

1 SUPPLEMENTARY DATA

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3 **ChAdOx1 nCoV-19 (AZD1222) or ChAdOx1 nCoV-19-Beta (AZD2816) protect Syrian hamsters**
4 **against the Beta, Delta, and Omicron variants of concern**

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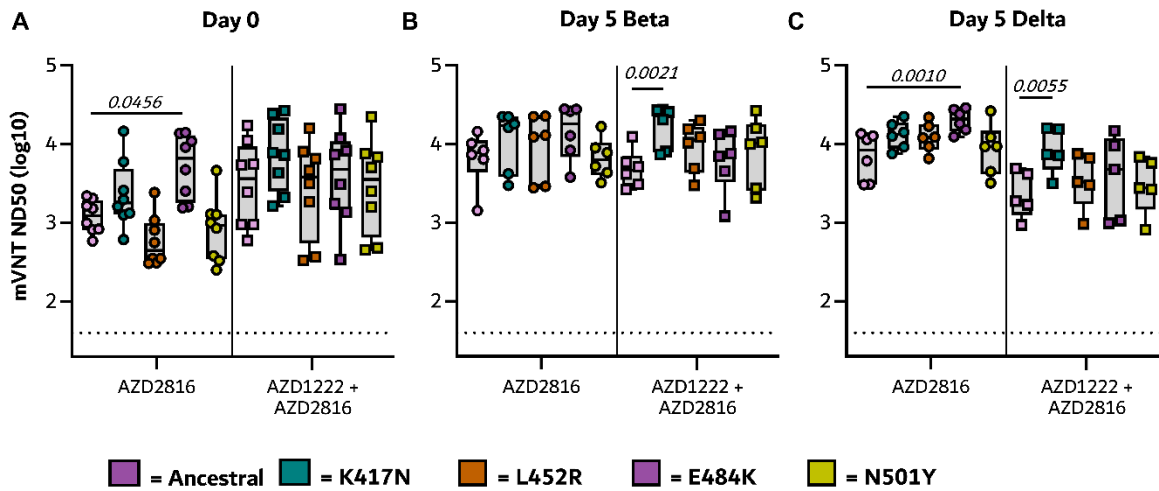
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26 **Supplementary Table 1. Pathological scoring of lung tissue samples.** The tissue slides were examined
 27 by a board-certified veterinary anatomic pathologist blinded to study group allocations. Scoring was done
 28 as follows. H&E; no lesions = 0; less than 1% = 0.5; minimal (1-10%) = 1; mild (11-25%) = 2; moderate
 29 (26-50%) = 3; marked (51-75%) = 4; severe (76-100%) = 5. IHC attachment; none = 0; less than 1% =
 30 0.5; rare/few (1-10%) = 1; scattered (11-25%) = 2; moderate (26-50%) = 3; numerous (51-75%) = 4;
 31 diffuse (76-100%) = 5.
 32

Beta VoC challenge							
Group	Day	H&E			IHC		
		% affected	Interstitial pneumonia	Bronchiolitis	% distribution	Type I and II pneumocytes	Bronchiolar epithelium
AZD2816	3	0	0	0	0	0	0
		0	0	0	0	0	0
		0	0	0	0	0	0
		0	0	0	0	0	0
		0	0	0	0	0	0
	5	0	0	0	0	0	0
		0	0	0	0	0	0
		0.5	1	0	0	0	0
		0	0	0	0	0	0
		0	0	2	0	0	0
AZD1222+ AZD2816	3	0	0	0	0	0	0
		0.5	0	2	0.5	0	3
		0	0	0	0	0	0
		0	0	0	0	0	0
		0.5	0	1	0.5	1	3
	5	0	0	0	0.5	0	2
		0	0	0	0	0	0
		0.5	1	0	0.5	1	2
		0.5	1	0	0	0	0
		0.5	1	0	0	0	0
Control	3	0.5	0	1	0.5	2	4
		0.5	1	1	0.5	2	4
		0.5	0	2	0.5	2	4
		0.5	0	1	0.5	2	4
		0	0	0	0.5	2	4
	5	0.5	0	2	0.5	2	4
		40	3	1	40	4	2
		40	3	2	40	4	3
		30	3	2	50	4	3
		40	3	2	30	4	3
Delta VoC challenge	3	0.5	0	1	0.5	1	2
		0.5	0	1	0.5	0	3
		0.5	0	3	0.5	1	4
		0.5	0	2	0.5	1	3
		0.5	1	0	0.5	1	1
	5	0.5	0	2	0.5	0	2
		0	0	0	0	0	0
		0	0	0	0	0	0
		0	1	0	0	0	0
		0.5	0	0	0	0	0

