Report Title

Introduction

The research report delves into the complexities of cellular responses and gene expression variations within individual cells, and their implications for disease progression and therapeutic interventions. It is contextualized, particularly, within the backdrop of the COVID-19 pandemic, where an understanding of cellular responses and gene expression profiles in patients has significant relevance to comprehend disease severity and to modify therapeutic interventions accordingly. The report aims to investigate the multi-omics profiles of children with COVID-19 and multisystem inflammatory syndrome in children (MIS-C), enabling the identification of distinct immunopathological signatures in both conditions. These findings could aid in understanding the pathophysiology of these disorders and subsequently guide therapy. Furthermore, the paper focuses on the prevalence, longitudinal dynamics, and functional effects of neutralizing autoantibodies against type I interferons (IFNs) in COVID-19 patients experiencing critical disease. The implications of these autoantibodies have previously been found in a subset of patients with critical COVID-19, thus, understanding their effects on circulating leukocytes could have substantial therapeutic implications. Consequently, this range of research specific to the COVID-19 context collectively underscores the importance of studying cellular heterogeneity, gene expression variations, and immune responses at the single-cell level, taking into consideration that this might influence targeted interventions, disease severity scoring, and personalized treatments. The relevance of this endeavor is emphasized by the intention to comprehend the dynamic changes in immune cells from hospitalized COVID-19 patients, hoping to inform personalized treatment approaches and improve disease management. The overall importance of this research area extends beyond COVID-19 to other diseases characterized by cellular heterogeneity, which suggests broader potential implications for the study of immune responses in diverse contexts.

Literature

tal methods employed in the study include the analysis of gene expression signatures, inflammation signatures, and cytokine levels in COVID-19 patients, with a particular emphasis on the correlation between gene expression patterns and clinical parameters. The study also examines the dynamics of immune responses, focusing on the differences in immune cell populations and the coordinated antigen-specific adaptive immune responses in severe cases.

Results from the experiments highlight the association between variations in gene expression and disease severity in COVID-19 patients. The study observes changes in inflammatory and immune responses, cytokine levels, and antibody responses in patients with different disease outcomes, emphasizing the implications of heterogeneity for disease progression. Furthermore, the research identifies a heightened wave of inflammatory responses in critical patients, indicating a critical juncture in the disease course that contributes to disease severity.

The methods used to verify these findings involve gene set enrichment analysis, correlation analysis of cytokine levels and gene expression signatures, and single-cell analysis of immune cell heterogeneity.

These methods aim to provide a comprehensive understanding of the molecular and cellular mechanisms underlying the observed heterogeneity in COVID-19 disease progression, contributing to potential therapeutic interventions.

In conclusion, the literature review of the article provides a comprehensive overview of the impact of gene expression variations on cellular responses in COVID-19 patients. The experimental methods utilized offer valuable insights into the molecular and cellular mechanisms contributing to disease heterogeneity, laying the groundwork for potential therapeutic interventions.

References:

- (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9119950/pdf/)
- (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8601717/pdf/)
- (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9018908/pdf/)
- (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8523079/pdf/)
- (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7874909/pdf/)

Discussion

The discussion section of the paper aims to provide a comprehensive analysis of the implications of variations in gene expression within individual cells for disease progression and therapeutic interventions, particularly in the context of COVID-19. The provided content suggests several key findings and implications across the related papers, which can be discussed as follows:

Implications of Variations in Gene Expression for Disease Progression:

1. Robust Humoral Responses: All the articles highlight the robust humoral responses observed in COVID-19 patients, characterized by elevated levels of antibodies against SARS-CoV-2 proteins. This indicates a significant aspect of the immune response to the virus.

2. Cellular Heterogeneity and Disease Severity: The lack of coordination and delays in antigen-specific T and B cell responses in severe cases of COVID-19 are consistently associated with severe disease across the articles. This suggests the significance of cellular heterogeneity in the immune response and its potential implications for disease severity.

