Infectious disease research

Uncovering deep molecular insights into viral pathogenesis using SARS-CoV-2–related TaqMan Arrays

TaqMan Gene Expression Assays:

- More than 2.8 million assays covering over 32 species have been predesigned and optimized for gene expression analysis
- Easily modify (e.g., add, delete, or reorganize) predesigned TaqMan Assays on flexible arrays with our easy-to-use online configurator
- Enable quick, robust investigation of the impact of well-studied diseases on biological processes and alternative pathways

Introduction

In this application note, we show:

- How medium-throughput gene expression analysis of several SARS-CoV-2–associated genes involved in virus life cycle and host response can be used to understand the basis of pathogenesis in SARS-CoV-2 infection
- Workflow efficiency utilizing prespotted Applied Biosystems™ TaqMan™ Array Plates (containing predesigned Applied Biosystems™ TaqMan™ Gene Expression Assays) to perform gene expression analysis
- How this approach can be widely applied to other infectious disease research to gain deep genomic insights into the disease process, given the depth and flexibility of TaqMan qPCR solutions

Emerging infectious diseases caused by zoonotic transmission of pathogens pose a great concern to public health and the global economy. The SARS-CoV-2 outbreak in Wuhan in 2019 rapidly spread across the world in 2020 and continues to put the world on alert for emerging variants. While the mortality and morbidity associated with SARS-CoV-2 infection have significantly decreased due to a combination of vaccination drives, effective therapeutics, and attenuated pathogenicity of the current variant, many infected individuals continue to experience symptoms that outlast the active infection period. Why is it that certain individuals are more likely to experience a worse outcome of the infection, or develop more severe symptoms than others? Questions such as these are active areas of research to understand the molecular basis of SARS-CoV-2 pathogenicity and ultimately lead to the discovery of predictive biomarkers and development of novel, and potentially personalized, treatment strategies.

Several studies on SARS-CoV-2 have demonstrated that differences in host response to the infection can be attributed to the differential modulation of genes involved in virus entry [1], virus restriction [2], and inflammatory response [3]. In addition, age [1,4] or differences in genetic background, arising from sex, for instance [1,5], have also been shown to influence the expression of such genes and impact disease progression and outcome.

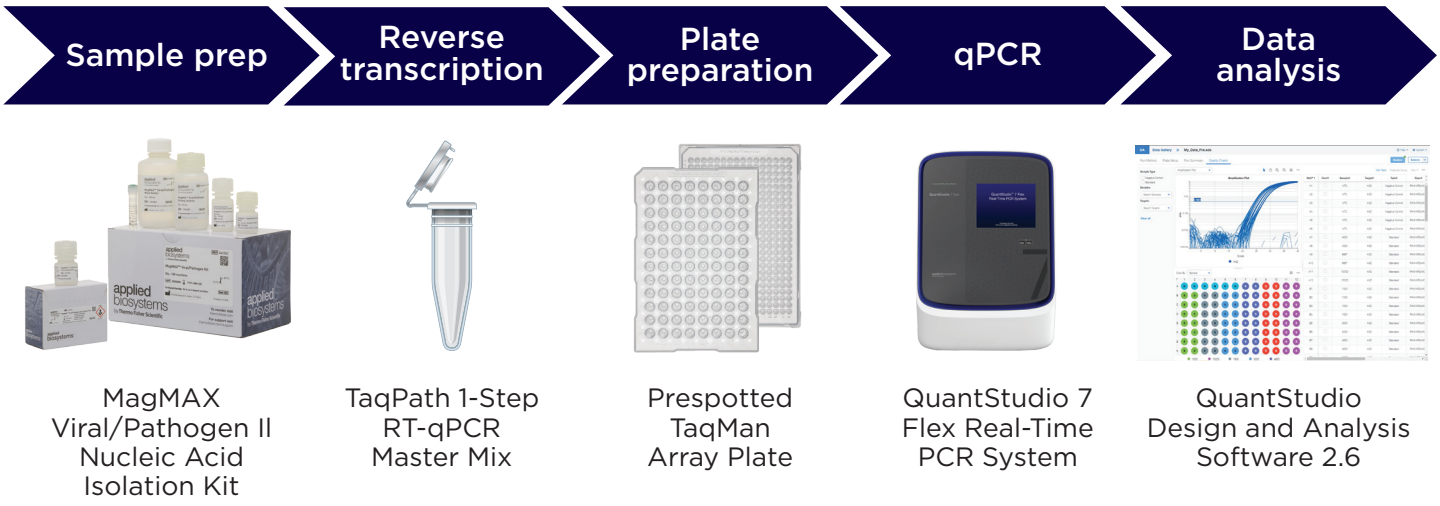

Figure 1. Simultaneous detection of gene expression changes using TaqMan Gene Expression Assays and analysis. A general real-time PCR workflow using TaqMan Array Plates is presented.

Using flexible TaqMan Array Plates, we investigated the genetic basis of SARS-CoV-2 pathogenesis in SARS-CoV-2–infected and control samples. Using qPCR panels interrogating the most cited genes involved in viral cell entry (13 genes), restriction factors (13 genes), and a large set of cytokines, chemokines, and growth factors (29 genes) associated with the SARS-CoV-2 infection (Table 1), we examined differences in the expression of these genes based on SARS-CoV-2 infection status, disease severity, and outcome. We observed that several viral life cycle and host response genes' expression were not only significantly different between these groups but were also differentially modulated between sexes. Many of our findings were in agreement with previously published data. Importantly, our analyses revealed several novel associations between the expression of certain genes with disease manifestation and the progress of SARS-CoV-2 infection. Such findings can lay the groundwork for discovery of potential biomarkers or therapeutic targets when validated in larger cohorts.