		0	0	0	0	0	0
		0	0	0	0	0	0
AZD1222+ AZD2816	3	0	0	0	0.5	0	2
		0	0	1	0.5	1	4
		0	0	0	0.5	0	4
		0	0	0	0.5	1	2
		0.5	0	1	0.5	1	2
	0	0	0	0.5	0	1	
	5	0	0	0	0	0	0
		0	0	0	0	0	0
		0	0	0	0	0	0
		10	2	0	0.5	1	0
0		0	0	0	0	0	
Control	3	0.5	0	3	0.5	2	4
		0.5	0	3	0.5	2	4
		0.5	0	3	0.5	2	4
		0.5	0	3	0.5	2	4
		0.5	0	3	0.5	2	4
	5	40	3	2	30	4	2
		40	3	2	30	4	2
		40	3	2	20	4	2
		50	3	2	30	4	2
		40	3	2	10	3	2
40	3	2	30	4	2		
Omicron VoC challenge							
AZD2816	3	0	0	0	0	0	0
		0	0	0	0	0	0
		0	0	0	0.5	0	1
		0	0	0	0	0	0
	5	0	0	0	0	0	0
		0	0	0	0	0	0
		0.5	1	0	0	0	0
		0	0	0	0	0	0
AZD1222	3	0	0	0	0.5	0	1
		0	0	0	0.5	0	1
		0	0	0	0.5	2	2
	5	0.5	0	1	0.5	0	1
		0	0	0	0	0	0
		0.5	1	0	0	0	0
		0	0	0	0	0	0
Control	3	0	0	0	0.5	0	3
		0	0	0	0	0	0
		0.5	0	1	0.5	0	3
		0.5	0	1	0.5	0	3
	5	0	0	0	0.5	0	1
		0	0	0	0.5	0	1
		0.5	0	1	0.5	1	2
0	0	0	0	0	0		
Ancestral challenge							
AZD1222	3	0.5	0	1	0.5	1	3
		0	0	0	0.5	0	1
		0.5	0	2	0.5	0	2
		0.5	0	2	0.5	0	3
	5	0.5	1	0	0	0	0
		10	1	0	0.5	1	0
		0	0	0	0	0	0

		0.5	1	1	0	0	0
Control	3	0.5	1	3	10	3	4
		0.5	1	2	10	3	4
		0.5	1	3	10	3	4
		0.5	0	3	0.5	2	4
		50	3	2	60	4	1
	5	50	3	2	40	4	2
		40	3	2	40	4	3