3. Proinflammatory Cytokines: Elevated levels of proinflammatory cytokines, particularly IL-6, are consistently noted as predictive of poor outcomes in COVID-19 patients. This emphasizes the role of inflammatory mediators in disease progression.

4. Attenuated Innate Immune Functions: Multiple articles underscore the attenuation of innate immune functions in response to SARS-CoV-2 infection, indicated by lower cell surface levels of HLA-DR in certain immune cells during active inflammation. This points to the impact of cellular heterogeneity on

immune responses.

Therapeutic Implications and Future Research Directions:

1. Single-Cell Profiling and Computational Approaches: The use of multimodal single-cell profiling and computational approaches across the articles provides a time-resolved single-cell atlas of COVID-19, revealing dynamically evolving cell-type-specific signatures linked to disease severity. This offers valuable insights into the immune cell dynamics associated with disease progression and potential therapeutic targets.

2. Type I Interferon Response: The significance of the type I interferon (IFN) response in protecting against severe disease is highlighted, supported by genetic evidence and the presence of autoantibodies against type I IFN in some critically ill patients. This suggests potential therapeutic targets related to the IFN response.

Unresolved Problems and Future Research Directions:

1. Limitations and Research Gaps: The articles acknowledge several limitations, such as the need for further validation of the findings in larger cohorts and the exploration of additional factors influencing disease heterogeneity. This paves the way for future research directions, focusing on elucidating the mechanisms underlying immune cell dysregulation and exploring potential therapeutic targets.

Innovative Scientific Method to Solve the Research Problem:

Considering the current findings, an innovative scientific method could involve further advancements in single-cell profiling techniques combined with functional assays to comprehensively characterize the evolving cellular responses in COVID-19. This method should aim to integrate multi-omics data and computational modeling to elucidate the complex interplay of immune responses at the single-cell level, providing a deeper understanding of the cellular heterogeneity and its implications for disease progression and therapeutic interventions.

Overall, the provided content offers valuable insights into the complex interplay of immune responses in COVID-19 and underscores the significance of cellular heterogeneity. However, further research is warranted to address the identified limitations and unanswered questions, leading to potential advancements in the understanding of the immune response to viral infections.

References:

1. [Link to the first source]
2. [Link to the second source]
3. [Link to the third source]
4. [Link to the fourth source]
5. [Link to the fifth source]

Idea

sure a solid understanding of the primary research study. Then, consider the related papers and entities to identify gaps, opportunities, or areas for further exploration within the field of systems immunology and COVID-19 research. Here is a potential research problem based on the information provided:

Research problem: How do the immunopathological signatures identified in severe COVID-19 patients, including the presence of type I interferon autoantibodies and impaired dendritic cell function, contribute to the late wave of inflammatory responses and divergent circulating protein trajectories observed in fatal COVID-19 outcomes, and how can this understanding inform the development of targeted therapeutic interventions at specific time points during the disease course?

This research problem aims to synthesize the findings from the target paper, related papers, and entities to delve deeper into the mechanisms underlying disease severity and outcome variability in COVID-19 patients. By investigating the impact of immunological dysregulation, autoantibody presence, and cellular dysfunction on the progression of severe cases towards fatal outcomes, this study can provide valuable insights into the critical windows for clinical intervention and personalized treatment strategies in the management of COVID-19 patients.

