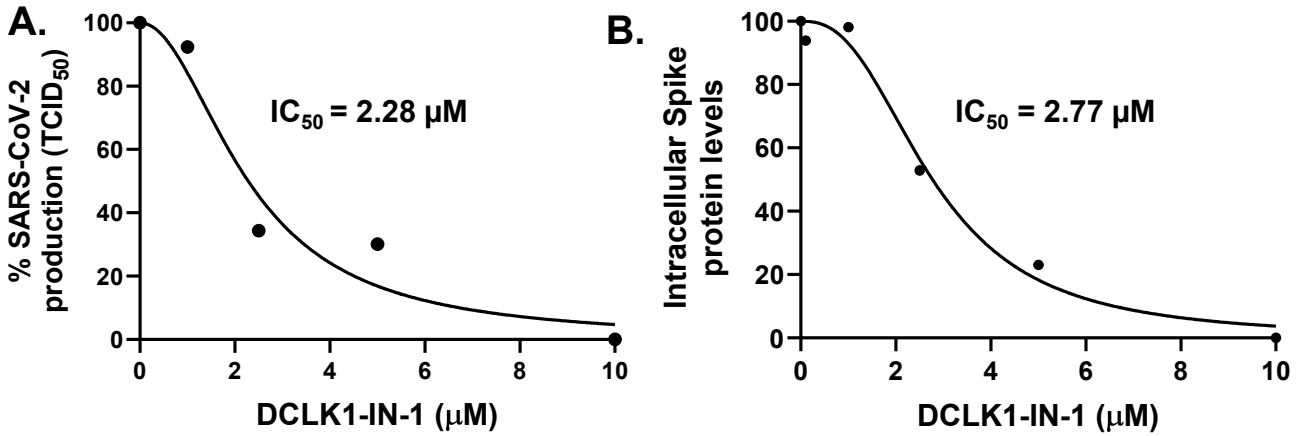



**Fig. S1.** Evaluation of $IC_{50}$ for DCLK1-IN-1 against SARS-CoV-2. (A) $IC_{50}$ of DCLK1-IN-1 (DCLK1 kinase inhibitor) for the inhibition of SARS-CoV-2 production. The virus-infected Calu 3 cells were treated with increasing amounts of DCLK1-IN-1 and the media supernatant were used for $TCID_{50}$ assay. (B) $IC_{50}$ for DCLK1-IN-1 against Spike expression was determined by Western blot of the infected Calu 3 cell lysates at varying concentrations of the inhibitor. The spike protein band intensities were quantitated by Image J.