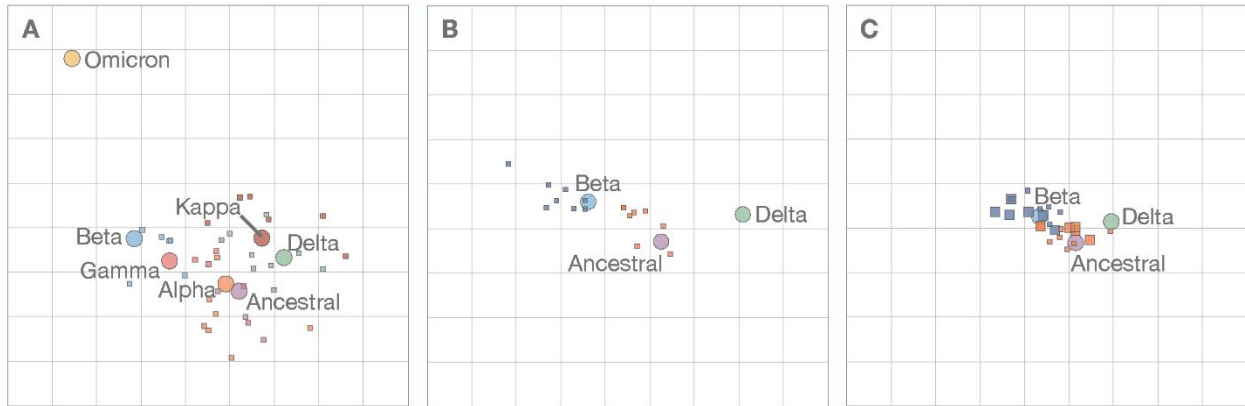


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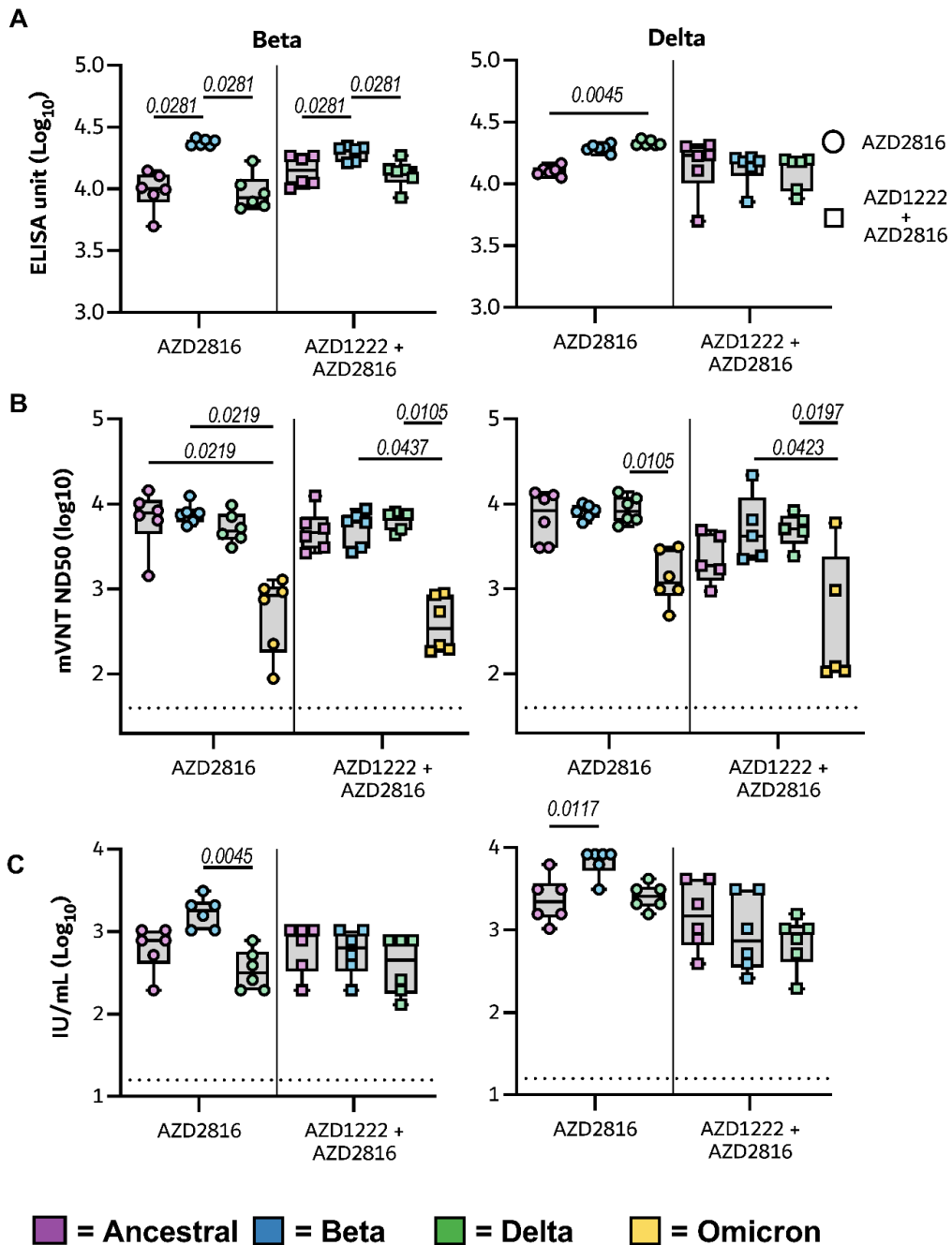
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37 **Supplementary Figure 1. Humoral response of vaccinated hamsters against single mutant**
 38 **pseudotypes.** Boxplots (minimum to maximum) of binding antibody titers as measured by pseudovirus
 39 VN titers in hamster sera obtained on day 0 (left panel), day 5 after Beta VoC challenge (middle panel),
 40 and day 5 after Delta VoC challenge (right panel). Statistical significance was determined via a Friedman
 41 test followed by Dunn's multiple comparisons test comparing ancestral against mutant, p-values in italic
 42 when significant. N=6 per group, day 5 Delta prime boost group N=5. All boxplots are drawn from first
 43 quartile to third quartile, with a line at the median. Whiskers go from each quartile to minimum or
 44 maximum values. Source data are provided as a Source Data file.