Method

thods, dsb significantly improves data quality by denoising and stabilizing protein detection across single cells, leading to more accurate identification of biologically relevant cell subsets and protein markers. The dsb method enhances the sensitivity of cell type discrimination, reveals consistent protein co-expression patterns, and uncovers novel biologically associated proteins that were previously masked by technical noise. Together, our work imparts a quantitative understanding of technical noise in droplet-based single-cell proteomic measurements and provides a powerful computational approach to address this issue, thereby offering improved insights into cellular heterogeneity.', 'The role of dendritic cells (DCs) in the context of coronavirus disease 2019 (COVID-19) is currently ill-defined. Here we dissect the phenotype and function of DCs isolated from the peripheral blood of 36 COVID-19 patients with different disease severities. We show that COVID-19 patients with moderate or severe diseases display a markedly impaired peripheral blood cDC1 and cDC2 compartment and reduced expression of human leukocyte antigen (HLA)-DR on these cells. Moreover, the CD1c+ DC compartment exhibited an altered phenotype with a decreased expression of C-type lectin and chemokine receptors. These phenotypic changes in DCs correlated with disease severity, inflammatory cytokine levels, and lymphopenia. Mechanistically, we found that blood and lung DCs exhibited a gene expression profile associated with cell death and impaired metabolic fitness. Proportions of peripheral blood DCs expressing CD38 positively correlated with lactate dehydrogenase, C-reactive protein, ferritin, but inversely correlated with lymphocyte numbers, T lymphocytes, CD4+, or CD8+ T effector memory RA', 'Expressed as percent in peripheral blood lymphocyte', '+ CD8+ T cells. Finally, functional analyses indicated a reduced ability of DCs from moderate or severe COVID-19 patients to stimulate allogeneic T cell proliferation. Thus, these findings establish the presence of an impaired function and delayed regeneration of dendritic cells in COVID-19.']

Based on the provided research problem, existing studies, and entities, the method for addressing the research problem within the field of systems immunology and COVID-19 research can be developed as follows:

1. In-depth Review of Core Concepts: Begin by thoroughly reading the target paper to comprehend the investigations, observations, and conclusions regarding the immunological signatures, circulating protein trajectories, and disease progression in severe and fatal COVID-19 outcomes. Pay special attention to the analysis of immune-cell-specific responses, identified gene expression signatures, and the temporal dynamics of immunopathological processes.

2. Analysis of Related Papers: Review the titles and abstracts of the related papers to gain insights into the specific abnormalities, immune alterations, autoantibody presence, and cellular dysfunctions observed in severe and critical COVID-19 patients. Identify the unique immunopathological signatures, such as type I interferon autoantibodies, dendritic cell phenotypes, and T cell activation patterns, detailed in these studies to assess the critical components necessary for addressing the research problem.

3. Exploration of Entities: Expand your understanding by exploring the entities relevant to the immunological mechanisms, gene expression signatures, dysregulated cellular functions, and interactions between immune cells and proteins in the context of COVID-19. Delve into the comprehensive understanding of multisystem responses, B cell mutations, genetic susceptibilities, and the influence of specific alleles in disease pathophysiology.

4. Integration and Synthesis: Integrate and synthesize the information from the target paper, related papers, and entities to dissect the immunological dysregulation that contributes to the late wave of inflammatory responses and fatal outcomes in severe COVID-19 patients. Focus on identifying the causative links between type I interferon autoantibodies, dendritic cell impairment, intra- and intercellular communication, and systemic protein trajectories with disease severity and fatality. Determine the potential therapeutic windows and personalized interventions based on the critical junctures of immunological transitions throughout the disease course.

5. Development of Hypotheses and Methodological Framework: Formulate hypotheses based on the critical immunopathological signatures identified, and propose a methodological framework to investigate these signatures specifically in relation to the temporal dynamics of severe COVID-19 outcomes. Consider the design of longitudinal studies, multivariate immune profiling, and advanced computational approaches to model the trajectories of immunopathological perturbations, identify prognostic factors, and develop targeted therapeutic interventions aligned with the temporal progression of the disease.

Through the method developed, this approach will offer an innovative, rigorous, valid, and generalizable framework to gain deep insights into the immunological mechanisms underlying

COVID-19 severity and fatality, and to devise critical interventions based on the systemic trajectory of immune responses and cellular aberrations.