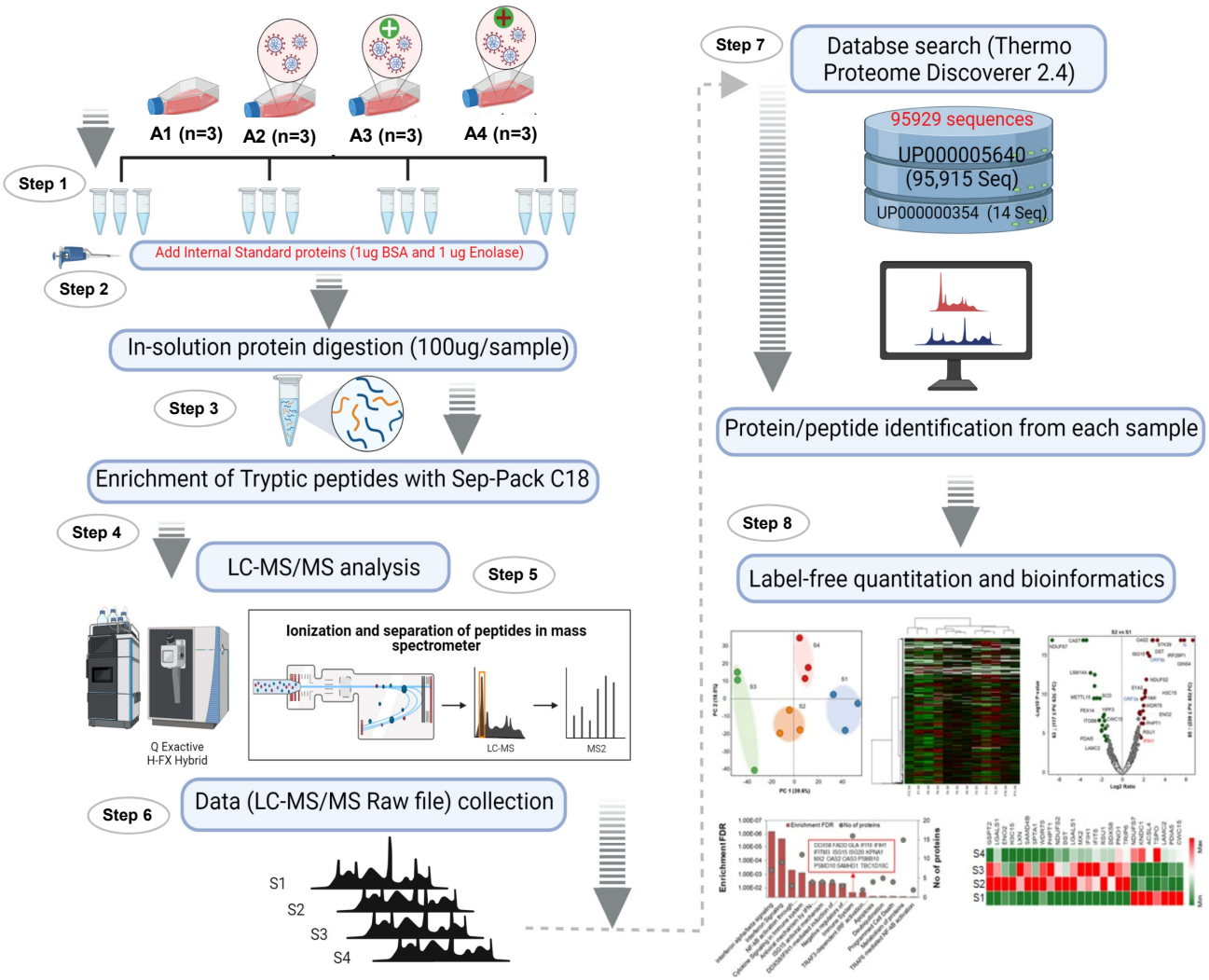
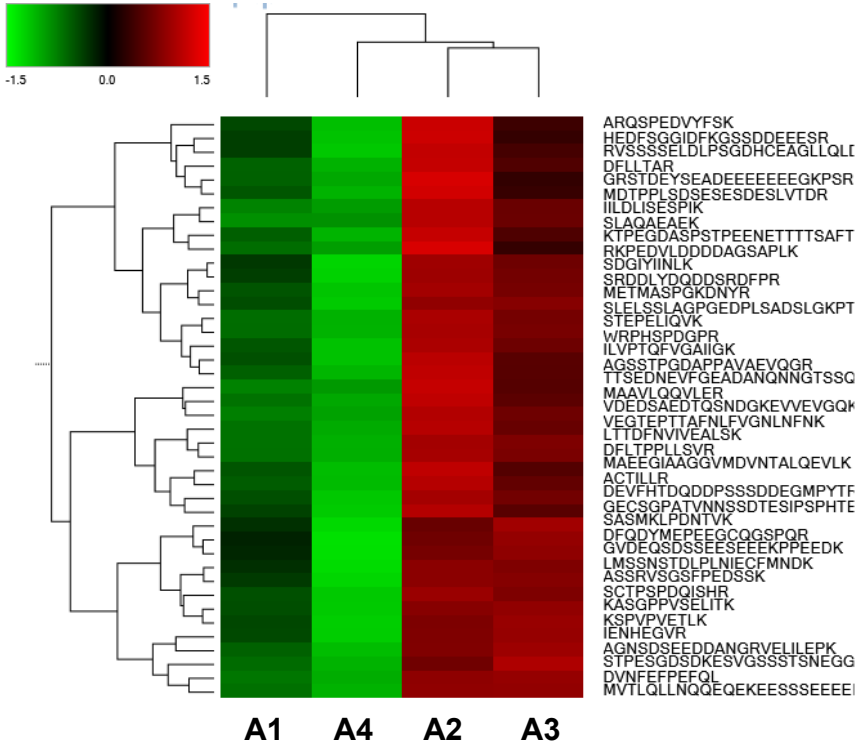