Together, our data demonstrate how simultaneous interrogation of several genes involved in SARS-CoV-2 pathogenesis, using the TaqMan Array Plates, can reveal novel molecular insights and advance our understanding of the disease process. This simple, medium-throughput workflow can easily be extended to any disease area of interest or genetic pathway. While this study employed these flexible panels in their default configuration, they can easily be modified to include additional or fewer targets as needed.

Materials and methods

Workflow for detecting changes in gene expression using TaqMan Gene Expression Assays

A curated selection of predesigned TaqMan Gene Expression Assays for signature genes identified in the targeted host response were used. These Applied Biosystems™ FAM™ dye–labeled assays were preloaded on three flexible-content TaqMan Array Plates, to target (1) viral entry factors, (2) viral restriction factors, and (3) immune signaling genes (Table 1). This TaqMan Array Plate format supports 384-well real-time PCR accommodating up to 381 targets plus controls.

Infection status of the SARS-CoV-2–infected and control samples was determined by qPCR using Applied Biosystems™ TaqPath™ 1-Step RT-qPCR Master Mix, CG (Cat. No. A15299) and run on the Applied Biosystems™ QuantStudio™ 7 Flex Real-Time PCR System. Manufacturer-recommended conditions were followed. Figure 1 shows a schematic of the workflow.

Viral nucleic acid was extracted from nasopharyngeal samples using the Applied Biosystems™ MagMAX™ Viral/Pathogen II Nucleic Acid Isolation Kit (Cat. No. A48383R) on the Thermo Scientific™ KingFisher™ Flex Purification System, following the workflow from the instructions for the Applied Biosystems™ TaqPath™ COVID-19 Combo Kit (400 µL sample input, 2 wash steps).

Bioinformatics analysis

Expression of inflammatory mediator genes, receptor expression genes, and restriction factors in 30 SARS-CoV-2–positive (i.e., SARS-CoV-2–infected) and 30 negative (i.e., SARS-CoV-2–uninfected) subjects were evaluated using the TaqMan Array Plates. The demographics and clinical characteristics of the

Table 1. Preconfigured, flexible TaqMan Arrays for SARS-CoV-2 research.

Viral entry factors		Viral restriction factors		Immune signaling genes: cytokines, chemokines, and growth factors		
ACE2	*CLEC4G*	*LY6E*	*ELF1*	*IL1ß*	*IFNß1*	*CCL2*
TMPRSS2	*FURIN*	*IFITM1*	*REC8*	*IL2*	*IFNG*	*CCL3/MIP1a*
TMPRSS4	*CTSL*	*IFITM2*	*IFIT3*	*IL4*	*TNF*	*CCL5*
TMPRSS11A	*CTSB*	*IFITM3*	*DNAJC6*	*IL5*	*TGFß1*	*CCL11*
TMPRSS11B	*DPP4*	*ZAP/ZC3HAV1*	*ZBP1*	*IL6*	*M-CSF/CSF1R*	*CCL27*
BSG	*NRP1*	*BST2*	*CH25H*	*IL7*	*MIF*	*CXCL1*
ANPEP		*CLEC4D*		*IL10*	*VEGF*	*CXCL10*
				IL12	*SCGF*	*CXCL12*
				IL13	*HGF*	
				IL16	*TNFSF10*	
				IL18		

samples used in this study are shown in Figure 2. For each sample, target gene expression was normalized to the geometric mean of the housekeeping (HK) genes 18S, *GAPDH*, and *PPIA*. Normalized values were reported as ΔC_t between target gene expression and HK expression geomeans for each positive and negative subject.

Expression-dependent analysis (infected only): Differences in target gene expression (i.e., $2^{-\Delta C_t}$) between SARS-CoV-2–positive symptomatic subjects (alive and deceased subjects treated as one group, and alive and deceased subjects treated as two separate groups) and asymptomatic subjects were assessed utilizing the Student's *t*-test or the Tukey-Kramer HSD test. Target gene expression differences between males and females were assessed using the Student's *t*-test. Univariate regression analysis was used to determine the relationship between target gene expression and age. Multivariate regression analysis was used to evaluate the relationship between target gene expression and age, sex, symptomatic/asymptomatic status, and alive (A)/deceased (D) status of the SARS-CoV-2–infected subjects.

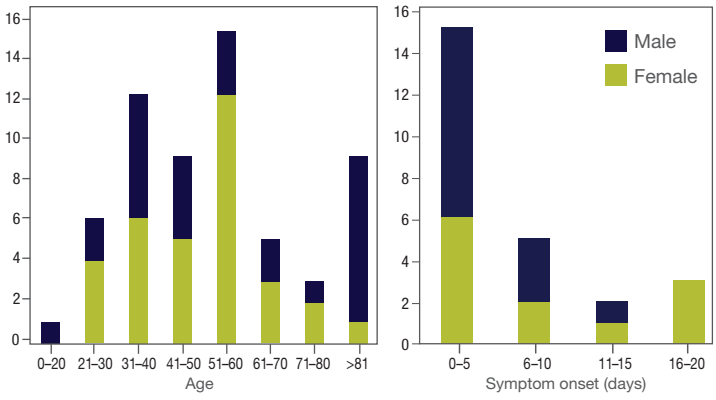

Figure 2. Demographics and clinical characteristics of study samples. Distribution of age, sex, and time of symptom onset for the 30 SARS-CoV-2–positive samples used in this study.