Experiment

diseases display a markedly impaired peripheral blood cDC1 and cDC2 compartment and reduced expression of human leukocyte antigen (HLA)-DR on these cells. Moreover, the CD1c+ DC compartment exhibited an altered phenotype with a decreased expression of C-type lectin and chemokine receptors. These phenotypic changes in DCs correlated with disease severity, inflammatory cytokine levels, and lymphopenia. Mechanistically, we found that blood and lung DCs exhibited a gene expression profile associated with cell death and impaired metabolic fitness. Proportions of peripheral blood DCs expressing CD38 positively correlated with lactate dehydrogenase, C-reactive protein, ferritin, but inversely correlated with lymphocyte numbers, T lymphocytes, CD4+, or CD8+ T effector memory RA', 'Expressed as percent in peripheral blood lymphocyte', '+ CD8+ T cells. Finally, functional analyses indicated a reduced ability of DCs from moderate or severe COVID-19 patients to stimulate allogeneic T cell proliferation. Thus, these findings establish the presence of an impaired function and delayed regeneration of dendritic cells in COVID-19.'] Based on the provided research problem, existing studies, and entities, the method for addressing the research problem within the field of systems immunology and COVID-19 research can be developed as follows: 1. In-depth Review of Core Concepts: Begin by thoroughly reading the target paper to comprehend the investigations, observations, and conclusions regarding the immunological signatures, circulating protein trajectories, and disease progression in severe and fatal COVID-19 outcomes. Pay special attention to the analysis of immune-cell-specific responses, identified gene expression signatures, and the temporal dynamics of immunopathological processes. 2. Analysis of Related Papers: Review the titles and abstracts of the related papers to gain insights into the specific abnormalities, immune alterations, autoantibody presence, and cellular dysfunctions observed in severe and critical COVID-19 patients. Identify the unique immunopathological signatures, such as type I interferon autoantibodies, dendritic cell phenotypes, and T cell activation patterns, detailed in these studies to assess the critical components necessary for addressing the research problem. 3. Exploration of Entities: Expand your understanding by exploring the entities relevant to the immunological mechanisms, gene expression signatures, dysregulated cellular functions, and interactions between immune cells and proteins in the context of COVID-19. Delve into the comprehensive understanding of multisystem responses, B cell mutations, genetic susceptibilities, and the influence of specific alleles in disease pathophysiology. 4. Integration and Synthesis: Integrate and synthesize the information from the target paper, related papers, and entities to dissect the immunological dysregulation that contributes to the late wave of inflammatory responses and fatal outcomes in severe COVID-19 patients. Focus on identifying the causative links between type I interferon autoantibodies, dendritic cell impairment, intra- and intercellular communication, and systemic protein trajectories with disease severity and fatality. Determine the potential therapeutic windows and personalized interventions based on the critical junctures of immunological transitions throughout the disease course. 5. Development of Hypotheses and Methodological Framework: Formulate hypotheses based on the critical immunopathological signatures identified, and propose a methodological framework to investigate these signatures specifically in relation to the temporal dynamics of severe COVID-19 outcomes. Consider the design of longitudinal studies, multivariate immune profiling, and advanced computational approaches to model the trajectories of immunopathological perturbations, identify prognostic factors, and develop targeted therapeutic interventions aligned with the temporal progression of the disease. Through the method developed, this approach will offer an innovative, rigorous, valid, and generalizable framework to gain deep insights into the immunological mechanisms underlying COVID-19 severity and fatality, and to devise critical interventions based on the systemic trajectory of immune responses and cellular aberrations.

More related paper

Paper 1
Title: Immunopathological signatures in multisystem inflammatory syndrome in children and pediatric COVID-19.

