

mRNA-based influenza vaccine expands the B cell response breadth in humans

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Supplementary Table 1

2022-2024 Northern Hemisphere HA proteins

Cell culture- or recombinant-based vaccines (mRNA-1010)

A/Wisconsin/588/2019 (H1N1)pdm09-like virus (2022-2023)
A/Wisconsin/67/2022 (H1N1)pdm09-like virus (2023-2024)
A/Darwin/6/2021 (H3N2)-like virus
B/Austria/1359417/2021 (B/Victoria lineage)-like virus
B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

Egg-based vaccines (Fluarix)

A/Victoria/2570/2019 (H1N1)pdm09-like virus (2022-2023)
A/Victoria/4897/2022 (H1N1)pdm09-like virus (2023-2024)
A/Darwin/9/2021 (H3N2)-like virus
B/Austria/1359417/2021 (B/Victoria lineage)-like virus
B/Phuket/3073/2013 (B/Yamagata lineage)-like virus

Virus strains included in 2022-2024 Northern Hemisphere influenza virus vaccines.

Supplementary Table 2

Participant	Time Point	Tissue	Sorting	Replicate	BCR		5' gene expression			
					Pre-QC number of cells	Post-QC number of cells	Pre-QC number of cells	Post-QC number of cells	Median number of UMIs per cell	Median number of genes per cell
397-05	d0	blood	IgDlo	1	2788	2448	3263	3237	4170	1506
397-05	d0	blood	IgDlo	2	3191	2779	3718	3680	4172	1508
397-05	d0	LN	NS	1	514	458	1558	1391	3278	1453
397-05	d0	LN	NS	2	523	479	1659	1477	3443	1505
397-05	d8	blood	PB	1	4369	3758	5409	4839	5080	1799
397-05	d8	blood	PB	2	4139	3647	5259	4738	5783.5	1829.5
397-05	d15	LN	NS	1	935	855	4229	4013	4018	1627
397-05	d15	LN	NS	2	1505	1379	5206	4961	4079	1631
397-05	d57	LN	NS	1	706	647	2581	2480	3646	1499
397-05	d57	LN	NS	2	798	706	2976	2891	3500	1447
397-05	d121	LN	NS	1	1014	900	3493	3345	3782	1548
397-05	d121	LN	NS	2	1254	1139	4102	3934	3852	1562
397-05	d180	blood	IgDlo	1	6143	4844	5958	5929	4237	1517
397-05	d180	blood	IgDlo	2	6838	5342	7045	7016	4147	1476
397-05	d181	LN	NS	1	450	406	2998	1672	3811	1543
397-05	d181	LN	NS	2	404	358	2706	1417	3877	1582
397-06	d0	blood	IgDlo	1	9544	8085	9071	8952	4768	1596
397-06	d0	blood	IgDlo	2	7594	6477	7292	7183	4895	1578
397-06	d0	LN	NS	1	251	234	6298	6075	3492	1431
397-06	d0	LN	NS	2	273	244	5313	5122	3411.5	1391
397-06	d8	blood	PB	1	6258	5692	7956	6937	11145	2311
397-06	d8	blood	PB	2	4845	4391	6590	5772	11244.5	2279
397-06	d15	LN	NS	1	254	225	6975	6905	3362	1346
397-06	d15	LN	NS	2	240	222	6086	6036	3286.5	1326.5
397-06	d57	LN	NS	1	118	107	3408	3234	3156	1291
397-06	d57	LN	NS	2	98	85	2438	2312	3253.5	1309.5
397-06	d121	LN	NS	1	234	218	3678	3088	3378.5	1394
397-06	d121	LN	NS	2	270	251	3379	2886	3306.5	1376
397-06	d180	blood	IgDlo	1	8581	7559	8634	8567	4956	1665
397-06	d180	blood	IgDlo	2	7185	6339	7388	7329	4853	1626
397-06	d181	LN	NS	1	349	313	7271	6899	3616	1421
397-06	d181	LN	NS	2	448	414	8281	7822	3724	1430

Processing of BCR and 5' gene expression data from scRNA-seq of WU397 participants 397-05 and 397-06. LN, lymph node; NS, no sorting.