Expression-dependent analysis (SARS-CoV-2–uninfected and infected): Target gene expression differences between SARS-CoV-2–positive and negative subjects were assessed using the Student's *t*-test.

Results

Gene expression analysis of entry factor panel

Host cell receptors like the protease furin and the serine protease TMPRSS2 have been shown to play an important but not essential role in the cleavage of the SARS-CoV-2 spike (S) protein for cell entry. Functional redundancy of receptors has been observed in the SARS-CoV-2 life cycle, wherein blocking of a key entry receptor such as angiotensin-converting enzyme-2 (ACE2) may not inhibit virus infection in specific cells [6]. The complexity of viral entry therefore makes it crucial to understand how differences in the expression levels of these factors between different cell types and genetic backgrounds may impact pathogenesis. To determine the expression levels of SARS-CoV-2–associated viral entry factors (listed in Table 1) in our samples, we used the predesigned TaqMan Array Plates and investigated gene expression differences relative to disease status, disease severity, and sex and age in the infected cohort.

We observed that several entry factors were upregulated in SARS-CoV-2–infected samples compared to healthy controls. These included coronavirus docking receptors *ANPEP* (*APN/CD13*) and *BSG* (*CD147*); lysosomal proteases *CTSB* and *CTSL*; and S priming proteases *FURIN*, *TMPRSS2*, and *TMPRSS4* (Figure 3A). In contrast, *TMPRSS11A* (*ECRG1*) and *TMPRSS11B* had lower relative expression in the nasopharyngeal samples from SARS-CoV-2–infected individuals than from uninfected individuals (Figure 3A). The differences in receptor levels between infected and uninfected individuals may indicate the impact of virus infection on the cellular environment to support the viral life cycle.