Abstract: Pediatric Coronavirus Disease 2019 (pCOVID-19) is rarely severe; however, a minority of children infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might develop multisystem inflammatory syndrome in children (MIS-C), with substantial morbidity. In this longitudinal multi-institutional study, we applied multi-omics (analysis of soluble biomarkers, proteomics, single-cell gene expression and immune repertoire analysis) to profile children with COVID-19 (nâ■■=â■■110) and MIS-C (nâ■■=â■■76), along with pediatric healthy controls (pHCs; nâ■■=â■■76). pCOVID-19 was characterized by robust type I interferon (IFN) responses, whereas prominent type II IFN-dependent and NF-ÎºB-dependent signatures, matrisome activation and increased levels of circulating spike protein were detected in MIS-C, with no correlation with SARS-CoV-2 PCR status around the time of admission. Transient expansion of TRBV11-2 T cell clonotypes in MIS-C was associated with signatures of inflammation and T cell activation. The association of MIS-C with the combination of HLA A*02, B*35 and C*04 alleles suggests genetic susceptibility. MIS-C B cells showed higher mutation load than pCOVID-19 and pHC. These results identify distinct immunopathological signatures in pCOVID-19 and MIS-C that might help better define the pathophysiology of these disorders and guide therapy.

DOI: 10.1038/s41591-022-01724-3
The impact factor: 87.241

Paper 2

Title: Human immune diversity: from evolution to modernity.

Abstract: The extreme diversity of the human immune system, forged and maintained throughout evolutionary history, provides a potent defense against opportunistic pathogens. At the same time, this immune variation is the substrate upon which a plethora of immune-associated diseases develop. Genetic analysis suggests that thousands of individually weak loci together drive up to half of the observed immune variation. Intense selection maintains this genetic diversity, even selecting for the introgressed Neanderthal or Denisovan alleles that have reintroduced variation lost during the out-of-Africa migration. Variations in age, sex, diet, environmental exposure, and microbiome each potentially explain the residual variation, with proof-of-concept studies demonstrating both plausible mechanisms and correlative associations. The confounding interaction of many of these variables currently makes it difficult to assign definitive contributions. Here, we review the current state of play in the field, identify the key unknowns in the causality of immune variation, and identify the multidisciplinary pathways toward an improved understanding.

DOI: 10.1038/s41590-021-01058-1
The impact factor: 31.25

Paper 3

Title: Type I interferon autoantibodies are associated with systemic immune alterations in patients with COVID-19.

Abstract: Neutralizing autoantibodies against type I interferons (IFNs) have been found in some patients with critical coronavirus disease 2019 (COVID-19), the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). However, the prevalence of these antibodies, their longitudinal dynamics across the disease severity scale, and their functional effects on circulating leukocytes remain unknown. Here, in 284 patients with COVID-19, we found type I IFNâ■■specific autoantibodies in peripheral blood samples from 19% of patients with critical disease and 6% of patients with severe disease. We found no type I IFN autoantibodies in individuals with moderate disease. Longitudinal profiling of over 600,000 peripheral blood mononuclear cells using multiplexed single-cell epitope and transcriptome sequencing from 54 patients with COVID-19 and 26 nonâ■■COVID-19 controls revealed a lack of type I IFNâ■■stimulated gene (ISG-I) responses in myeloid cells from patients with critical disease. This was especially evident in dendritic cell populations isolated from patients with critical disease producing type I IFNâ■■specific autoantibodies. Moreover, we found elevated expression of the inhibitory receptor leukocyte-associated immunoglobulin-like receptor 1 (LAIR1) on the surface of monocytes isolated from patients with critical disease early in the disease course. LAIR1 expression is inversely correlated with ISG-I expression response in patients with COVID-19 but is not expressed in healthy controls. The deficient ISG-I response observed in patients with critical COVID-19 with and without type I IFNâ■■specific autoantibodies supports a unifying model for disease pathogenesis involving ISG-I suppression through convergent mechanisms.

DOI: 10.1126/scitranslmed.abh2624
The impact factor: 19.319

Paper 4

Title: Normalizing and denoising protein expression data from droplet-based single cell profiling.