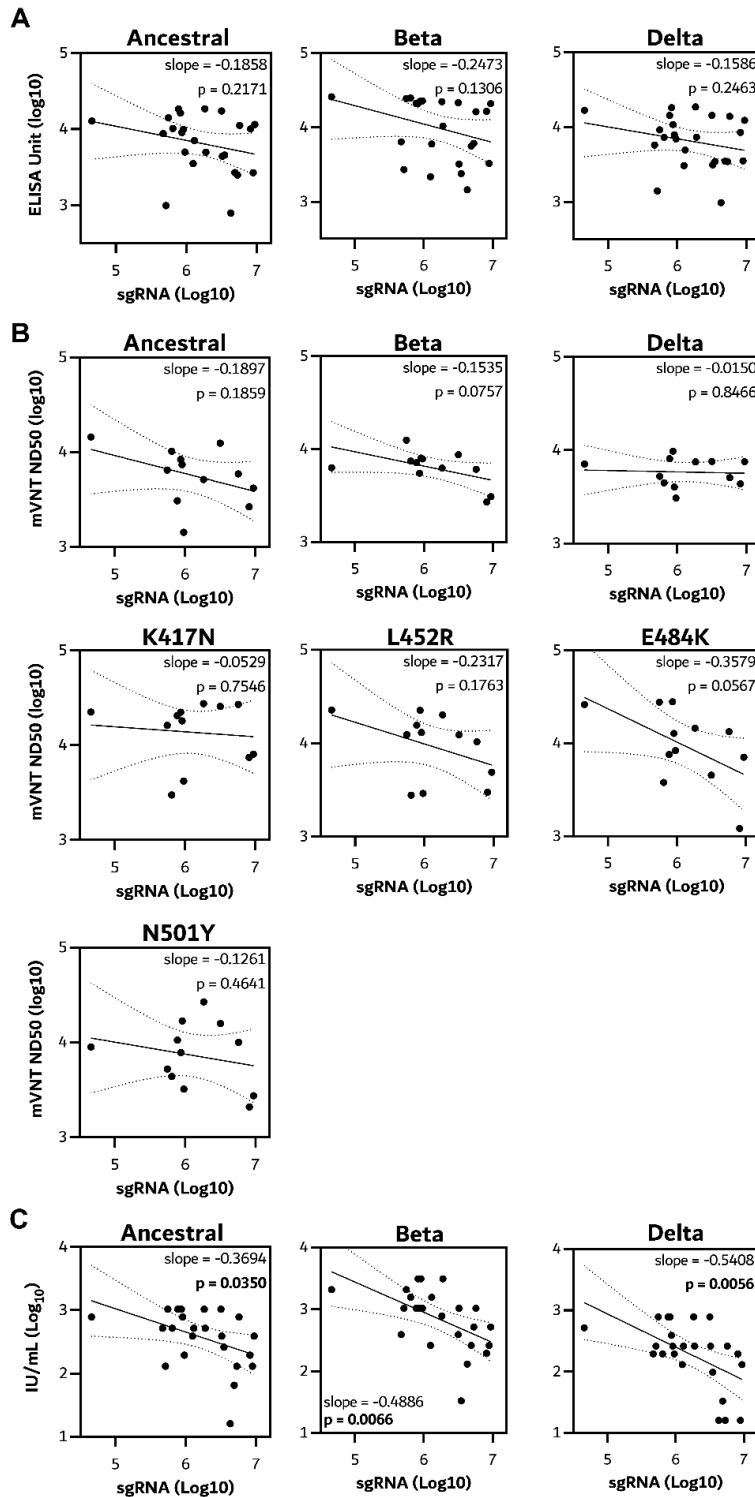
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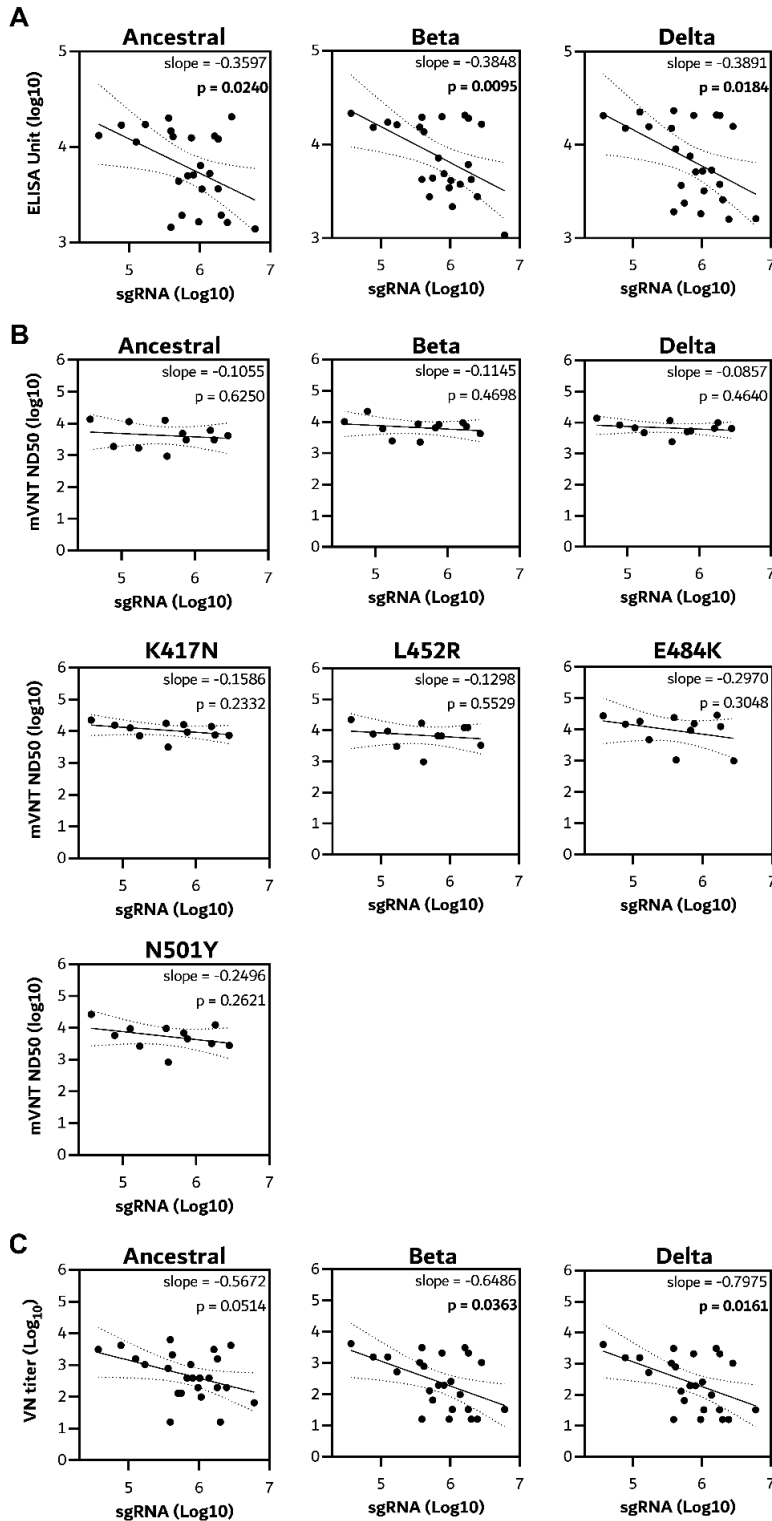
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 47 **Supplementary Figure 2. Antigenic map using live VN assays.** Multidimensional scaling was used to
 48 make maps showing the antigenic distance between different antigens and sera obtained from hamsters,
 49 based on live VN titers. (A) Mapping of live VN titers of sera obtained from hamsters challenged with
 50 ancestral virus, Alpha, Beta, Gamma, Kappa, Delta, or Omicron VoCs against the same VoCs. Antigens
 51 are shown as circles, sera is shown as squares. Sera is color-matched against antigen, e.g. sera obtained
 52 from hamsters challenged with the Beta VoC is blue. (B) Mapping of live VN titers of sera obtained from
 53 vaccinated hamsters at 0 days post challenge against ancestral virus, Beta, or Delta VoCs. Blue squares =
 54 AZD2816-vaccinated hamsters; Orange squares = AZD1222+AZD2816-vaccinated hamsters. (C)
 55 Mapping of live VN titers of sera obtained from vaccinated hamsters at 5 days post challenge against
 56 ancestral virus, Beta, or Delta VoCs. Blue squares = AZD2816-vaccinated hamsters; Orange squares =
 57 AZD1222+AZD2816-vaccinated hamsters; Large squares = hamsters challenged with Beta VoC; Small
 58 squares = hamsters challenged with Delta VoC. Source data are provided as a Source Data file.