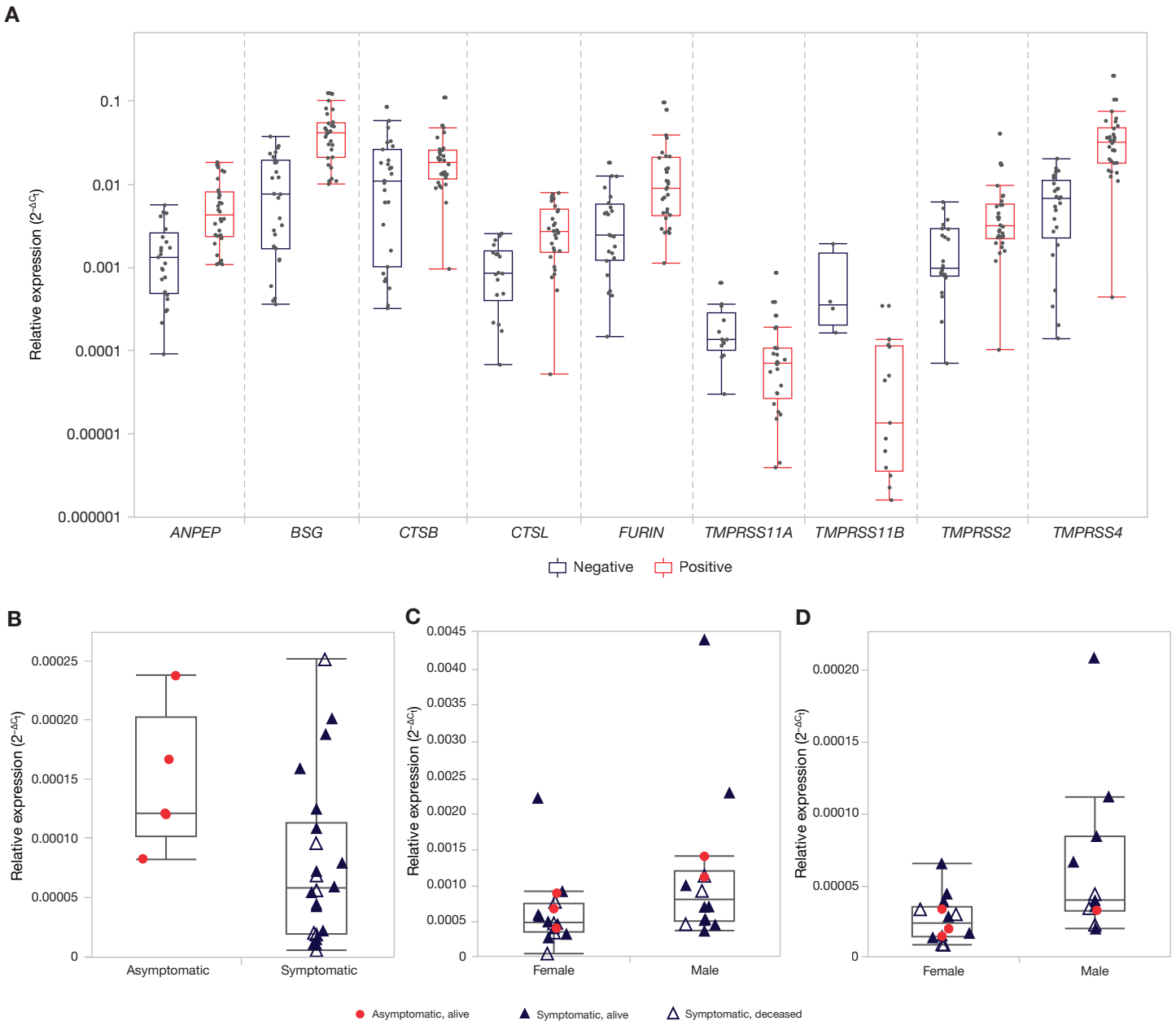

Figure 3. Detection of gene expression changes of entry factors. (A) Comparison between uninfected and SARS-CoV-2–infected samples. **(B)** Comparison of *ACE2* between asymptomatic and symptomatic SARS-CoV-2–individuals. Comparison of **(C)** *TMPRSS2* and **(D)** *TMPRSS11A* between females and males with SARS-CoV-2 infection.

Next, we examined differences in receptor expression based on disease severity (i.e., samples from symptomatic and asymptomatic subjects). ACE2 is a well-studied enzyme that also functions as the cognate docking receptor for SARS-CoV-2, and it is expressed throughout the body, including the lungs, cardiovascular system, central nervous system, and gastrointestinal system. Consistent with several studies, *ACE2* was found to be significantly downregulated in symptomatic individuals compared to asymptomatic individuals, indicating a correlation with disease severity (Figure 3B) [1,4,5]. ACE2 plays a crucial role in regulating inflammation, and its downregulation can worsen the disease pathology via the renin-angiotensin system [7].

We also observed sex-related differences in that an increase in *TMPRSS2* and *TMPRSS11A* expression was seen in infected males compared to infected females (Figure 3C and 3D). Published gene expression data on the lungs of healthy males and females do not show any differences in *TMPRSS2* level [8], similar to our observation in healthy controls (data not shown). However, a preliminary study reported an increased prevalence of androgen-related hair loss in hospitalized SARS-CoV-2–infected

men and suggested a possible link between androgens and SARS-CoV-2 infection [9]. If androgens are indeed increased in men during infection, it might explain our finding, as *TMPRSS2* is positively upregulated by this hormone.

Gene expression analysis of host antiviral restriction factor panel

Several host antiviral effector molecules function as restriction factors to inhibit early viral replication and propagation. Expression of several of these restriction factors is induced by interferons (IFNs), which play a key role in the antiviral response of the body. SARS-CoV-2 is shown to be inhibited by Type I IFNs [10,11], suggesting that interferon-stimulated genes (ISGs) and the antiviral effectors they induce play an important role in host defense against the infection [12]. To determine the expression levels of host restriction factors in SARS-CoV-2–positive and control samples, and investigate their association with disease severity, infection, sex, and disease outcomes, we used the TaqMan Array Plate panel for host restriction factors implicated in the SARS-CoV-2 antiviral response (Table 1).

In this analysis, we observed that several interferon-stimulated genes, including *BST2*, *ELF1*, *LY6E*, and *ZAP*, and the viral nucleic acid binder *ZBP1* were upregulated in SARS-CoV-2–infected samples (Figure 4A). This finding is consistent with studies of *BST2*, *ELF1*, *LY6E*, and *ZBP1* in which these antiviral restriction