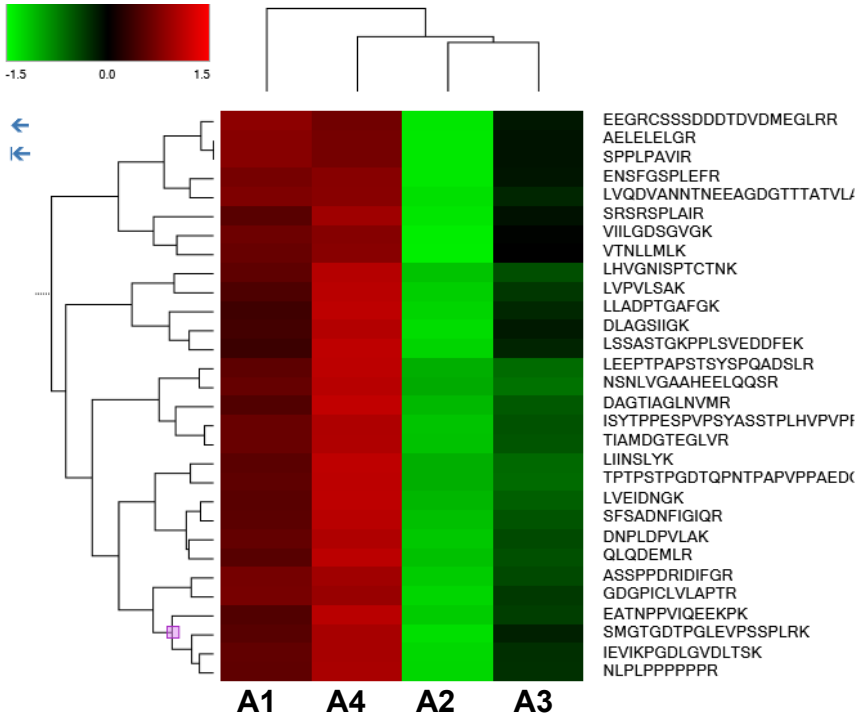

**Fig. S2.** Strategy for the quantitative proteomic and bioinformatic analysis and the number of replicates for each group. A1 (uninfected), A2 (infected), A3 (infected and treated with DMSO), and A4 (infected and treated with DCLK1-IN-1).


**Fig. S3.** Heat map of protein abundance in all four conditions as indicated. (A) upregulation of protein levels by SARS-CoV-2 infection (average of triplicate, red, A2 an), which were normalized by DCLK1-IN-1, green, A4) but not by vehicle (A3). (B) Infection-induced downregulated proteins (A2, green) were restored by DCLK1-IN-1 (red, A4) similar to uninfected levels (A1)

