Supplemental Information

Loss of Bcl-6-Expressing T Follicular Helper Cells and Germinal Centers in COVID-19

Naoki Kaneko, Hsiao-Hsuan Kuo, Julie Boucau, Jocelyn R. Farmer, Hugues Allard-Chamard, Vinay S. Mahajan, Alicja Piechocka-Trocha, Kristina Lefteri, Matthew Osborn, Julia Bals, Yannic C. Bartsch, Nathalie Bonheur, Timothy M. Caradonna, Josh Chevalier, Fatema Chowdhury, Thomas J. Diefenbach, Kevin Einkauf, Jon Fallon, Jared Feldman, Kelsey K. Finn, Pilar Garcia-Broncano, Ciputra Adijaya Hartana, Blake M. Hauser, Chenyang Jiang, Paulina Kaplonek, Marshall Karpell, Eric C. Koscher, Xiaodong Lian, Hang Liu, Jinqing Liu, Ngoc L. Ly, Ashlin R. Michell, Yelizaveta Rassadkina, Kyra Seiger, Libera Sessa, Sally Shin, Nishant Singh, Weiwei Sun, Xiaoming Sun, Hannah J. Ticheli, Michael T. Waring, Alex L. Zhu, Galit Alter, Jonathan Z. Li, Daniel Lingwood, Aaron G. Schmidt, Mathias Lichterfeld, Bruce D. Walker, Xu G. Yu, Robert F. Padera Jr., Shiv Pillai, and the Massachusetts Consortium on Pathogen Readiness Specimen Working Group
Table S1 (Related to Figs. 1-4). Autopsied COVID-19 Patients studied by immunofluorescence and multispectral imaging

| Duration of hospital stay | 1-8 days | 16-36 days |
|---------------------------|----------|------------|
|                           | n=5      | n=6        |

**Clinical Course**

| Duration of hospital stay | 1-8 days | 16-36 days |
|---------------------------|----------|------------|
|                           | n=5      | n=6        |

**Demographics**

| Demographics        | 1-8 days | 16-36 days |
|---------------------|----------|------------|
| Gender (% male)     | 60%      | 80%        |

**Maximum Laboratory Values**

| Laboratory Value     | 1-8 days | 16-36 days |
|----------------------|----------|------------|
| CRP (mg/L)           | 199.2 (+ 102.3) | 74.5 (+ 44.8) |
| LDH (U/L)            | 590.0 (+ 149.9) | 423.0 (+ 128.2) |
| Ferritin (ug/L)      | 703 (+ 618.0) | 410.8 (+ 166.1) |
| D-dimer (ng/mL)      | 1374 to >4000 | 725 to >4000 |

Body mass index (BMI), C-reactive protein (CRP), lactate dehydrogenase (LDH), standard deviation (s.d.)
### Table S2 (Related to Figs. 1, 3 and 4). Non-COVID-19 Autopsied Controls

| Age | Gender | Presumed Cause of Death                                      |
|-----|--------|-------------------------------------------------------------|
| 77  | F      | Multi-organ system failure, pancreatitis                     |
| 78  | M      | Non-metastatic bladder malignancy                            |
| 64  | M      | Multi-organ system failure, thromboembolic infarcts         |
| 78  | M      | Respiratory failure, treatment resistant MAC                 |
| 69  | M      | Cerebellar hemorrhage                                        |
| 66  | F      | Fibrinous pericarditis, subpleural fibrosis                  |
Table S3 (Related to Figs. 2-4). Control Spleen Samples from Massachusetts General Hospital

| Age | Gender |
|-----|--------|
| 61  | M      |
| 20  | M      |
| 54  | F      |
| 74  | F      |
| 59  | M      |
| 68  | F      |
| 58  | M      |
**Table S4 (Related to Figs. 5-7).** Summary of information on COVID-19 patients (n=68) in whom circulating B cells were analyzed by flow cytometry.

|                        | Convalescence | Moderate | Severe (CRP int) | Severe (CRP hi) |
|------------------------|---------------|----------|------------------|-----------------|
|                        | mean (+ SD)   | mean (+ SD) | mean (+ SD)       | mean (+ SD)     |
| n=39                   | n=4           | n=10     | n=15             |
| Demographics           |               |          |                  |                 |
| Age (years)            | 44.8 (+ 15.1) | 35.5 (+ 15.4) | 59.3 (+ 11.0)**  | 58.0 (+ 13.9)** |
| Deceased (%)           | 0.0           | 0.0      | 10.0             | 13.3            |
| Gender (% male)        | 28.2          | 50.0     | 60.0             | 66.7*           |
| BMI (kg/m²)            | 24.5 (+ 4.6)  | 31.1 (+ 8.7) | 35.7 (+ 8.1)**   | 33.5 (+ 8.7)**  |
| Clinical Course        |               |          |                  |                 |
| Hospitalized due to COVID-19 (%) | 0.0          | 0.0      | 100.0            | 100.0           |
| Admitted to ICU due to COVID-19 (%) | 0.0          | 0.0      | 70.0             | 86.7            |
| Mechanically ventilated due to COVID-19 (%) | 0.0          | 0.0      | 70.0             | 86.7            |
| ECMO received due to COVID-19 (%) | 0.0          | 0.0      | 0.0              | 6.7             |
| Total Hospitalization (days) | na           | na       | 26.5 (+ 17.9)    | 55.5 (+ 35.3)*  |
| Symptom Duration at Draw (days) | na           | 17.0 (+ 9.7) | 15.2 (+ 12.3)    | 32.6 (+ 14.4)** |
| Convalescence Period at Draw (days) | 39.9 (+ 15.0) | na       | na               | na              |
| Maximum Laboratory Values |               |          |                  |                 |
| CRP (mg/L)             | na            | na       | 103.3 (+ 40.2)   | 314.6 (+ 72.5)**|
| ESR (mm/h)             | na            | na       | 70.6 (+ 44.1)    | 102.0 (+ 36.7)  |
| LDH (U/L)              | na            | na       | 526.5 (+ 240.5)  | 707.2 (+ 399.7) |
| Ferritin (ug/L)        | na            | na       | 2843.7 (+ 5616.7)| 3535.9 (+ 3955.3)|
| D-dimer (ng/mL)        | na            | na       | 4399.0 (+ 3157.5)| 7669.3 (+ 2691.4)* |
| Day of Draw Laboratory Values |             |          |                  |                 |
| ALC (K/uL)             | 1.50 (+ 0.40) | na       | 1.40 (+ 0.62)    | 1.55 (+ 0.65)   |
| CRP (mg/L)             | na            | na       | 39.8 (+ 47.8)    | 74.4 (+ 72.3)   |

Convalescence was defined as a clinically asymptomatic state on the date of blood draw, either from a baseline asymptomatic state or recuperated from moderate clinical symptoms of COVID-19. Moderate disease was defined as active clinical symptoms of COVID-19 on the date of blood draw that did not necessitate a hospital admission. Severe disease was defined as active clinical symptoms of COVID-19 on the date of blood draw that did necessitate a hospital admission. Severe disease was further subdivided by maximum CRP level during hospital admission as CRP < 200 mg/L ‘CRP intermediate (int)’ and CRP > 200 mg/L ‘CRP high (hi).’ Absolute lymphocyte count (ALC), Body mass index (BMI), C-reactive protein (CRP), extracorporeal membrane oxygenation (ECMO), erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), not available (na), standard deviation (SD), *significance by Student’s t-test to ‘convalescence’ group, +significance by Student’s t-test to ‘severe (CRP int)’ group.