Abstract: Multimodal single-cell profiling methods that measure protein expression with oligo-conjugated antibodies hold promise for comprehensive dissection of cellular heterogeneity, yet the resulting protein counts have substantial technical noise that can mask biological variations. Here we integrate experiments and computational analyses to reveal two major noise sources and develop a method called "dsb" (denoised and scaled by background) to normalize and denoise droplet-based protein expression data. We discover that protein-specific noise originates from unbound antibodies encapsulated during droplet generation; this noise can thus be accurately estimated and corrected by utilizing protein levels in empty droplets. We also find that isotype control antibodies and the background protein population average in each cell exhibit significant correlations across single cells, we thus use their shared variance to correct for cell-to-cell technical noise in each cell. We validate these findings by analyzing the performance of dsb in eight independent datasets spanning multiple technologies, including CITE-seq, ASAP-seq, and TEA-seq. Compared to existing normalization methods, our approach improves downstream analyses by better unmasking biologically meaningful cell populations. Our method is available as an open-source R package that interfaces easily with existing single cell software platforms such as Seurat, Bioconductor, and Scanpy and can be accessed at "dsb [https://cran.r-project.org/package=dsb]".

DOI: 10.1038/s41467-022-29356-8
The impact factor: 17.694

Paper 5

Title: Impaired function and delayed regeneration of dendritic cells in COVID-19.

Abstract: Disease manifestations in COVID-19 range from mild to severe illness associated with a dysregulated innate immune response. Alterations in function and regeneration of dendritic cells (DCs) and monocytes may contribute to immunopathology and influence adaptive immune responses in COVID-19 patients. We analyzed circulating DC and monocyte subsets in 65 hospitalized COVID-19 patients with mild/moderate or severe disease from acute illness to recovery and in healthy controls. Persisting reduction of all DC subpopulations was accompanied by an expansion of proliferating Lineage-HLADR+ cells lacking DC markers. Increased frequency of CD163+ CD14+ cells within the recently discovered DC3 subpopulation in patients with more severe disease was associated with systemic inflammation, activated T follicular helper cells, and antibody-secreting cells. Persistent downregulation of CD86 and upregulation of programmed death-ligand 1 (PD-L1) in conventional DCs (cDC2 and DC3) and classical monocytes associated with a reduced capacity to stimulate naÃ¯ve CD4+ T cells correlated with disease severity. Long-lasting depletion and functional impairment of DCs and monocytes may have consequences for susceptibility to secondary infections and therapy of COVID-19 patients.

DOI: 10.1371/journal.ppat.1009742
The impact factor: 7.464

Paper 6

Title: Cell specific peripheral immune responses predict survival in critical COVID-19 patients.

Abstract: SARS-CoV-2 triggers a complex systemic immune response in circulating blood mononuclear cells. The relationship between immune cell activation of the peripheral compartment and survival in critical COVID-19 remains to be established. Here we use single-cell RNA sequencing and Cellular Indexing of Transcriptomes and Epitomes by sequence mapping to elucidate cell type specific transcriptional signatures that associate with and predict survival in critical COVID-19. Patients who survive infection display activation of antibody processing, early activation response, and cell cycle regulation pathways most prominent within B-, T-, and NK-cell subsets. We further leverage cell specific differential gene expression and machine learning to predict mortality using single cell transcriptomes. We identify interferon signaling and antigen presentation pathways within cDC2 cells, CD14 monocytes, and CD16 monocytes as predictors of mortality with 90% accuracy. Finally, we validate our findings in an independent transcriptomics dataset and provide a framework to elucidate mechanisms that promote survival in critically ill COVID-19 patients. Identifying prognostic indicators among critical COVID-19 patients holds tremendous value in risk stratification and clinical management.

DOI: 10.1038/s41467-022-28505-3
The impact factor: 17.694

Paper 7

Title: Activation or exhaustion of CD8(+) T cells in patients with COVID-19.

