# Supplementary information

## Supplementary Table 1. Global statistics of the dataset used in the analysis.

| Dataset       | TPI          | SRA accession | Total reads   | Selected transcripts$^1$ | Transcripts per GEM | Selected GEMs$^3$ | Selected genes$^4$ |
|---------------|--------------|---------------|---------------|--------------------------|---------------------|------------------|-------------------|
| Bronchial     | Mock         | SRR13711613   | 604,127,582   | 92,488,540               | 1,878-16,810        | 16,331           |
| epithelial    | 1 dpi        | SRR13711614   | 589,830,183   | 75,836,207               | 1,232-30,555        | 9,345            |
| cells         |              |               |               |                          |                     |                  |
|              | 2 dpi        | SRR13711615   | 653,390,536   | 90,806,792               | 1,752-20,120        | 12,472           |
|              | 3 dpi        | SRR13711616   | 573,563,158   | 91,799,408               | 1,781-13,181        | 17,820           |
| Colon*        | Mock         | SRR12508049   | 294,735,427   | 71,838,718               | 1,030-47,489        | 4,024            |
| organoids     |              | SRR12508050   | 107,844,234   | 30,338,763               | 1,149-46,952        | 3,992            |
|              | 12 hpi       | SRR12508052   | 304,892,652   | 79,187,463               | 1,149-46,952        | 3,992            |
|              |              | SRR12508053   | 123,149,496   | 37,510,656               |                     |                  |
|              | 24 hpi       | SRR12508055   | 307,339,187   | 79,260,961               | 1,232-31,513        | 4,407            |
|              |              | SRR12508056   | 121,191,449   | 35,611,648               |                     |                  |
| Ileum*        | Mock         | SRR12508058   | 310,516,022   | 77,784,527               | 968-40,234          | 3,457            |
| organoids     |              | SRR12508059   | 115,263,635   | 35,651,119               |                     |                  |
|              | 12 hpi       | SRR12508061   | 308,565,909   | 73,011,266               | 1,100-40,163        | 4,115            |
|              |              | SRR12508062   | 116,802,746   | 33,699,484               |                     |                  |
|              | 24 hpi       | SRR12508064   | 304,036,624   | 69,478,009               | 908-42,604          | 3,629            |
|              |              | SRR12508065   | 115,167,592   | 33,137,814               |                     |                  |
|               |              |               | 1,270,352,528 | 322,762,219              | 12,201              | 8,334            |

$^1$Only transcripts unambiguously attributed to a single gene and a single unique molecular identifier (UMI) were included in the analysis.

$^2$Specifies the minimum and maximum number of transcripts required for a cell in the corresponding dataset to be included in the analysis.

$^3$Total number of cells selected based on the number of transcripts.

$^4$Total number of genes included in the analysis for each cell type. Selected genes required to expressed in a minimum of one thousand cells.

$^*$Datasets from colon and ileum organoids comprised two separate files per experiment that were merged for subsequent analyses.

Abbreviations: GEM: Gel Bead-in Emulsion, SRA: Sequence read archive, TPI: time post-inoculation, dpi: days post-infection, hpi: hours post-infection.

Aggregated values for selected columns are shown in bold.
Supplementary Figure 1. Filtering of void GEMs and multiplets. GEMs were ordered with respect to the number of transcripts the local standard deviation of the log_{10} using window size of five datapoints. Upper and lower thresholds delimiting multiples and voids GEMS were determined using 1.5×IQR rule. The cells used in this study correspond to the grey area.
Supplementary Figure 2. Global composition of the scRNA-seq datasets.  
a Proportion of GEMs from mock and infected treatments from each dataset.  
b Proportion of bystanders, infected, mock, and infected mock cells in each dataset.  
c Distribution of cells with respect to viral loads for each treatment.  
Statistics presented in these plots correspond to observed counts.  
d Selecting cell with respect to number of individual transcripts, instead of number of detected genes increases the proportion of cells with high viral accumulations.
Supplementary Figure 3. Transcriptional response of ileum organoid cells infected with human astrovirus 1 (HAstV1). a Proportion of selected cells at each time post-infection. b Distribution of HAstV1 accumulations in the infected cell subset. c Average transcriptional response of ileum cells illustrating a very different response than SARS-CoV-2. d Response profiles of genes from components 1 (global SARS-CoV-2 response), 2 (genes involved in translation), and 3 (mitochondrial-encoded genes) to HAstV1 infection.
Supplementary Data 1. Database of reference human messenger RNAs and SARS-CoV-2 genomes used for mapping reads. Raw count matrices.

Supplementary Data 2. Expression matrices and transcript levels in uninfected cells.

Supplementary Data 3. Differential Expressed Gene analysis used in the volcano plots analysis. Datasets and results used in the Gene Ontology analyses. Classification of outliers.

Supplementary Data 4. Transcriptional profiles for all genes in each cell type.

Supplementary Data 5. Networks used in the analyses presented in Figs. 5 and 6.

Supplementary Data 6. Transcriptional analysis of human astrovirus 1 infection in ileum organoids.