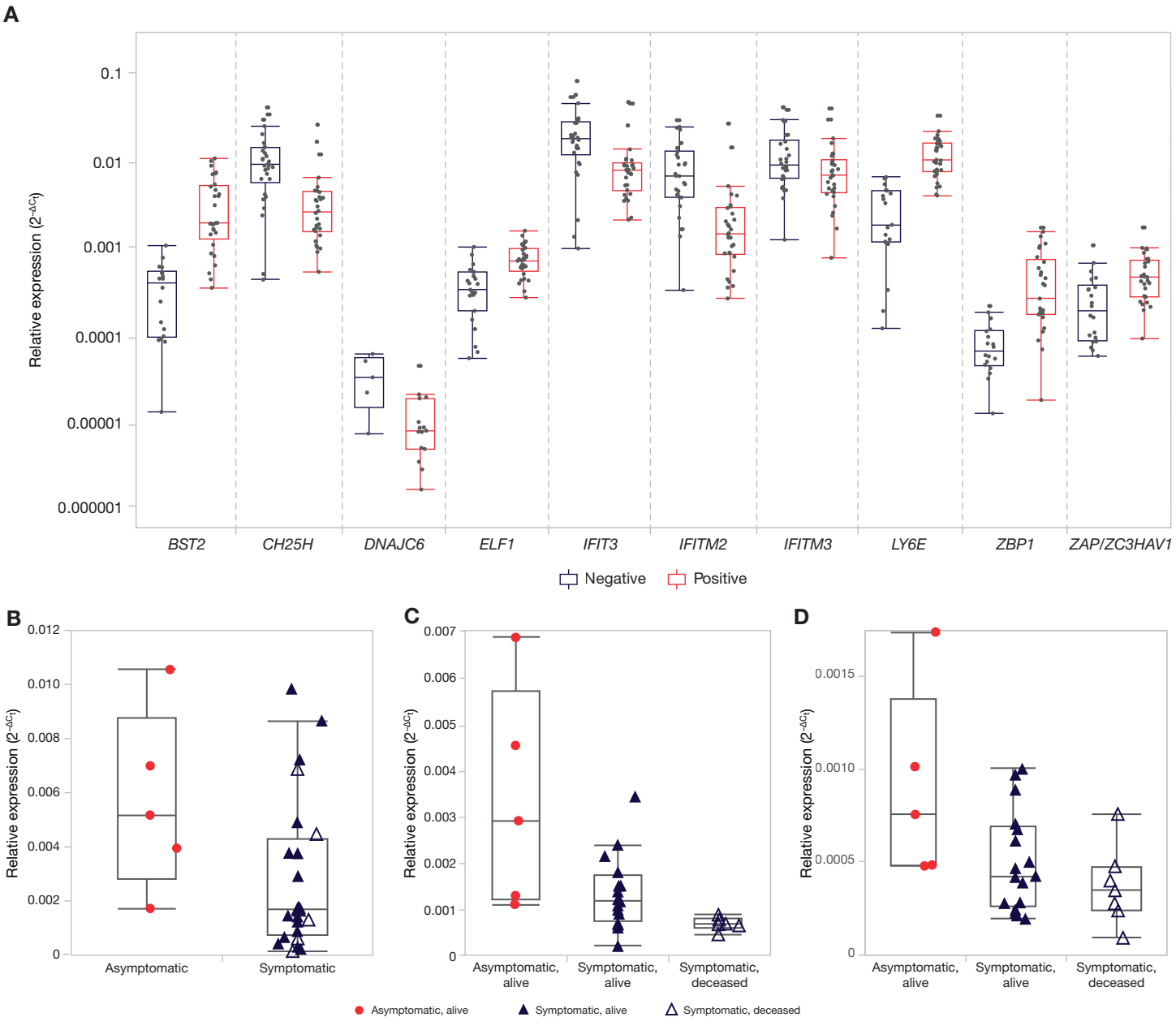

Figure 4. Detection of gene expression changes of host antiviral restriction factors. (A) Comparison between uninfected and SARS-CoV-2–infected samples. **(B)** Comparison of *BST2* between asymptomatic and symptomatic SARS-CoV-2–infected individuals. **(C–D)** Comparison between asymptomatic, symptomatic alive, and symptomatic deceased SARS-CoV-2–infected individuals for **(C)** *REC8* and **(D)** *ZAP/ZC3HAV1*.

