Supplementary Figure Legends

Supplementary Figure S1. Study schema.

Supplementary Figure S2. B cell responses in vaccinated rhesus macaques. Frequencies of RBD- and S-specific B cells in total IgG+ B cell populations following Ad26.COV2.S immunization. (A) Representative flow cytometry of PBMCs from one monkey in the 1x10^{11} vp dose group at days 0, 7, 14, and 28 after vaccination gated on class-switched IgG+ B cells. (B) Expression level of CD27 and CD95 on RBD-specific B cells. (C) Flow cytometry showing activated memory (AM) and resting memory (RM) B cells, gated on RBD-specific IgG+ B cells.

Supplementary Figure S3. Correlations of B cell responses with adaptive immune responses. Correlations of RBD-specific activated memory B cell frequencies with log NAb, log ELISA, and ELISPOT responses in vaccinated rhesus macaques. Red lines reflect the best linear fit relationship between these variables. P and R values reflect two-sided Spearman rank-correlation tests. n=25 biologically independent animals.

Supplementary Figure S4. SARS-CoV-2 associated pathology in sham rhesus macaques following SARS-CoV-2 challenge. Focal to locally extensive SARS CoV-2 associated pathological lesions were observed in sham vaccinated monkeys 10 days following challenge. (A) Bronchoepithelial syncytia (arrow, inset) within alveolus; (B) Multifocal Type II pneumocyte hyperplasia; (C) Inset from (B) showing type II pneumocyte hyperplasia (arrow) and endothelial reactivity (arrowhead); (D) Inset from (C) showing hyperplastic pneumocytes
(arrow) and occasional polymorphonuclear cells (PMNs); (E) thrombus (arrow); (F) focal edema and consolidation due to pneumocyte hyperplasia; (G) multifocal interstitial pneumonia; (H) Inset from (G) showing large reactive cells. Lesions shown are from 4 animals. Scale bars = 20 microns (G), 50 microns (A, C, E, F), 200 microns (B).

**Supplementary Figure S5.** Pathology in sham vaccinated animals corresponds to viral replication and inflammation following SARS-CoV-2 challenge. (A) H&E showing type II pneumocyte hyperplasia; (B) Immunohistochemistry for SARS nucleocapsid protein; (C) RNAscope in situ hybridization for viral RNA (vRNA) in hyperplastic pneumocytes. Immunohistochemistry for (D) Iba-1 (macrophages), (E) CD3 (T lymphocytes) and (F) CD20 (B lymphocytes) in regions of lung pathology. All images from one representative sham animal 10 days following SARS-CoV-2 challenge. Scale bars = 20 microns (A, B, D-F), 50 microns (C).
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Figure S3

RBD+AM / IgG+B cells (%)

Log NAb Titer

R = 0.7997
P < 0.0001

Log ELISA Titer

R = 0.8851
P < 0.0001

IFN-γ SFU/ 10⁶ PBMC

R = 0.5310
P = 0.0063
Figure S4