Supplementary Table 3

Participant	Time Point	Tissue	Sorting	Replicate	BCR		5' gene expression			
					Pre-QC number of cells	Post-QC number of cells	Pre-QC number of cells	Post-QC number of cells	Median number of UMIs per cell	Median number of genes per cell
397-09	d0	blood	IgDlo	1	10857	7697	10514	10429	4429	1542
397-09	d0	blood	IgDlo	2	13440	9494	13753	13702	4209	1507
397-09	d0	LN	NS	1	707	633	4575	3858	4012	1605
397-09	d0	LN	NS	2	826	755	5007	4220	3829	1583
397-09	d8	blood	PB	1	3887	3237	4584	4017	8045	1904
397-09	d8	blood	PB	2	3970	3305	4631	4154	8030	1902.5
397-09	d15	LN	NS	1	601	527	2176	2070	3393	1328
397-09	d15	LN	NS	2	616	555	2217	2138	3260	1296
397-09	d57	LN	NS	1	1067	953	6250	6181	3746	1442
397-09	d57	LN	NS	2	1017	910	6688	6616	3741.5	1455
397-09	d121	blood	IgDlo	1	7293	5456	7212	7083	3901	1400
397-09	d121	blood	IgDlo	2	7900	6011	7624	7494	3849	1406
397-09	d121	LN	NS	1	1243	1141	4802	4643	4016	1594
397-09	d121	LN	NS	2	1398	1286	5424	5251	3655	1516
397-17	d0	blood	IgDlo	1	4320	3884	4456	4216	4137.5	1485
397-17	d0	blood	IgDlo	2	4030	3490	4252	4044	4164	1472
397-17	d0	LN	NS	1	1799	1683	5707	5642	3561	1455
397-17	d0	LN	NS	2	1959	1823	6095	6028	3542.5	1442
397-17	d8	blood	PB	1	3305	3060	6676	3460	15321	2474
397-17	d8	blood	PB	2	4561	3447	6157	3576	11379.5	2180.5
397-17	d15	LN	NS	1	2458	2274	14245	13624	3330	1371.5
397-17	d15	LN	NS	2	2849	2600	15818	14963	3283	1364
397-17	d57	LN	NS	1	3062	2847	13994	10534	3710	1489
397-17	d57	LN	NS	2	3534	3277	14734	10845	3713	1474
397-17	d121	blood	IgDlo	1	3381	2677	6488	4546	5141.5	1646
397-17	d121	blood	IgDlo	2	5658	4010	8870	6265	4747	1531
397-17	d121	LN	NS	1	1925	1739	9508	8736	3255.5	1304
397-17	d121	LN	NS	2	1917	1686	9765	8911	3257	1316
397-17	d181	LN	NS	1	2061	1960	10632	10529	3509	1438
397-17	d181	LN	NS	2	2032	1933	10799	10701	3509	1472

Processing of BCR and 5' gene expression data from scRNA-seq of WU397 participants 397-09 and 397-17. LN, lymph node; NS, no sorting.

