Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix

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Supplemental Methods

Samples. Day 43 and 57 data are missing for one 18-55 year-old participant, and for Day 209 for one subject in the 71+ group, because they did not have samples collected at those time points. In addition, one subject in the 56-70 group did not get the second dose, therefore data after Day 29 were not included in analysis.

Statistical Analysis. Confidence intervals of the geometric means were calculated with the Student's t distribution on log-transformed data and then back transformed. Age group titers were compared using the Kruskal-Wallis test and, if significant, individual pairs were compared using the Wilcoxon test. Antibody decay rates and half-life were calculated using both exponential and power law models fit to data starting at Study Day 43 and beyond. Both models were implemented, and 95% confidence interval of fixed effects computed using the lme4 package in R 3.6.3 or higher. 95% confidence intervals of fixed effects are calculated by computing a likelihood profile and finding the appropriate cut-offs based on the likelihood ratio test as implemented in the lme4 package[1]. The exponential model after $\log_{10}$ transformation of titers takes the following form[2]:

$$log_{10}(Titer_{ij}) = \alpha + \beta * (study\ day_{ij}) + u_i + e_{ij}$$

where α and β are the fixed effects, intercept and decay rate, respectively. u_i is the random intercept for each participant *i* and e_{ij} are the model errors for participant *i* at study day *j*. The fixed effect decay rate and 95% confidence intervals are reported. The half-life was calculated using the following formula:

$$t_{1/2} = \frac{log_{10}(0.5)}{\hat{\beta}}$$

Where $t_{1/2}$ is the day when the titer has decayed to half of its starting value and $\hat{\beta}$ is the estimated model decay rate. The 95% confidence interval of the half-life was computed using the delta method. The power law model after $\log_{10}$ transformation of titers and study day takes the following form[3]:

$$log_{10}(Titer_{ij}) = \alpha + \beta * \left(log_{10}(study\ day_{ij} - 29)\right) + u_i + e_{ij}$$

where α and β are the fixed effects, intercept and decay rate, respectively. u_i is the random intercept for each participant and e_{ij} are the model errors for participant *i* at study day *j*. Study day was offset by 29 days to account for the 2 dose regimen. The fixed effect decay rate and 95% confidence intervals are reported. The half-life was calculated using the following formula:

$$log_{10}(t_{1/2}) = log_{10}(study\ day - 29) + \frac{log_{10}(0.5)}{\hat{\beta}}$$

Where $t_{1/2}$ is the day when the titer has decayed to half of its starting value and $\hat{\beta}$ is the estimated model decay rate. The 95% confidence interval of the half-life was computed using1000 bootstrap simulations. Model fit was compared using the AIC_c criteria. This is AIC with a small sample size correction.

Supplemental Tables

Supplemental Table 1: Serum RBD-Binding IgG ELISA Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Age Group

Time Point	Statistic	100 mcg mRNA-1273 18-55 years (N=15)	100 mcg mRNA-1273 56-70 years (N=10)	100 mcg mRNA-1273 ≥71 years (N=10)	100 mcg mRNA-1273 (N=35)
Day 1 (Pre-Vaccination 1)	n	15	10	10	35
	GMT	166	223	503	248
	95% CI	82, 337	64, 775	174, 1455	148, 417
Day 15 (14 Days Post Vaccination 1)	n	15	10	10	35
	GMT	34073	30981	25670	30582
	95% CI	21688, 53531	15901, 60362	12394, 53168	22524, 41523
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n	15	10	10	35
	GMT	93231	45690	56343	65852
	95% CI	59895, 145123	26314, 79330	35052, 90567	50065, 86618
Day 36 Post Vaccination 1 (7 Days Post Vaccination 2)	n	15	9	10	34
	GMT	499539	1471882	711752	737938
	95% CI	400950, 622370	560108, 3867893	368657, 1374153	531937, 1023717
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n	14	9	10	33
	GMT	558905	1005639	694471	700636
	95% CI	462908, 674810	445521, 2269948	465032, 1037111	549265, 893723
Day 57 Post Vaccination 1 (28 Days Post Vaccination 2)	n	14	9	10	33
	GMT	371271	506364	453506	429317
	95% CI	266721, 516804	235654, 1088051	255624, 804573	327770, 562325
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n	15	9	10	34
	GMT	235228	151761	157946	186308
	95% CI	177236, 312195	88571, 260033	94345, 264420	148772, 233314
Day 209 Post Vaccination 1 (180 Days Post Vaccination 2)	n	15	9	9	33
	GMT	92451	62424	49373	70000
	95% CI	57148, 149562	36765, 105990	25171, 96849	51866, 94474

Supplemental Table 2: **Pseudovirus Neutralization Assay ID_{50} Geometric Mean (GM) Results with 95% Confidence Intervals by Time Point and Age Group**

