Supplementary Table 1. Characteristics of the study population

Characteristics	<60 years	≥60 years	Total cohort number (%)
Total	178 (57.1)	134 (42.9)	312
Gender			
Male (%)	51 (28.3)	79 (61.7)	130 (41.7)
Female (%)	127 (69.7)	55 (30.3)	182 (58.3)
Ethnicity			
Chinese (%)	106 (46.9)	120 (53.1)	226 (72.4)
Indians (%)	14 (60.9)	9 (39.1)	23 (7.6)
Malays (%)	26 (89.7)	3 (10.3)	29 (8.8)
Others (%)	32 (94.1)	2 (5.9)	34 (11.2)
Median years (minimum-maximum)	35 (22-59)	69 (60-82)	50.85 (22-82)

Supplementary table 2. Immune reactivity across timepoints

Assays	Proportion of volunteers with response above individual baseline * (%)		
	At day 21	At day 90	At day 180
Anti-spike protein IgG (SFB)	306/312 (98)	311/312 (99)	311/312 (99)
Anti-RBD IgG (Roche S)	310/312 (99.3)	312/312 (100)	312/312 (100)
sVNT	247/312 (79.1)	309/312 (99)	293/312 (93.9)
B cell Elispot	17/35 (48.6)	28/35 (80)	30/35 (85.7)
IL-2 T cells	155/155 (100)	155/155 (100)	155/155 (100)
IFNγ T cells	144/155 (92.9)	149/155 (96.1)	153/155 (98.7)
CD8 T cell Elispot	39/72 (54.2)	54/72 (75)	29/72 (40.3)
CD4 Th1 Elispot	54/78 (69.2)	66/78 (84.6)	65/78 (83.3)
CD4 Th2 Elispot	42/71 (59)	42/71 (59)	35/71 (49)

* Paired samples

Supplementary table 3. Long-term immune responses in vaccinated individuals

Assays	Proportion of individuals with a lower response at day 180 compared with day 90 (%)*			
	Total population	< 60 years	≥60 years	*P value***
Anti-spike protein IgG (SFB)	243/312 (78)	176/178 (98.9)	66/134 (49.2)	0.0001
Anti-RBD IgG (Roche S)	243/312 (77.8)	153/178 (85.9)	89/134 (66.4)	0.0001
sVNT	243/312 (77.5)	119/178 (66.8)	123/134 (91.8)	NS
B cell Elispot	10/34 (29.4)	3/16 (18.75)	7/18 (52.9)	NS
IL-2 T cells	97/155 (62.5)	56/81 (69.1)	40/74 (54)	NS
IFNγ T cells	72/155 (46.5)	49/81 (60.4)	24/74 (32)	0.0003
CD8 T cell Elispot	45/72 (67.9)	31/45 (68.9)	13/27 (48.1)	NS
CD4 Th1 Elispot	37/79 (46.8)	21/51 (41.2)	16/28 (57.1)	NS
CD4 Th2 Elispot	35/71 (50.7)	30/51 (58.2)	11/20 (55)	NS

* Paired samples

** Difference between age groups

Supplementary table 4. Low responders as determined by the SFB assay

Days	21		90		180	
Median antibody response (% binding)	28.3%		41.98%		23.35%	
Proportion of low responders* (n / tested number)	-		37.2 (116/312)		22.2 (88/312)	
Age (Years)	N	% of total cohort	N	% of total cohort	N	% of total cohort
<60	57	18.2	42	13.5	40	12.8
>60	99	31.7	74	23.7	48	13.5

* Low responders are defined as fully vaccinated individuals with antibody response below cohort's median response at consecutive timepoints (%). For example, the low responders, at day 90, have antibody response below cohort's median response at both day 21, 90 and 180.

Supplementary table 5. Low responders as determined by Roche S

Days	21		90		180	
Median antibody response (U/ml)	50.28		927		677	
Proportion of low responders* (n/tested number)	-		36.5 (114/312)		31.4 (98/312)	
Age (Years)	N	% of total cohort	N	% of total cohort	N	% of total cohort
<60	60	19.2	32	10.25	26	8.3
>60	99	31.7	82	26.2	69	22

* These values were determined as in Supplementary table 4.

Supplementary table 6. Low responders as determined by sVNT

Days	21		90		180	
Median inhibition (%l)	56.39		89.87		67.4	
Proportion of low responders* (n/tested number)	-		39.1 (122/312)		34.9 (109/312)	
Age (Years)	N	% of total cohort	N	% of total cohort3	N	% of total cohort
<60	53	16.9	38	12.18	35	11.2
>60	104	33	84	26.9	74	23.7

* These values were determined as in Supplementary table 4.