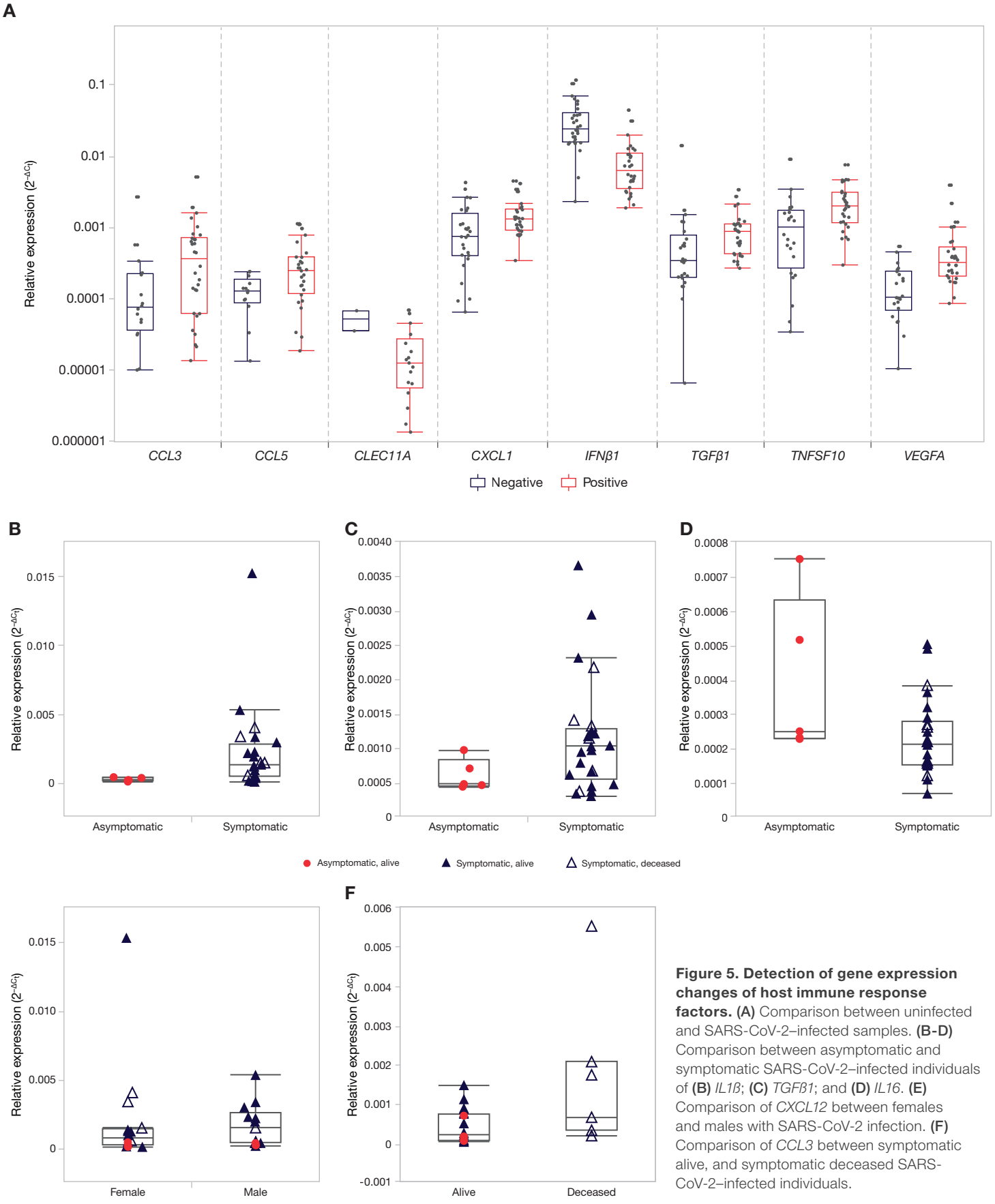

Figure 5. Detection of gene expression changes of host immune response factors. (A) Comparison between uninfected and SARS-CoV-2–infected samples. **(B-D)** Comparison between asymptomatic and symptomatic SARS-CoV-2–infected individuals of **(B)** *IL1ß*; **(C)** *TGFß1*; and **(D)** *IL16*. **(E)** Comparison of *CXCL12* between females and males with SARS-CoV-2 infection. **(F)** Comparison of *CCL3* between symptomatic alive, and symptomatic deceased SARS-CoV-2–infected individuals.

factors are observed to be elevated in SARS-CoV-2–infected subjects compared to uninfected controls [2,13]. Conversely, host antiviral restriction factors *CH25H*, *DNAJC6*, *IFIT3*, *IFITM2*, and *IFITM3* (inhibitors of viral entry) were observed to have lower relative gene expression in SARS-CoV-2–infected samples than in uninfected controls. Contrary to this observation, some studies have reported an increase in *DNAJC6*, *IFIT3*, *IFITM2*, and *IFITM3* expression in SARS-CoV-2–infected samples [2,14,15]. Variance in observations is expected to arise, as different cell types are likely to respond differently to infection. In addition, factors such as genetic backgrounds, comorbidities, and age can influence the inflammatory response and disease progression.

From our panel analysis, we observed that the interferon-stimulated genes *BST2* (*CD317*), *REC8*, and zinc finger antiviral protein (*ZC3HAV1*/*ZAP*) had lower relative gene expression in SARS-CoV-2–infected symptomatic individuals than in asymptomatic individuals (Figure 4B–D). Further, *ZAP* was observed to have lower gene expression in fatal cases than in those that had survived. These results are consistent with published studies that suggest these three restriction factors (i.e., BST2, REC8, and ZAP) support a role in the host immune response to SARS coronaviruses [2,16-18].

Gene expression analysis of inflammatory mediator panel

Understanding how the immune system responds to SARS-CoV-2 infection and its dependence on age, sex, viral load, and genetics, among other known and unknown variables, can be useful in finding potential therapeutics and disease preventatives. During a SARS-CoV-2 viral infection, the immune system's first level of defense is the innate immune response, which includes the IFN response, other cytokines, and chemokines to inhibit viral replication. Studies have found that infected individuals with severe symptoms or a fatal outcome, however, exhibit an exaggerated innate immune response, the hallmark of which is a cytokine storm that can lead to systemic organ failure and death [19,20]. To better understand the host response during SARS-CoV-2 infection, we utilized our TaqMan Array Plate system to investigate correlations between gene expression and infection, disease severity, sex, and/or disease outcomes (Table 1).

Consistent with several published studies, we observed elevated expression of chemokine genes *CCL3*, *CCL5*, and *CXCL1* (Figure 5A) in individuals infected with SARS-CoV-2 [13,21-27]. In addition, we observed elevated expression of the cytokine genes *TGFß1*, *TNFSF10*, and *VEGFA*, which are known to play a role in cell proliferation and apoptosis (Figure 5A). These results are in agreement with several studies that have also identified these inflammatory cytokines as elevated in SARS-CoV-2 infection [3,22,26]. In contrast, we observed that the cytokine genes *CLEC11A* and, surprisingly, *IFNß1* had lower relative expression in SARS-CoV-2–infected individuals than in uninfected individuals (Figure 5A). IFNß1 belongs to the Type I class of interferons and is central to the innate antiviral immune response. Current research studies report heterogeneous findings related to *IFNß1* expression in SARS-CoV-2 infection [3,28]. However, there are reports of delayed type I interferon responses in the nasal epithelium during SARS-CoV-2 infection [29] and inhibition of IFNß activation by various SARS-CoV-2 proteins [30] that may, at least in part, explain our finding.

In our gene expression analysis of inflammatory mediators expressed differentially between SARS-CoV-2–infected symptomatic and asymptomatic individuals, we observed that the genes for both the pro-inflammatory cytokine IL1ß and the anti-inflammatory cytokine TGFß1 were more highly expressed (Figure 5B, C) in symptomatic subjects, whereas expression of the lymphocyte chemoattractant factor *IL16* (Figure 5D) was lower in this population than in asymptomatic individuals. These findings are in concordance with several published studies that reported high *IL1ß* expression in severe disease [18,21,23,31,32]. The observed increase in TGFß1 is consistent with studies on hospitalized patients with severe SARS-CoV-2 infections [25,33]. Modulation of the TGFß signaling pathway during viral infection has been shown to promote fibroblast proliferation and myofibroblast differentiation, ultimately contributing to pulmonary fibrosis as observed in severe SARS-CoV-2 infection.