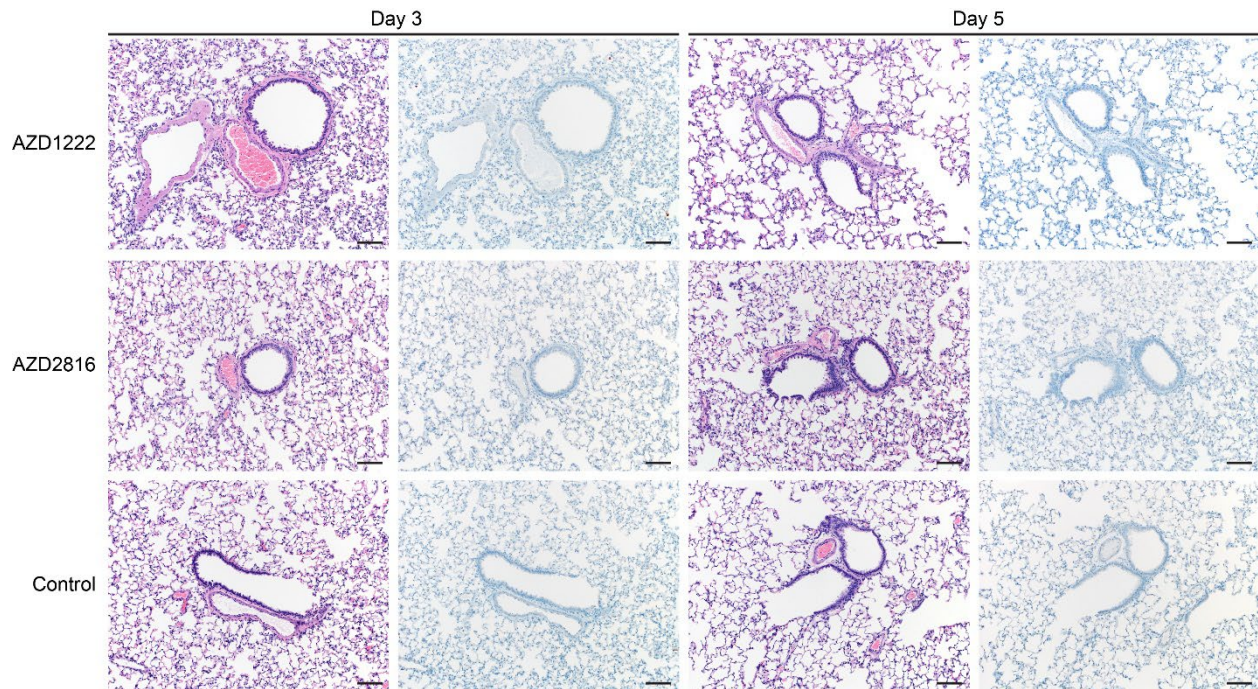
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60 **Supplementary Figure 3. Humoral response of vaccinated hamsters upon challenge with the Beta**
61 **(left panels) or Delta (right panels) VoC.** Boxplots (minimum to maximum) of binding antibody titers
62 as measured by ELISA (A), pseudovirus VN titers (B), and live virus VN titers (C) in hamster sera
63 obtained on day 5. Statistical significance was determined via a Friedman test followed by Dunn's
64 multiple comparisons test, p-values in italic when significant. N=6 per group, N=5 for pseudovirus VN
65 after Delta challenge. All boxplots are drawn from first quartile to third quartile, with a line at the median.
66 Whiskers go from each quartile to minimum or maximum values. Source data are provided as a Source
67 Data file.