Abstract: In addition to CD4(+) T cells and neutralizing antibodies, CD8(+) T cells contribute to protective immune responses against SARS-CoV-2 in patients with coronavirus disease 2019 (COVID-19), an ongoing pandemic disease. In patients with COVID-19, CD8(+) T cells exhibiting activated phenotypes are commonly observed, although the absolute number of CD8(+) T cells is decreased. In addition, several studies have reported an upregulation of inhibitory immune checkpoint receptors, such as PD-1, and the expression of exhaustion-associated gene signatures in CD8(+) T cells from patients with COVID-19. However, whether CD8(+) T cells are truly exhausted during COVID-19 has been a controversial issue. In the present review, we summarize the current understanding of CD8(+) T-cell exhaustion and describe the available knowledge on the phenotypes and functions of CD8(+) T cells in the context of activation and exhaustion. We also summarize recent reports regarding phenotypical and functional analyses of SARS-CoV-2-specific CD8(+) T cells and discuss long-term SARS-CoV-2-specific CD8(+) T-cell memory.

DOI: 10.1038/s41423-021-00750-4
The impact factor: 22.096

Paper 8

Title: Natural killer cells in antiviral immunity.

Abstract: Natural killer (NK) cells play an important role in innate immune responses to viral infections. Here, we review recent insights into the role of NK cells in viral infections, with particular emphasis on human studies. We first discuss NK cells in the context of acute viral infections, with flavivirus and influenza virus infections as examples. Questions related to activation of NK cells, homing to infected tissues and the role of tissue-resident NK cells in acute viral infections are also addressed. Next, we discuss NK cells in the context of chronic viral infections with hepatitis C virus and HIV-1. Also covered is the role of adaptive-like NK cell expansions as well as the appearance of CD56(-) NK cells in the course of chronic infection. Specific emphasis is then placed in viral infections in patients with primary immunodeficiencies affecting NK cells. Not least, studies in this area have revealed an important role for NK cells in controlling several herpesvirus infections. Finally, we address new data with respect to the activation of NK cells and NK cell function in humans infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) giving rise to coronavirus disease 2019 (COVID-19).

DOI: 10.1038/s41577-021-00558-3
The impact factor: 108.555

Paper 9

Title: Multiomics: unraveling the panoramic landscapes of SARS-CoV-2 infection.

Abstract: In response to emerging infectious diseases, such as the recent pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), it is critical to quickly identify and understand responsible pathogens, risk factors, host immune responses, and pathogenic mechanisms at both the molecular and cellular levels. The recent development of multiomic technologies, including genomics, proteomics, metabolomics, and single-cell transcriptomics, has enabled a fast and panoramic grasp of the pathogen and the disease. Here, we systematically reviewed the major advances in the virology, immunology, and pathogenic mechanisms of SARS-CoV-2 infection that have been achieved via multiomic technologies. Based on well-established cohorts, omics-based methods can greatly enhance the mechanistic understanding of

diseases, contributing to the development of new diagnostics, drugs, and vaccines for emerging infectious diseases, such as COVID-19.

DOI: 10.1038/s41423-021-00754-0
The impact factor: 22.096

Paper 10

Title: COVID-19 patients exhibit unique transcriptional signatures indicative of disease severity.

Abstract: COVID-19 manifests a spectrum of respiratory symptoms, with the more severe often requiring hospitalization. To identify markers for disease progression, we analyzed longitudinal gene expression data from patients with confirmed SARS-CoV-2 infection admitted to the intensive care unit (ICU) for acute hypoxic respiratory failure (AHRF) as well as other ICU patients with or without AHRF and correlated results of gene set enrichment analysis with clinical features. The results were then compared with a second dataset of COVID-19 patients separated by disease stage and severity. Transcriptomic analysis revealed that enrichment of plasma cells (PCs) was characteristic of all COVID-19 patients whereas enrichment of interferon (IFN) and neutrophil gene signatures was specific to patients requiring hospitalization. Furthermore, gene expression results were used to divide AHRF COVID-19 patients into 2 groups with differences in immune profiles and clinical features indicative of severe disease. Thus, transcriptomic analysis reveals gene signatures unique to COVID-19 patients and provides opportunities for identification of the most at-risk individuals.

DOI: 10.3389/fimmu.2022.989556
The impact factor: 8.786