There are studies that have examined the levels of *IL-16* expression in SARS-CoV-2 infection and have found them to be elevated in severe disease; however, most of these studies are limited to plasma cytokine analysis as opposed to gene expression [34].

Next, to determine if inflammatory mediators are affected by sex differences, we compared gene expression between male and female SARS-CoV-2–infected individuals. In this analysis, we observed that the chemokine gene *CXCL12* had elevated expression in infected males compared to females (Figure 5E). While studies have observed elevated expression of *CXCL12* during viral infections and in critically ill SARS-CoV-2–infected patients, there is currently a lack of data on sex-based variation of this cytokine during infection [35-37]. No significant difference in the expression of this gene was observed between healthy males and females (data not shown).

Finally, our analysis to determine the relationship between inflammatory mediators and disease outcome revealed that the chemokine and acute inflammatory responder *CCL3* had higher relative gene expression in deceased individuals than in those who survived (Figure 5F). This observation is consistent with BALF (bronchoalveolar lavage fluid) studies that found several

cytokines including *CCL3* to be elevated in severe cases where ICU admission was required [24,25].

Conclusions

Given the severe impact that SARS-CoV-2 has had on healthcare and the global economy, and its ongoing evolution, there remains an urgent need to deeply understand the virus biology to develop effective therapeutics and biomarkers to predict disease severity.

In our pilot analysis, we observed differential expression of several genes involved in host cell entry, regulatory factors, and inflammatory response factors based on the infection status of the individuals, disease severity, and disease outcomes, as well as sex. Several of our findings (e.g., elevated expression of cell entry factors *BSG*, *FURIN*, *TMPRSS2*; host restriction factors *BST2*, *ELF1*, *LY6E*, and *ZBP1*; and inflammatory mediators *CCL3*, *CCL5*, *CXCL1*, *TGFß1*, *TNFSF10*, and *VEGFA* in SARS-CoV-2–infected individuals) were largely consistent with published studies. In addition, our analyses revealed associations between several genes involved in various aspects of the viral life cycle or host response with disease severity, outcome, and sex, that have previously not been described. For instance, our study showed sex-related differences in the expression of specific virus entry receptors and inflammatory mediators between infected males and females, which warrant further investigation.

In conclusion, our study illustrates the utility of flexible TaqMan Arrays to investigate the molecular basis of disease development of SARS-CoV-2 through interrogation of genes involved in virus entry and restriction, and the inflammatory response. Identification of differentially expressed genes based on infection status, disease severity, and/or sex can potentially reveal targets for therapeutic treatment and predictive biomarkers, in addition to shedding light on the biology of infection. The flexible TaqMan Arrays offer a versatile, highly sensitive, medium-throughput solution for obtaining novel molecular insights into any disease of interest through simultaneous gene expression analysis of relevant targets.

Learn more about our solutions for SARS-CoV-2 research at **thermofisher.com/qpcr4sarscov2**

Explore our full portfolio of TaqMan Cards and Plates at **thermofisher.com/taqmanarrays**

References

1. Hou Y., et al. Aging-related cell type-specific pathophysiologic immune responses that exacerbate disease severity in aged COVID-19 patients. *Aging Cell,* 2022. 21(2):e13544.
2. Martin-Sancho L., et al. Functional landscape of SARS-CoV-2 cellular restriction. *Mol Cell*, 2021. 81(12):2656-2668.e8.
3. Galbraith M.D., et al. Specialized interferon action in COVID-19. *Proc Natl Acad Sci U S A*, 2022. 119(11):e2116730119.
4. Rossi Á.D., et al. Association between *ACE2* and *TMPRSS2* nasopharyngeal expression and COVID-19 respiratory distress. *Scientific Reports*, 2021. 11:9658.
5. Mukherjee S. and Pahan K. Is COVID-19 gender-sensitive? *J Neuroimmune Pharmacol*, 2021. 16:38–47.
6. Wang S., et al. AXL is a candidate receptor for SARS-CoV-2 that promotes infection of pulmonary and bronchial epithelial cells. *Cell Res*, 2021. 31:126–140.
7. Mehrabadi M.E., et al. Induced dysregulation of *ACE2* by SARS-CoV-2 plays a key role in COVID-19 severity. *Biomed Pharmacother*, 2021. 137:111363.
8. Asselta R., et al. *ACE2* and *TMPRSS2* variants and expression as candidates to sex and country differences in COVID-19 severity in Italy. *Aging*, 2020. 512:10087-10098.
9. Goren A., et al. A preliminary observation: Male pattern hair loss among hospitalized COVID-19 patients in Spain - A potential clue to the role of androgens in COVID-19 severity. *J Cosmet Dermatol*, 2020. 19(7):1545-1547.
10. Mantlo E., et al. Antiviral activities of type I interferons to SARS-CoV-2 infection. *Antiviral Res*, 2020. 179:104811.
11. Sallard E., et al. Type 1 interferons as a potential treatment against COVID-19. *Antiviral Res*, 2020. 178:104791.
12. Mathew D., et al. Deep immune profiling of COVID-19 patients reveals distinct immunotypes with therapeutic implications. *Science, 2020*. 369(6508):eabc8511.
13. Zhao X., et al. LY6E restricts entry of human coronaviruses, including currently pandemic SARS-CoV-2. *J Virol*, 2020. 94(18):e00562-20.
14. Gao X., et al. Genome-wide screening of SARS-CoV-2 infection-related genes based on the blood leukocytes sequencing data set of patients with COVID-19. *J Med Virol*, 2021. 93:5544-5554.
15. Park A. and Harris L.K. Gene expression meta-analysis reveals interferon-induced genes associated with SARS infection in lungs. *Front Immunol*, 2021. 12:694355.
16. Wang S-M, et al. Severe acute respiratory syndrome coronavirus spike protein counteracts BST2-mediated restriction of virus-like particle release. *J Med Virol*, 2019. 91:1743-1750.
17. Nchioua R., et al. SARS-CoV-2 is restricted by zinc finger antiviral protein despite preadaptation to the low-CpG environment in humans. *mBio*, 2020. 11(5):e01930-20.
18. Sposito B., et al. The interferon landscape along the respiratory tract impacts the severity of COVID-19. *Cell*, 2021. 19(184):4953-4968.
19. Zhou X. and Ye Q. Cellular immune response to COVID-19 and potential immune modulators. *Frontiers in Immunology*, 2021. 12:646333.
20. Li Q., et al. Immune response in COVID-19: what is next? *Cell Death Differ*, 2022. 29:1107–1122.
21. Li S., et al. SARS-CoV-2 triggers inflammatory responses and cell death through caspase-8 activation. *Sig Transduct Target Ther*, 2020. 5:235.
22. Chua R.L., et al. COVID-19 severity correlates with airway epithelium-immune cell interactions identified by single-cell analysis. *Nat Biotechnol*, 2020. 38(8):970-979.
23. Khan S., et al. SARS-CoV-2 spike protein induces inflammation via TLR2-dependent activation of the NF-κB pathway. *Elife*, 2021. 10:e68563.