Supplementary table 7. Low responders as determined by measurement of IL-2 production by T cells

Days	21		90		180	
Median antibody response (pg/ml)	54.48		89.39		78.06	
Proportion of low responders* (n / tested number)	-		29.7 (46/155)		25.2 (39/155)	
Age (Years)	N	% of total cohort	N	% of total cohort	N	% of total cohort
<60	40	25.8	25	16.1	21	13.5
>60	37	23.9	21	13.5	18	11.6

* These values were determined as in Supplementary table 4.

Supplementary table 8. Low responders as determined by measurement of IFN-γ production by T cells

Days	21		90		180	
Median antibody response (U/ml)	11.69		33.81		32.43	
Proportion of low responders* (n / tested number)	-		32.2 (50/155)		26.5 (41/155)	
Age (Years)	N	% of total cohort	N	% of total cohort	N	% of total cohort
<60	33	21.2	22	14.2	20	12.9
>60	45	29	28	18	21	13.5

* These values were determined as in Supplementary table 4. The median values were at day 21: 11.69 pg/ml, at day 90: 33.81 pg/ml and day 180: 32.43 pg/ml).

Supplementary table 9. Low responders as determined by CD4 Th1 ELISPOT

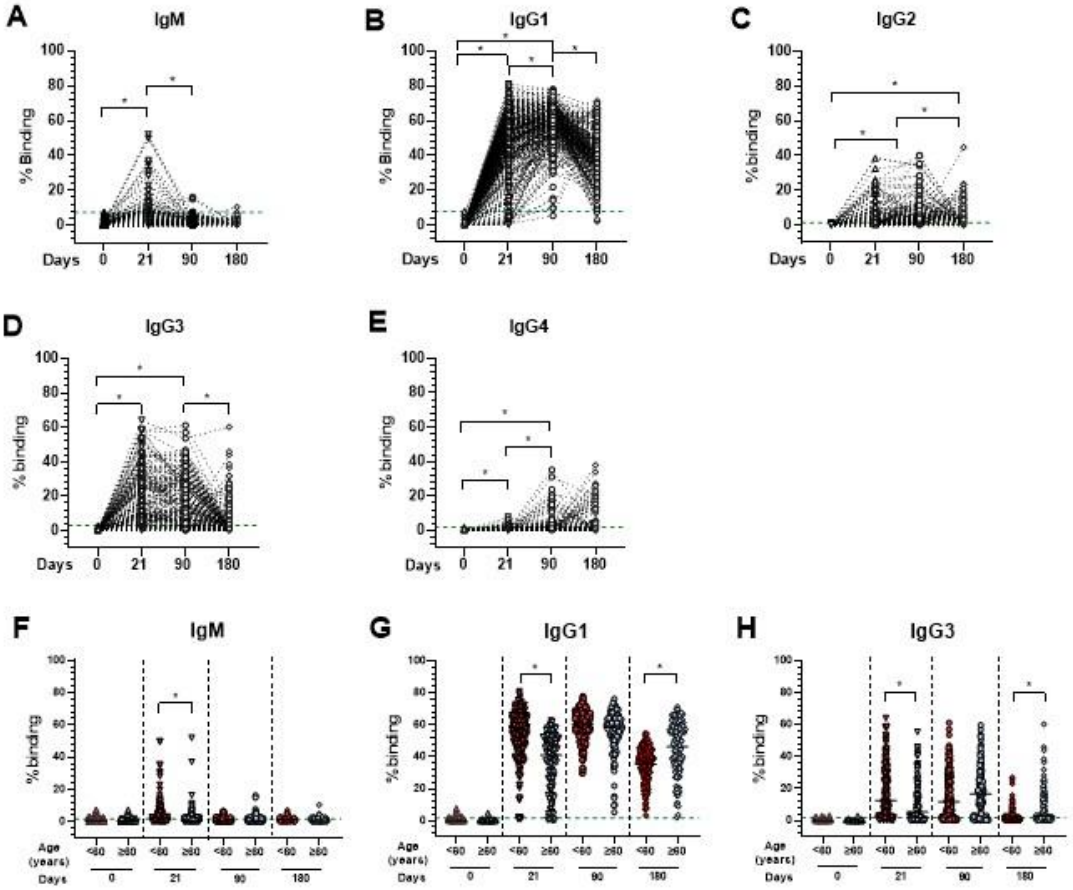
Days	21		90		180	
Median antibody response (Spot forming units)	53.48		89.39		78.06	
Proportion of low responders* (n / tested number)	-		19.2 (15/78)		6.4 (5/78)	
Age (Years)	N	% of total cohort	N	% of total cohort	N	% of total cohort
<60	22	28.2	8	10.2	1	1.2
>60	13	16.7	7	9	4	6.4

* These values were determined as in Supplementary table 4.

