## SARS-CoV-2 Cellular Tropism

| Panel Specimen                      | Case(s) | Cell type(s)                                      |
|-------------------------------------|---------|--------------------------------------------------|
| a Sinus turbinate                   | P42     | Mucus secreting epithelium                       |
| b Lip, oral mucosa                  | P18     | Squamous epithelium                              |
| c Lip, minor salivary gland         | P18     | Minor salivary gland (lip)                        |
| d Bronchus                          | P18     | Bronchial epithelium, endothelium (*)            |
| e Bronchus                          | P20     | Mucus secreting epithelium                       |
| f Lung                              | P42     | Pneumocytes, Type I (*), Type II (#)             |
| g Lung                              | P24     | Hyaline membrane (*) mononuclear leukocyte (#) (60X) |
| h Heart                             | P19     | Cardiac myocyte                                  |
| i Aorta                             | P19     | Tunica intima                                    |
| j Aorta                             | P19     | Tunica media                                     |
| k Trachea                           | P19     | Endothelium(*), smooth muscle (#)                |
| l Esophagus                         | P18     | Stratified squamous epithelum                    |
| m Appendix                          | P19     | Colonic epithelium(*), mononuclear leukocytes (#) |
| n Colon                             | P16     | Colonic epithelium(*), mononuclear leukocytes (#) |
| o Liver                             | P19     | Hepatocyte (*), bile duct epithelium (#)         |
| p Liver                             | P19     | Hepatocyte (*), Kupffer cell (#)                 |
| q Pancreas                          | P18     | Exocrine pancreatic cells                        |
| r Adrenal gland                     | P19     | Adrenal cortical epithelium                      |
| s Thyroid                           | P19     | Follicular cells                                 |
| t Kidney                            | P18     | Glomerular epithelium                            |
| u Kidney                            | P18     | Tubular epithelium                               |
| v Uterus                            | P35     | Endometrial stroma (*), endometrial glandular epithelium (#) |
| w Uterus                            | P35     | Myometrium                                       |
| x Ovary                             | P20     | Ovarian stromal cells                            |
| y Testis                            | P20     | Sertoli cells (*), spermatid (#)                 |
| z Testis                            | P20     | Sertoli cells (*), Leydig cells (#)              |
| aa Testis, seminiferous tubules     | P19     | Seminiferous tubule epithelium                   |
| bb Lymph node                       | P19     | Mononuclear leukocytes                            |
| cc Lymph node                       | P19     | Mononuclear leukocytes                            |
| dd Spleen                           | P19     | Mononuclear leukocytes                            |
| ee Pancreas                         | P18     | Arterial smooth muscle                            |
| ff Ileum                            | P19     | Intestinal epithelium (*), smooth muscle (#)     |
| gg Trachea                          | P27     | Chondrocyte (60X)                                |
| hh Skin                             | P43     | Epithelium, outer root sheath of a hair follicle |
| ii Pericardium                      | P18     | Fibroblast                                       |
| jj Bronchus                         | P43     | Endothelium (*), smooth muscle (#)               |
| kk Psoas muscle                     | P18     | Skeletal muscle                                  |
| ll Sciatic nerve                    | P20     | Schwann cells                                    |
| mm Brain, frontal lobe              | P40     | NOS                                              |
| nn Brain, parietal lobe             | P38     | NOS                                              |
| oo Brain, occipital lobe            | P38     | Endothelium (#), NOS (*)                         |
| pp Brain, corpus callosum           | P38     | NOS                                              |
| qq Brain, thalamus                  | P33     | NOS                                              |
| rr Brain, hypothalamus              | P40     | NOS                                              |
| ss Brain, basal ganglia             | P40     | NOS                                              |
| tt Brain, midbrain                  | P43     | NOS                                              |
| uu Brain, cerebellum                | P42     | Granular layer neurons                           |
| vv Cervical spinal cord             | P38     | Ependymal cells                                  |
| ww Brain, temporal lobe             | P43     | NOS                                              |
| xx Cervical spinal cord             | P40     | NOS within white matter                          |
| yy Lung and basal ganglia           | P40     | Table of chromogenic IHC and ISH validation images |
| zz Basal ganglia, cervical spinal cord, lung, hypothalamus | P42, P38 | IF validation images |
| aaa Hypothalamus, cervical spinal cord, and cerebellum | P38, P42 | Table of additional chromogenic IHC and ISH control images for Fig. 3 |
| bbb Cortex, brain NOS, cervical spinal cord, and cerebellum | P38, P42 | Table of additional CNS chromogenic and ISH validation images |
| ccc Heart, interventricular septum   | P18, P29 | Examples of image analysis with and without markup |
| VY | Lung | Brain, basal ganglia |
|----|------|---------------------|
|    | P18  | Pre-pandemic        |
|    | P40  | Pre-pandemic        |

**Chromogenic immunohistochemistry**
- **Anti-nucleocapsid Ab**
- **Rabbit IgG isotype control**

**In situ hybridization**
- **Spike**
- **Nucleocapsid**
- **Positive control human housekeeping gene**
- **Negative Control E. coli gene**
zz) To confirm SARS-CoV-2 antibody specificity within CNS and lung tissues, sections of pre-pandemic lung (top left), basal ganglia (top middle), and spinal cord (top right) were labeled with primary antibodies against NP1 (lung and CNS, green) and NeuN (CNS only, magenta). As a positive control, lung from P42 was labeled for SARS-CoV-2 NP1 (bottom left, green). Within the CNS, microglial cells were identified via TMEM119 labeling (bottom right, magenta) and were consistently found to be negative for SARS-CoV-2 protein (green). Hoechst 33342 was used to identifying nuclei and is shown in blue.
|          | P38 Hypothalamus | P42 Cervical spinal cord | P38 Cerebellum |
|----------|------------------|--------------------------|----------------|
| ISH positive control human housekeeping gene | ![ISH positive control human housekeeping gene](image) | ![ISH positive control human housekeeping gene](image) | ![ISH positive control human housekeeping gene](image) |
| ISH negative control E. Coli gene | ![ISH negative control E. Coli gene](image) | ![ISH negative control E. Coli gene](image) | ![ISH negative control E. Coli gene](image) |
| Chromogenic IHC Rabbit IgG isotype control | ![Chromogenic IHC Rabbit IgG isotype control](image) | ![Chromogenic IHC Rabbit IgG isotype control](image) | ![Chromogenic IHC Rabbit IgG isotype control](image) |

RNA ISH and chromogenic IHC controls from P40 are contained in panel yy (page 7)
### Adequate pre-pandemic ISH controls were not available for cerebellum
### in situ hybridization quantification of interventricular septum (n=16)

| Patient ID | ddPCR N copies per ng RNA (mean) | Positive cells (median) |
|------------|----------------------------------|-------------------------|
| P18        | 60.2478                          | 110.0                   |
| P37        | 47.3838                          | 80.5                    |
| P27        | 24.1469                          | 50.5                    |
| P32        | 14.7105                          | 46.0                    |
| P24        | 4.2594                           | 74.5                    |
| P16        | 1.0061                           | 28.0                    |
| P21        | 0.5922                           | 23.0                    |
| P7         | 0.3116                           | 89.5                    |
| P39        | 0.1489                           | 26.5                    |
| P38        | 0.0632                           | 52.0                    |
| P15        | 0.0519                           | 52.5                    |
| P29        | 0.0081                           | 21.5                    |
| P42        | 0.0027                           | 28.0                    |
| P12        | 0.0000                           | 21.0                    |
| P17        | 0.0000                           | 18.0                    |
| P31        | 0.0000                           | 26.0                    |