animal experiments were approved by the ministere de l’enseignement superieur, de la recherche et de l’innovation – France (APAFIS#25418-2020051512242806 v2).

Data sharing, handling, and access

BIOTURNING BROWSER: INTERACTIVELY EXPLORE PUBLIC SINGLE CELL SEQUENCING DATA
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Background Single-cell sequencing technology has opened an unprecedented ability to interrogate cancer. It reveals significant insights into the intratumoral heterogeneity, metastasis, therapeutic resistance, which facilitates target discovery and validation in cancer treatment. With rapid advancements in throughput and strategies, a particular immuno-oncology study can produce multi-omics profiles for several thousands of individual cells. This overflow of single-cell data poses formidable challenges, including standardizing data formats across studies, performing reanalysis for individual datasets and meta-analysis.

Methods N/A

Results We present BioTuring Browser, an interactive platform for accessing and reanalyzing published single-cell omics data. The platform is currently hosting a curated database of more than 10 million cells from 247 projects, covering more than 120 immune cell types and subtypes, and 15 different cancer types. All data are processed and annotated with standardized labels of cell types, diseases, therapeutic responses, etc. to be instantly accessed and explored in a uniform visualization and analytics interface. Based on this massive curated database, BioTuring Browser supports searching similar expression profiles, querying a target across datasets and automatic cell type annotation. The platform supports single-cell RNA-seq, CITE-seq and TCR-seq data. BioTuring Browser is now available for download at www.bioturing.com.

Conclusions N/A

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