**A.** **Clustering of phosphorylated peptides that are upregulated by SARS-CoV-2 infection**




**B.** **Clustering of phosphorylated peptides that are downregulated by SARS-CoV-2 infection**



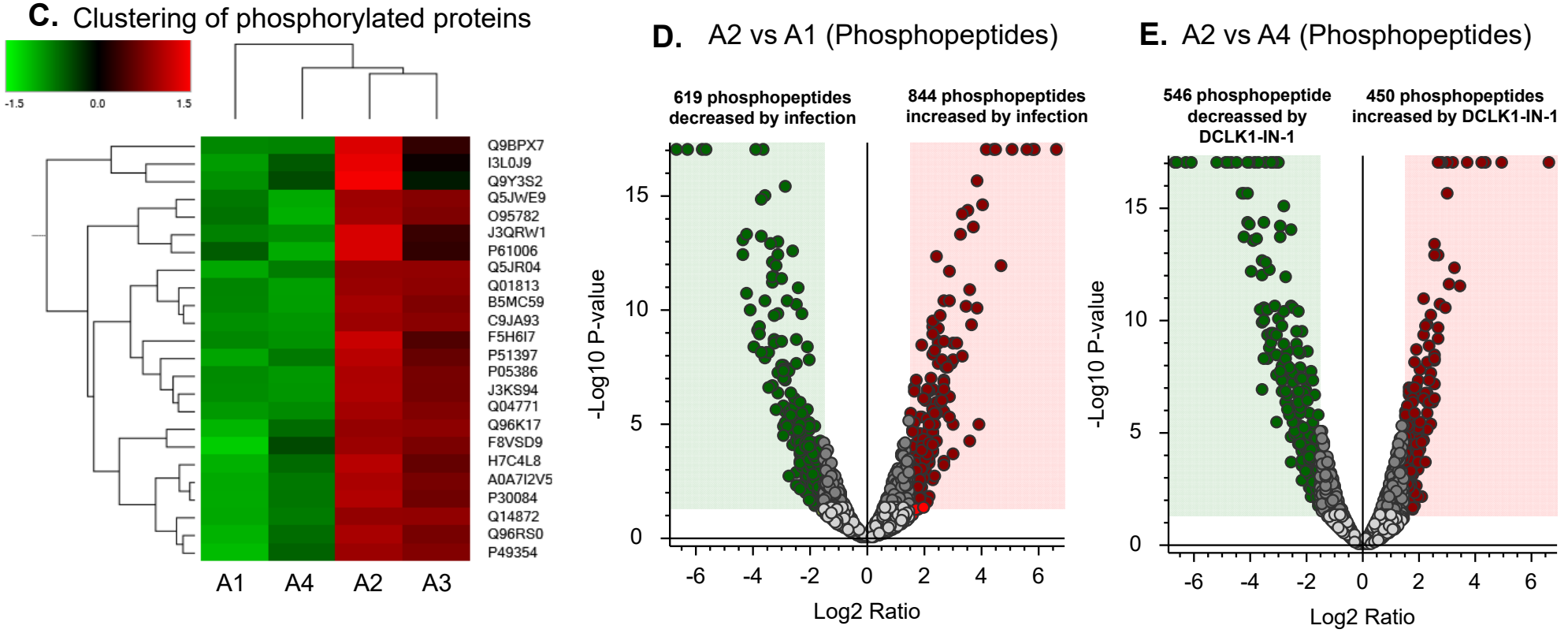



**Fig. S4**. Cluster analyses of the infection-induced upregulated (A) and downregulated (B) phosphorylated peptides detected during phosphoproteomic quantitation. A1 through A4 are as indicated in Fig. S3. (C) Overall status of phosphorylated proteins under all four condition. A1 (uninfected) and A4 (infected and DCLK1-IN-1 treated) cluster together whereas A2 (infected and untreated) and A3 (infected and DMSO-treated) show heightened phosphorylation of the proteins. (D and (E) Volcano plot showing relative increase (red) or decrease (green) of the phosphorylated peptides under four conditions described above.

