

Supplementary Table 1 Participant characteristics and sample collection information

Variable	BNT162b2 (n=52)
Age, years (median [IQR])	4 [32.3-54]
Female [Male]	46 [6]
Seropositivity to SARS-CoV-2 (Reactive [Non-reactive])	2 [50]
Blood sample collected post 1 st vaccine (Yes [No])	47 [5]
Blood sample collected post 2 nd vaccine (Yes [No])	18 [34]
Baseline stool samples collected (Yes [No])	48 [4]
Twelve-weeks post 1 st vaccine stool samples collected (Yes [No])	41 [11]
Matching baseline and twelve-week stool samples collected (Yes [No])	38 [14]
Dietary fibre grouping (Low [Moderate] High) (n=41)	13 [14] 14
Total dietary fibre intake, g/day (mean [SD]) (n=41)	24.7 [11.9]
Vegetarian (Yes [No]) (n=41)	4 [37]
Antibiotics taken within 9 months of collecting stool (Yes [No]) (n=41)	3 [38]
Significant* change in weight or food intake over the past year (Yes [No]) (n=41)	7 [34]

IQR – inter quartile range, SD – standard deviation. * Significant body weight changes >10% weight gain or loss and significant changes in food intake included becoming vegetarian/vegan, stopped consuming gluten, dairy or sugar, increased fruit, or vegetable intake, etc.

Supplementary Table 2 Gut microbiota species significantly positively or negatively associated ($p < 0.01$; statistical test) with higher avidity after the 2nd dose of the BNT162b2 vaccine (D2) in a subset of participants ($n=15$)

	baseMean	log2FoldChange	lfcSE	stat	pvalue	padj	Kingdom	Phylum	Class	Order	Family	Genus	Species
ASV_12	652.6828066	16.61603655	1.12976698	14.70748999	5.77085204873443E-49	4.0395964341141E-47	Bacteria	Firmicutes	Negativicutes	Acidaminococcales	Acidaminococcaceae	Phascolarctobacterium	succinatutens
ASV_40	856.3116714	15.01679959	1.12976278	13.29199355	2.57621721167962E-40	1.20223469878382E-38	Bacteria	Synergistota	Synergistia	Synergistales	Synergistaceae	Cloacibacillus	evryensis
ASV_56	1163.66926110663	18.9073311	1.129781224	16.73539151	7.23796558640599E-63	1.01331518209684E-60	Bacteria	Firmicutes	Negativicutes	Veillonellales-Selenomonadales	Selenomonadaceae	Megamonas	funiformis
ASV_90	299.9462157	-11.55809526	1.09781944	-10.52822972	6.40272464578869E-26	1.12047681301302E-24	Bacteria	Firmicutes	Negativicutes	Acidaminococcales	Acidaminococcaceae	Acidaminococcus	intestinalis
ASV_104	165.2171921	-7.257755983	1.094064509	-6.633755071	3.27252692455385E-11	3.81794807864615E-10	Bacteria	Bacteroidota	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	massiliensis
ASV_123	100.8114371	-5.521510801	1.091821644	-5.057154555	4.25558338438288E-07	4.58293595241233E-06	Bacteria	Actinobacteriota	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	bifidum
ASV_177	53.6415468	4.110286262	1.128616539	3.641880232	0.000270654	0.00270654	Bacteria	Actinobacteriota	Actinobacteria	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium	animalis
ASV_202	127.887441	14.00883584	1.12979702	12.39942714	2.63198463344399E-35	9.21194621705396E-34	Bacteria	Bacteroidota	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	plebeius
ASV_217	45.77577167	12.5267809	1.129873892	11.08688411	1.45259641590064E-28	3.38939163710149E-27	Bacteria	Bacteroidota	Bacteroidia	Bacteroidales	Tannerellaceae	Parabacteroides	johnsonii
ASV_309	60.52674668	12.85841755	1.129833358	11.38080891	5.21140863375641E-30	1.45919441745179E-28	Bacteria	Desulfobacterota	Desulfovibrionia	Desulfovibrionales	Desulfovibrionaceae	Desulfovibrio	fairfieldensis
ASV_328	27.36761572	11.33415571	1.123464443	10.08857537	6.20636856209842E-24	9.65435109659754E-23	Bacteria	Bacteroidota	Bacteroidia	Bacteroidales	Bacteroidaceae	Bacteroides	ovatus
ASV_384	36.43927284	12.11973529	1.129888243	10.72649031	7.64447009656451E-27	1.5288940193129E-25	Bacteria	Firmicutes	Clostridia	Lachnospirales	Lachnospiraceae	Eisenbergiella	tayi
ASV_635	21.05201209	11.23206477	1.138659715	9.864285715	5.9456105183706E-23	8.32385472571884E-22	Bacteria	Firmicutes	Clostridia	Oscillospirales	Ruminococcaceae	Negativibacillus	massiliensis

Supplementary Table 3 Equations used to calculate absolute (U/mL) and relative fractional avidity (%), and total absolute and relative fractional avidity indices

	Very low	Low	Medium	High	Very high
Absolute fractional avidity (U/mL)	$AFA_{vlo} = Y_0 - Y_{0.5}$	$AFA_{lo} = Y_{0.5} - Y_{0.75}$	$AFA_{med} = Y_{0.75} - Y_1$	$AFA_{hi} = Y_1 - Y_2$	$AFA_{vhi} = Y_2$
Total absolute fractional avidity index	$2 * AFA_{vhi} + 1 * AFA_{hi} + 0.25 * AFA_{med} + 0.25 * AFA_{lo} + 0.5 * AFA_{vlo}$				
Relative fractional avidity (%)	$RFA_{vlo} = \frac{AFA_{vlo}}{Y_0} * 100\%$	$RFA_{lo} = \frac{AFA_{lo}}{Y_0} * 100\%$	$RFA_{med} = \frac{AFA_{med}}{Y_0} * 100\%$	$RFA_{hi} = \frac{AFA_{hi}}{Y_0} * 100\%$	$RFA_{vhi} = \frac{AFA_{vhi}}{Y_0} * 100\%$
Total relative fractional avidity (TRFA)*	$TRFA = -0.533 * RFA_{vlo} + 0.0269 * RFA_{lo} + 0.477 * RFA_{med} + 0.492 * RFA_{hi} + 0.495 * RFA_{vhi}$				

AFA – absolute fractional avidity, RFA – relative fractional avidity

*Based on eigenvalue plot loadings of each avidity for PC1 of all avidity data