Supplementary Table 4

Participant	Time Point	Tissue	Sorting	Replicate	BCR		5' gene expression			
					Pre-QC number of cells	Post-QC number of cells	Pre-QC number of cells	Post-QC number of cells	Median number of UMIs per cell	Median number of genes per cell
397-22	d0	blood	IgDlo	1	6467	4516	5535	5356	4767.5	1573
397-22	d0	blood	IgDlo	2	7884	5152	6670	6508	4556.5	1505
397-22	d0	LN	NS	1	697	618	4624	4335	4304	1578
397-22	d0	LN	NS	2	934	797	4790	4526	3916.5	1443.5
397-22	d8	blood	PB	1	3647	3047	3854	3528	10356.5	2095.5
397-22	d8	blood	PB	2	2870	2440	3284	3012	9889	2027
397-22	d15	LN	NS	1	890	808	5045	4965	4374	1613
397-22	d15	LN	NS	2	1369	1248	6101	6015	4320	1574
397-22	d57	LN	NS	1	103	96	5447	2947	4547	1684
397-22	d57	LN	NS	2	92	80	6373	3481	4530	1645
397-22	d121	LN	NS	1	727	682	4897	4619	4453	1680
397-22	d121	LN	NS	2	922	858	6007	5720	4292.5	1590
397-22	d180	blood	IgDlo	2	5589	3896	6311	6061	3292	1136
397-22	d181	LN	NS	1	997	927	3908	3447	4016	1430
397-22	d181	LN	NS	2	1269	1177	4824	4315	3959	1400
397-28	d0	blood	IgDlo	1	4785	4343	5362	4856	4687.5	1569
397-28	d0	blood	IgDlo	2	5990	5367	6760	6174	4952.5	1584.5
397-28	d0	LN	NS	1	1687	1605	6908	6884	2645	1124
397-28	d0	LN	NS	2	1058	1015	4342	4325	2598	1075
397-28	d8	blood	PB	1	1629	1328	2138	1178	14806	2599
397-28	d8	blood	PB	2	1978	1615	2869	1636	13439	2407
397-28	d15	LN	NS	1	2704	2579	6788	6620	3688.5	1401
397-28	d15	LN	NS	2	2785	2653	6568	6421	3735	1367
397-28	d57	LN	NS	1	2665	2399	8524	7426	3503	1316
397-28	d57	LN	NS	2	2454	1846	9418	8260	3300	1281
397-28	d121	LN	NS	1	306	285	2371	2065	3112	1253
397-28	d121	LN	NS	2	425	410	3284	2924	3062	1206
397-28	d180	blood	IgDlo	1	5668	4946	6199	5872	4320	1358.5
397-28	d180	blood	IgDlo	2	6389	5285	7233	6774	4712	1433
397-28	d181	LN	NS	1	2509	2397	13723	13699	3561	1340
397-28	d181	LN	NS	2	2240	2133	13580	13546	3726.5	1342

Processing of BCR and 5' gene expression data from scRNA-seq of WU397 participants 397-22 and 397-28. LN, lymph node; NS, no sorting.

Supplementary Table 5

Participant	Time Point	Tissue	Sorting	Replicate	BCR		5' gene expression			
					Pre-QC number of cells	Post-QC number of cells	Pre-QC number of cells	Post-QC number of cells	Median number of UMIs per cell	Median number of genes per cell
397-29	d0	blood	IgDlo	1	961	862	929	842	4791	1481.5
397-29	d0	blood	IgDlo	2	871	786	762	729	4289	1374
397-29	d0	LN	NS	1	1776	1660	7865	7772	3448	1297
397-29	d0	LN	NS	2	1762	1625	7593	7495	3201	1235
397-29	d8	blood	PB	1	3499	3156	6950	4072	14935	2309
397-29	d8	blood	PB	2	3472	2950	6983	3645	14930	2322
397-29	d15	LN	NS	1	973	907	6559	6508	3179	1248.5
397-29	d15	LN	NS	2	1101	1043	8649	8593	3501	1330
397-29	d57	LN	NS	1	2340	2126	8788	8496	3866	1385
397-29	d57	LN	NS	2	2515	2251	9449	9127	3894	1383
397-29	d121	LN	NS	1	1879	1751	7401	7276	3466.5	1269
397-29	d121	LN	NS	2	1951	1809	7959	7802	4042.5	1423
397-29	d180	blood	IgDlo	1	761	667	724	667	4136	1315
397-29	d180	blood	IgDlo	2	735	654	677	624	4264	1378
397-29	d181	LN	NS	1	5931	4849	9006	8925	3602	1420
397-29	d181	LN	NS	2	6181	5456	11286	11194	3618	1397

Processing of BCR and 5' gene expression data from scRNA-seq of WU397 participant 397-29.
LN, lymph node; NS, no sorting.