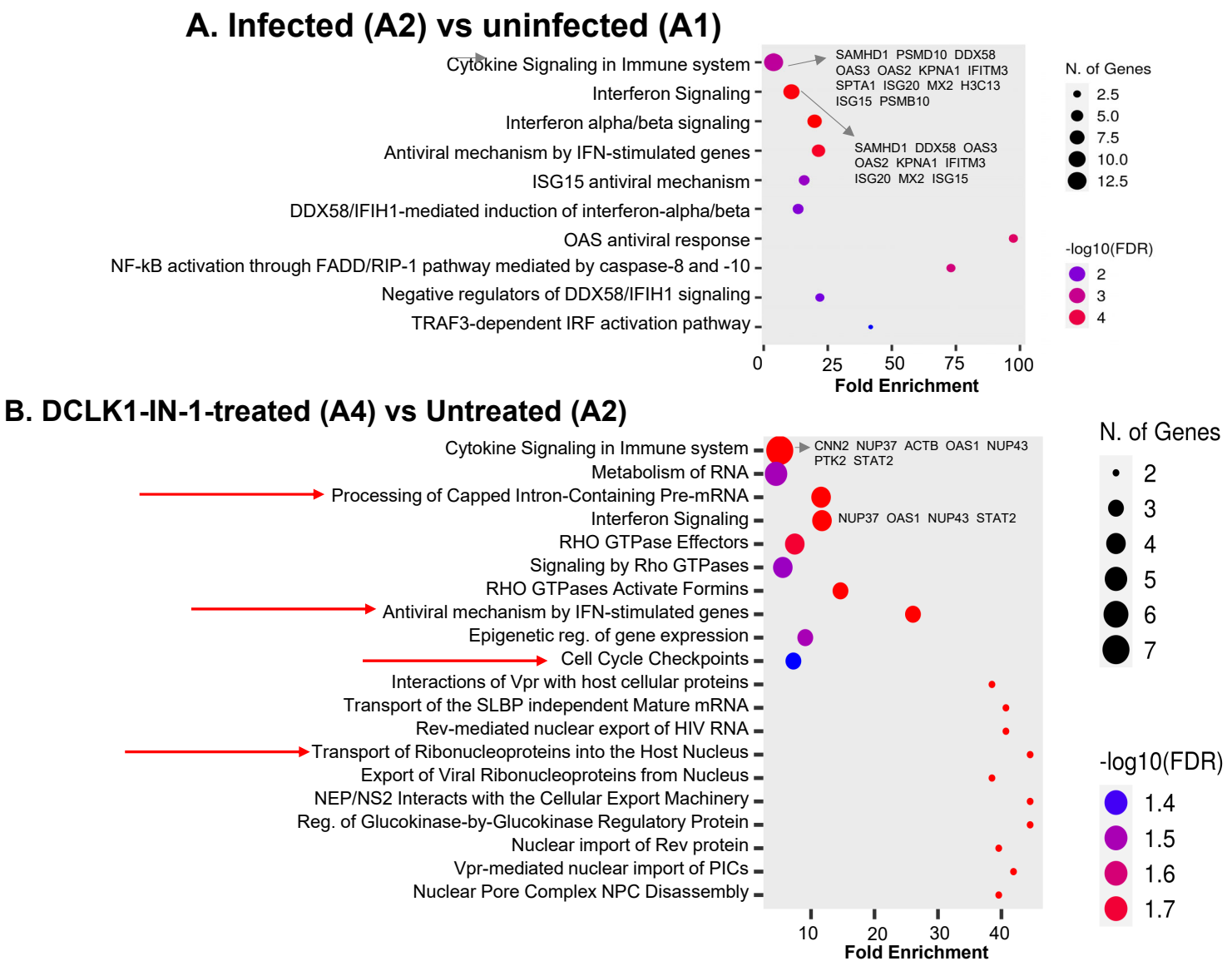



**Fig. S5** Pathway and gene ontology enrichment analyses for in SARS-CoV-2-infected cells. Gene ontology (GO) biological process of the upregulated proteins in A2 vs A1 (**A**) and A4 vs A2 (**B**) samples

## Table S1: reagents used in this paper

| Antibody and reagents | Cat# | Manufacturer |
|---|---|---|
| SARS-CoV-2 Nucleocapsid Protein (HL344) Rabbit mAb 100 µl | 26369S | Cell Signaling Technology |
| SARS-CoV-2 Spike Protein (RBD) (E7B3E) Rabbit mAb #63847 | 63847S | Cell Signaling Technology |
| Anti-SARS spike glycoprotein antibody [1A9] | ab273433 | Abcam |
| Anti-DCAMKL1/DCLK1 antibody [EPR6085] (ab109029) | ab109029 | Abcam |
| Licor beta-Actin Mouse Monoclonal Antibody, 100 uL | 926-42212 | LI-COR Biosciences |
| Licor beta-Actin Rabbit Monoclonal Antibody, 100 uL | 926-42210 | LI-COR Biosciences |
| WDR75 Polyclonal Antibody | PA5-70946 | Thermo Fisher Scientific |
| Anti-Galectin 1 antibody [EPR3206(2)] (ab138513) | ab138513 | Abcam |
| GSPT2 Antibody | PA5-100254 | Thermo Fisher Scientific |
| SAMD4B Antibody | NBP1-94045 | Novus Biologicals |
| NDUFS7 Polyclonal Antibody | PA5-106367 | Thermo Fisher Scientific |
| KNDC1 Polyclonal Antibody | BS-10056R | Thermo Fisher Scientific |
| TSPO Antibody (MA5-33203) in ICC/IF | MA5-33203 | Thermo Fisher Scientific |
| HLA-A Polyclonal Antibody, Unconjugated, | PA5-29911 | Thermo Scientific |
| SP-C (H-8) | sc-518029 | Santa Cruz Biotechnology |
| CD206 (15-2) | sc-58986 | Santa Cruz Biotechnology |
| Anti-Angiotensin Converting Enzyme 2 antibody (ab15348) | ab15348 | Abcam |
| DCLK1-IN-1 | 7285 | Tocris |
| DAPI ready made solution with Antifade | MBD0020-10ML | Sigma-Aldrich |
| New Coronavirus Nucleic Acid Detection Kit | 2019-NCOV-PCR-AUS | PerkinElmer |