24. Sheerin D., et al. Immunopathogenic overlap between COVID-19 and tuberculosis identified from transcriptomic meta-analysis and human macrophage infection. *iScience*, 2022. 25(6):104464.
25. Xiong Y., et al. Transcriptomic characteristics of bronchoalveolar lavage fluid and peripheral blood mononuclear cells in COVID-19 patients. *Emerg Microbes & Infect*, 2020. 9(1):761-770.
26. Xu G., et al. The differential immune responses to COVID-19 in peripheral and lung revealed by single-cell RNA sequencing. *Cell Discov*, 2020. 6:73.
27. Zeng Z., et al. CCL5/CCR5 axis in human diseases and related treatments. *Genes Dis*, 2022. 9(1):12-27.
28. Schaller M.A., et al. *Ex vivo* SARS-CoV-2 infection of human lung reveals heterogeneous host defense and therapeutic responses. *JCI Insight*, 2021. 6(18):e148003.
29. Hatton C.F., et al. Delayed induction of type I and III interferons mediates nasal epithelial cell permissiveness to SARS-CoV-2. *Nat Commun*, 2021. 12:7092.
30. Lei X., et al. Activation and evasion of type I interferon responses by SARS-CoV-2. *Nat Commun*, 2020. 11(1):3810.
31. Bell L.C.K., et al. Transcriptional response modules characterize IL-1β and IL-6 activity in COVID-19. *iScience*, 2021. 24(1):101896.
32. McElvaney O.J., et al. Characterization of the inflammatory response to severe COVID-19 illness. *Am J Respir Crit Care Med*, 2020. 202(6):812-821.
33. Witkowski M., et al. Untimely TGFβ responses in COVID-19 limit antiviral functions of NK cells. *Nature*, 2021. 600(7888):295-301.
34. Lucas C., et al. Longitudinal analyses reveal immunological misfiring in severe COVID-19. *Nature*, 2020. 584:463–469.
35. Ghanem M., et al. French COVID Cohort Study Group. Blood fibrocytes are associated with severity and prognosis in COVID-19 pneumonia. *Am J Physiol Lung Cell Mol Physiol*, 2021. 321(5):L847-L858.
36. Shaharuddin S.H., et al. Deleterious effects of SARS-CoV-2 infection on human pancreatic cells. *Front Cell Infect Microbiol*, 2021 11:678482.
37. Shao Y, et al. Endothelial immunity trained by coronavirus infections, DAMP stimulations and regulated by anti-oxidant NRF2 may contribute to inflammations, myelopoiesis, COVID-19 cytokine storms and thromboembolism. *Front Immunol*, 2021. 12:653110.

Ordering information

Cat No.	Description
A15299	TaqPath 1-Step RT-qPCR Master Mix, CG
A48383R	MagMAX Viral/Pathogen II Nucleic Acid Isolation Kit
RAH49YX	TaqMan Coronavirus Entry Factor Flexible Array Panel 96-well, 0.2 mL Human*
RAWCWKF	TaqMan Coronavirus Restriction Factor Flexible Array Panel 96-well, 0.2 mL Human*
RA322F2	TaqMan Coronavirus Immune Signaling Flexible Array Panel 96-well, 0.2 mL Human*

* Additional formats and species available.

Discover more TaqMan Array Panels at
thermofisher.com/taqmanarrays