Time Point	**Statistic**	**100 mcg mRNA-1273 18-55 years (N=15)**	**100 mcg mRNA-1273 56-70 years (N=10)**	**100 mcg mRNA-1273 ≥71 years (N=10)**	**100 mcg mRNA-1273 (N=35)**
Day 1 (Pre-Vaccination 1)	n	15	10	10	35
	GMT	10	10	10	10
	95% CI	NE	NE	NE	NE
Day 15 (14 Days Post Vaccination 1)	n	15	10	10	35
	GMT	24	12	27	20
	95% CI	13, 42	10, 15	12, 60	15, 28
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n	15	10	10	35
	GMT	18	11	20	16
	95% CI	12, 27	10, 12	12, 33	13, 20
Day 36 Post Vaccination 1 (7 Days Post Vaccination 2)	n	15	9	10	34
	GMT	263	340	310	295
	95% CI	188, 368	219, 527	202, 475	241, 363
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n	14	9	10	33
	GMT	360	404	317	358
	95% CI	273, 476	292, 561	198, 508	297, 430
Day 57 Post Vaccination 1 (28 Days Post Vaccination 2)	n	14	9	10	33
	GMT	276	424	231	294
	95% CI	193, 393	267, 673	150, 356	235, 368
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n	15	9	10	34
	GMT	182	167	109	153
	95% CI	112, 296	88, 318	68, 175	115, 203
Day 209 Post Vaccination 1 (180 Days Post Vaccination 2)	n	15	9	9	33
	GMT	80	57	59	67
	95% CI	48, 135	30, 106	29, 121	49, 92

Supplemental Table 3: FRNT mNG Geometric Mean (GM) ID_{50} Results with 95% Confidence Intervals by Time Point and Age Group

Time Point	Statistic	100 mcg mRNA-1273 18-55 years (N=15)	100 mcg mRNA-1273 56-70 years (N=10)	100 mcg mRNA-1273 ≥71 years (N=10)	100 mcg mRNA-1273 (N=35)
Day 1 (Pre-Vaccination 1)	n	15	10	10	35
	GMT	10	10	10	10
	95% CI	NE	NE	NE	NE
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n	15	10	10	35
	GMT	69	80	39	61
	95% CI	46, 102	52, 123	18, 86	46, 82
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n	14	9	10	33
	GMT	1388	1425	900	1226
	95% CI	1056, 1825	980, 2072	575, 1409	1008, 1491
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n	15	9	10	34
	GMT	775	685	552	679
	95% CI	560, 1071	436, 1077	321, 947	543, 848
Day 209 Post Vaccination 1 (180 Days Post Vaccination 2)	n	15	9	9	33
	GMT	361	171	131	236
	95% CI	258, 504	95, 307	69, 251	173, 321

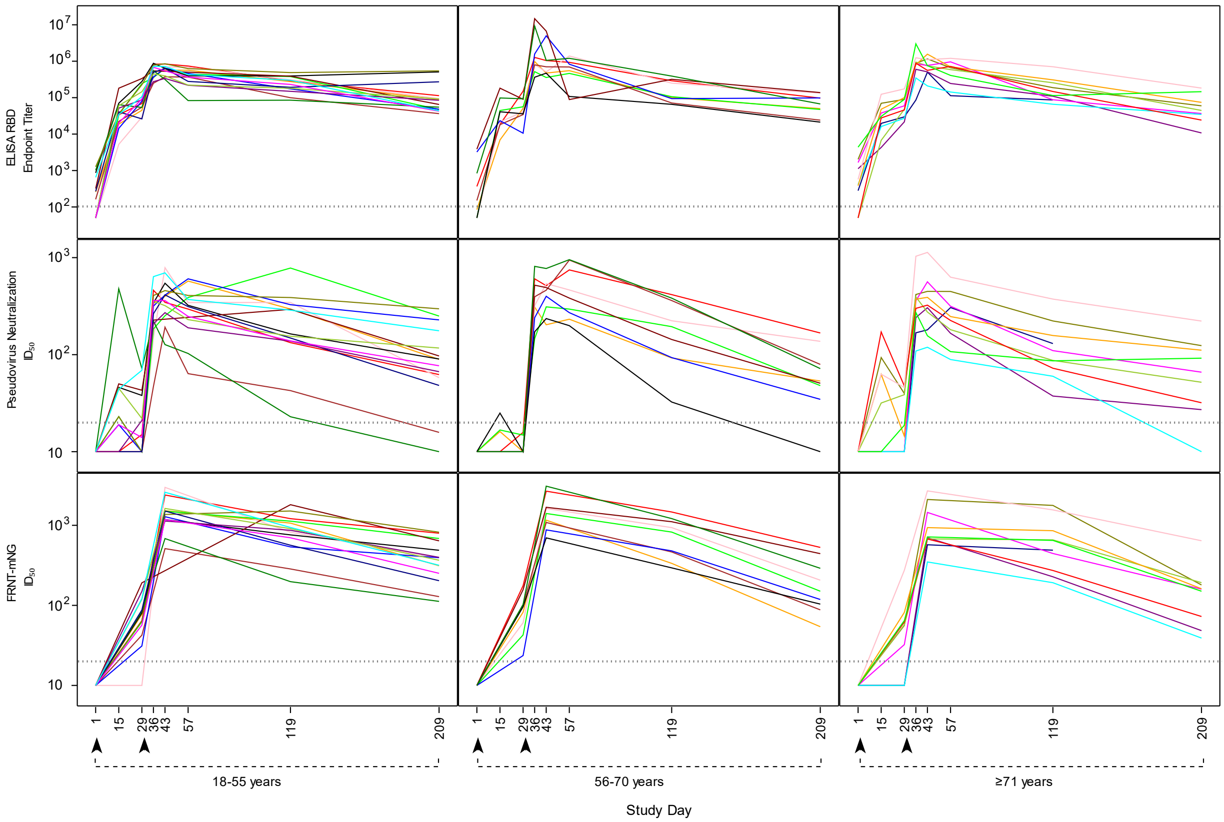
Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Supplemental Table 4: Estimates of antibody half-life