68
 69 **Supplementary Figure 4. Linear correlation plots between sgRNA load in oropharyngeal swabs and**
 70 **antibodies found in serum at day of necropsy post Beta challenge.** A) Binding antibodies as
 71 determined via ELISA S. B) Pseudo VN titers. C) Live VN titers. Significance is calculated using simple
 72 linear regression. Source data are provided as a Source Data file.



82
 83 **Supplementary Figure 6. Linear correlation plots between sgRNA load in oropharyngeal swabs and**
 84 **antibodies found in serum at day of necropsy post Delta challenge.** A) Binding antibodies against
 85 Delta S. B) Pseudo VN titers against Delta. C) Live VN titers against the Delta variant. Significance is
 86 calculated using simple linear regression. Source data are provided as a Source Data file.



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89 **Supplementary Figure 7. Pulmonary effects of intranasal challenge with the Omicron VoC in**
 90 **vaccinated and control hamsters at day 3 and 5.** H&E staining (1st and 3rd column) and IHC staining
 91 against N protein (brown, 2nd and 4th column), 100x, scale bar = 100 μ m. N=4. Most vaccinated and
 92 control animals showed no pathology in the lower respiratory tract, except for minimal interstitial
 93 pneumonia on day 5 in 1/4 animals in each vaccine group. Antigen staining was limited to bronchial and
 94 bronchiolar epithelium in 2/4 control animals on day 5 and 1/4 AZD1222 vaccinated animals on day 3, as
 95 well as in type I and II pneumocytes in 1/4 animals in control animals on day 5.