Supplementary table 10. Low responders as determined by CD8 ELISPOT

Days	21		90		180	
Median antibody response (Spot forming units)	44.85		71.65		180.42	
Proportion of low responders* (n / tested number)	-		36 (26/72)		23.6 (17/72)	
Age (Years)	N	% of total cohort	N	% of total cohort	N	% of total cohort
<60	25	42.3	18	11.5	13	1.2
>60	11	57.7	8	7.7	4	6.4

* These values were determined as in Table S4. The median values were at day 21: 44.85 SFU, at day 90: 71.65 SFU and day 180: 42.1 SFU).



Supplementary Figure 1. Anti-SARS-CoV-2 spike protein antibody isotype response after vaccination. A flow cytometry-based assay using the full Spike protein (SFB) assay was used to determine antibody isotype in the same 312 vaccinated individuals described in Figure 1. (A) IgM. Median (range) of values at day 0 was 0.4 (0.0098, 7.385). Antibody levels below the maximum range (7.385) were considered baseline values . *, $p < 0.001$, Friedman test; (B) IgG1. Median (range) of values at day 0 was 0.07 (0.0069, 7.893). Antibody levels below the maximum range (7.893) were considered baseline values. *, $p < 0.001$, Friedman test; (C) IgG2. Median (range) of values day 0 was 0.037 (0.008, 1.44). Antibody levels below the maximum range (1.44) were considered baseline values. *, $p < 0.001$, Friedman test; (D) IgG3. Median (range) of values at day 0 was 0.085 (0.0073-3.19). Antibody levels below the maximum range (3.19) were considered baseline values. *, $p < 0.001$, Friedman test; (E) IgG4. Median (range) of values at day 0 was 0.034 (0.0052, 1.953). Antibody levels below the maximum range (1.953) were considered baseline values. *, $p < 0.001$, Friedman test. . (F) IgM, (G) IgG1 and (H) IgG3 antibody levels comparison between the analyzed age groups: <60 (n=186) and ≥60 (n=144), at different time points (day 0, 21 and 90). The Media n of group values are represented as a line through the dots. The red lines or boxes represent the maximum range of the samples. *, $p < 0.001$, Mann Whitney test.