Assay	Age Group	Model	Decay Rate	Half-Life (days)	ΔAIC_c
ELISA RBD	Overall l	Exponential	-0.00579 (-0.00649, -0.00509)	52.0 (45.8, 58.3)	8.8
		Power Law	-0.876 (-0.982, -0.768)	108.6 (91.7, 135.8)	
	18-55 Years	Exponential	-0.00440 (-0.00521, -0.00360)	68.4 (56.0, 80.8)	4.3
		Power Law	-0.654 (-0.786, -0.522)	169.7 (124.5, 263.1)	
	56-70 Years	Exponential	-0.00689 (-0.00865, -0.00512)	43.7 (32.7, 54.7)	14.2
		Power Law	-1.079 (-1.326, -0.831)	81.1 (62.2, 116.9)	
	≥71 Years	Exponential	-0.00695 (-0.00797, -0.00591)	43.3 (37.0, 49.6)	5.0
		Power Law	-1.024 (-1.192, -0.853)	87.1 (69, 117.7)	
Pseudovirus Neutralization	Overall l	Exponential	-0.00439 (-0.00485, -0.00393)	68.6 (61.4, 75.7)	-8.7
		Power Law	-0.646 (-0.7226, -0.569)	173.4 (143.7, 225.2)	
	18-55 Years	Exponential	-0.0038 (-0.00451, -0.00309)	79.2 (64.6, 93.9)	3.1
		Power Law	-0.558 (-0.676, -0.440)	221.5 (154.1, 398.3)	
	56-70 Years	Exponential	-0.00541 (-0.0062, -0.00462)	55.6 (47.6, 63.6)	-5.1
		Power Law	-0.775 (-0.936, -0.615)	130.1 (95.5, 198.9)	
	≥71 Years	Exponential	-0.00432 (-0.00516, -0.00348)	69.7 (56.4, 83)	12.7
		Power Law	-0.655 (-0.775, -0.535)	169.3 (123.6, 265)	
FRNT-mNG	Overall l	Exponential	-0.00459(-0.00504,-0.00413)	65.6 (59.2,72)	-35.0
		Power Law	-0.605 (-0.698,-0.512)	181.7 (152.9, 254.4)	
	18-55 Years	Exponential	-0.00364 (-0.00417,-0.00310)	82.7 (70.7,94.7)	-4.2
		Power Law	-0.503 (-0.602,-0.401)	231 (187.1,444.2)	
	56-70 Years	Exponential	-0.00559 (-0.00632, -0.00485)	53.9 (47.0, 60.8)	-10.2
		Power Law	-0.740 (-0.932, -0.548)	139.6 (99.5, 230.9)	
	≥71 Years	Exponential	-0.00511 (-0.00607, -0.00415)	58.9 (48.1, 69.6)	-6.4
		Power Law	-0.640 (-0.853, -0.426)	176 (114.7, 350)	

Note: Power Law half-lives estimated at Day 119.
$\Delta AIC_c = AIC_c$(exponential) - AIC_c(Power Law). So positive ΔAIC_c are evidence that the power law model fits better and negative values are evidence that the exponential model fits better.

Supplemental Figure 1



Supplemental Figure 1. Each line represents a single subject over time. Data from 35 subjects are stratified by age: 18-55 (n=15), 56-70 (n=10), and ≥71 (n=10) years old. Dotted line indicates the limit of detection for each assay. Panels, in vertical order, show binding to RBD protein (endpoint dilution titer) on days 1, 15, 29, 36, 43, 57, 119, and 209; pseudovirus neutralization 50% inhibitory dilution (ID_{50}) titer on days 1, 15, 29, 36, 43, 57, 119, and 209; and focus-reduction neutralization mNeonGreen (FRNT-mNG) assay ID_{50} titer on days 1, 29, 43, 119, and 209. Arrows represent vaccination time points: 100 mcg of mRNA-1273 on days 1 and 29.

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