Statistical Methods

We fit two linear mixed-effect models to each biomarker dataset. One model included both time and the classification of R and S groups as predictors (alternative hypothesis):

$$Y_{it} = a + b_i + ct + dP + eG + \varepsilon_{it}$$

and the other model excluded the factor of R and S groups by removing the term dG (null hypothesis):

$$Y_{it} = a + b_i + ct + dP + \varepsilon_{it}$$

In the models, Y_{it} represents the predicted biomarker level of one type for patient i at time t. a and b_i are fixed and patient-specific random effects of the intercept and follows a normal distribution with a zero mean, i.e., $b_i \sim N(0, \sigma_1)$. c is the coefficient of the independent variable t (time). Considering the disease severity is associated with both virus-induced damage and immune response-induced inflammation, we introduced a new predictor P to indicate the period where virus-induced damage is relatively dominant. We set $P = 1$ for $t \leq 14$ days to indicate the existence of virus-caused damage before 14 days because SARS-CoV-2 virus was normally cleared within 14 days after disease onset(1-3) and $P = 0$ for $t > 14$ days. d is the coefficient of P. e is the coefficient of group-indicating variable G ($G = 0$ when the patient is in S group and $G = 1$ for the R group). ε_{it} is the observation error and follows $\varepsilon_{it} \sim N(0, \sigma_2)$.

We then performed a likelihood ratio test to examine if we should reject the null hypothesis (i.e., the R and S groups have no effect on the predicted biomarker level) based on a confidence level of 95% in order to conclude if the mean biomarker levels are statistically distinct between the R and S groups. Note that the analyses for CD4+ T cells and CD8+ T cells did not include the data from patient S6 due to the reason provided in the main text.

The analysis was performed in RStudio (version 1.1.383) using the package "lme4" (Bates et al. 2015. J Stat Softw, https://www.jstatsoft.org/%20article/view/v067i01/).

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2. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med.* 2020;26(5):672-5.
3. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N Engl J Med.* 2020;382(12):1177-9.