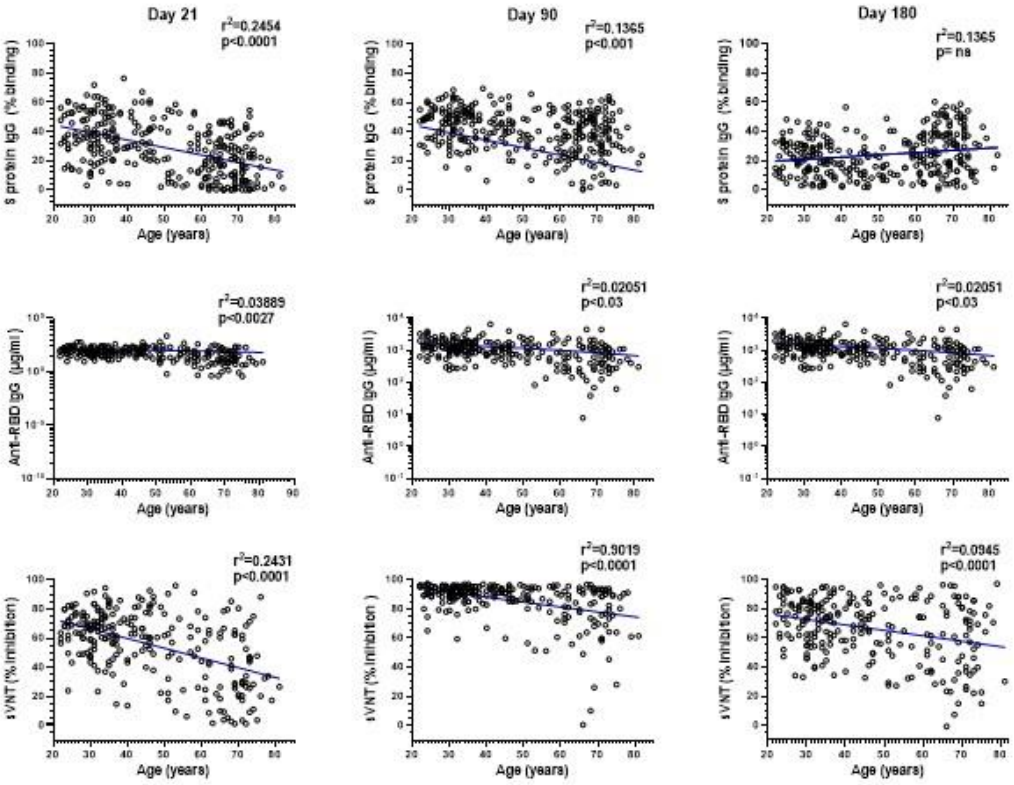


Figure S2. Linear correlations between participant's age and SARS-CoV-2 specific antibody titer measured at different time after vaccination. Correlation was analyzed by simple linear regression at day 21, 90 and 180 for the Flow cytometry-based assay for the S-pike protein (SFB) (Higher panels); the commercial RBD Roche S assay (mid panels) ; and the sVNT assay (Lower panels). $p < 0.05$ was considered statistically significant.

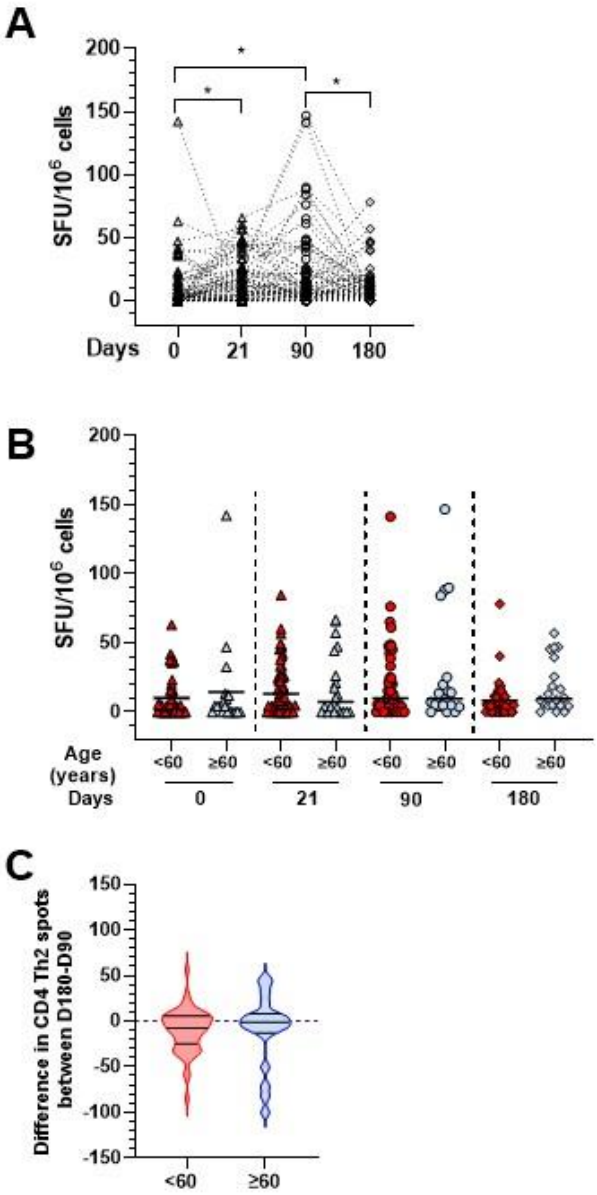


Figure S3. CD4 Th2 responses. (A) Kinetics of Spike-protein-specific Th2 cells overtime in vaccinees. CD4 Th2 cells were assayed on a subset of vaccinees \on a subset of vaccinees (n =71) by IL4/IL5/IL13 ELISPOT using 15 mer pool peptides. Data are presented are spot forming units (SFU) per million of PBMC from paired samples from vaccinated individuals at 4 time points. Each data point represents the normalized mean spot count from duplicate wells for one study participant, after subtraction of the medium-only control *, $p < 0.01$, (B) Comparison between the analyzed age groups at day 0, 21 , 90 and 180, (n=83), <60: (n= 51) and ≥60 (n=20). Median values are indicated by a dark line. *, $p < 0.01$Mann Whitney test. *, $p < 0.01$, Mann Whitney test. (C) Violin plots (with median and quartiles) showing difference in CD4 Th2 cell responses measure in the different assays between days 180 and 90 for paired samples for both age groups, <60: (n= 51), and ≥60 (n=20). $p = 0.003$, Mann Whitney test.