Supplementary Table 6

Participant	Overall cluster	Cell count (% of whole cells)	B cell cluster	Cell count (% of B cells)
397-05	B	36398 (64%)	PB	9617 (26.8%)
	CD4+ T	13865 (24.4%)	Naïve	4603 (12.8%)
	CD8+ T	4252 (7.5%)	ABC	1396 (3.9%)
	NK	946 (1.7%)	MBC	19647 (54.8%)
	Monocyte	1251 (2.2%)	GC	246 (0.7%)
	pDC	201 (0.4%)	LNPC	363 (1%)
397-06	B	46468 (48.9%)	PB	12506 (27.2%)
	CD4+ T	41920 (44.1%)	Naïve	3040 (6.6%)
	CD8+ T	4625 (4.9%)	ABC	510 (1.1%)
	NK	776 (0.8%)	MBC	29681 (64.6%)
	Monocyte	1116 (1.2%)	GC	135 (0.3%)
	pDC	193 (0.2%)	LNPC	59 (0.1%)
397-09	B	53702 (65.6%)	PB	9886 (18.6%)
	CD4+ T	19037 (23.3%)	Naïve	13254 (25%)
	CD8+ T	5373 (6.6%)	ABC	1937 (3.6%)
	NK	2278 (2.8%)	MBC	27348 (51.5%)
	Monocyte	1302 (1.6%)	GC	468 (0.9%)
	pDC	126 (0.2%)	LNPC	208 (0.4%)
397-17	B	48410 (38.2%)	PB	12597 (27.9%)
	CD4+ T	57264 (45.2%)	Naïve	14623 (32.4%)
	CD8+ T	16144 (12.8%)	ABC	209 (0.5%)
	NK	2910 (2.3%)	MBC	16930 (37.5%)
	Monocyte	1630 (1.3%)	GC	340 (0.8%)
	pDC	211 (0.2%)	LNPC	460 (1%)

Cell counts and frequencies of transcriptional clusters in scRNA-seq of WU397 participants 397-05, 397-06, 397-09, and 397-17. NK, natural killer cell. pDC, plasmacytoid dendritic cell. PB, plasmablast. MBC, memory B cell.

Supplementary Table 7

Participant	Overall cluster	Cell count (% of whole cells)	B cell cluster	Cell count (% of B cells)
397-22	B	30742 (44.7%)	PB	7851 (26.2%)
	CD4+ T	25357 (36.9%)	Naïve	2228 (7.4%)
	CD8+ T	9612 (14%)	ABC	902 (3%)
	NK	1526 (2.2%)	MBC	17484 (58.5%)
	Monocyte	1275 (1.9%)	GC	1169 (3.9%)
	pDC	290 (0.4%)	LNPC	278 (0.9%)
397-28	B	45430 (46.1%)	PB	3097 (7.3%)
	CD4+ T	42651 (43.3%)	Naïve	17462 (41.1%)
	CD8+ T	7516 (7.6%)	ABC	338 (0.8%)
	NK	1239 (1.3%)	MBC	19962 (47%)
	Monocyte	1425 (1.4%)	GC	1148 (2.7%)
	pDC	344 (0.3%)	LNPC	487 (1.1%)
397-29	B	32166 (34.3%)	PB	6039 (21.5%)
	CD4+ T	50195 (53.6%)	Naïve	4412 (15.7%)
	CD8+ T	8102 (8.6%)	ABC	222 (0.8%)
	NK	1195 (1.3%)	MBC	13509 (48.2%)
	Monocyte	1511 (1.6%)	GC	3302 (11.8%)
	pDC	520 (0.6%)	LNPC	540 (1.9%)

Cell counts and frequencies of transcriptional clusters in scRNA-seq of WU397 participants 397-22, 397-28, and 397-29. NK, natural killer cell. pDC, plasmacytoid dendritic cell. PB, plasmablast. MBC, memory B cell.

Supplementary Table 8

Monoclonal antibodies (mAbs) from WU397 participants							
Participant	Vaccine	mAbs expressed	HA+	H1+	H3+	B/Yam+	B/Vic+
397-06	mRNA-1010	439	259	126	89	39	46
397-17	mRNA-1010	411	215	53	114	41	33
397-28	mRNA-1010	174	81	26	32	25	16
397-29	mRNA-1010	569	229	70	126	27	40
397-05	Fluarix	412	165	66	29	65	67
397-09	Fluarix	493	54	21	6	22	18
397-22	Fluarix	491	38	12	10	8	13
	Total	2989	1041	374	406	227	233

Numbers of mAbs expressed from mRNA-1010 and Fluarix participants. Total numbers of mAbs determined by ELISA to bind HA and numbers of mAbs determined to bind each vaccine HA strain are shown.

Supplementary Table 9

Germinal center (GC) and week 1 plasmablast (PB) HA+ clones

Participant	Vaccine	Week 1 PB clones	GC clones	Clones in week 1 PB and GC	% overlap GC	% overlap week 1 PB
397-06	mRNA-1010	257	25	23	92.0	8.9
397-17	mRNA-1010	213	11	10	90.9	4.7
397-28	mRNA-1010	78	18	15	83.3	19.2
397-29	mRNA-1010	207	63	46	73.0	22.2
				Median	87.1	14.1
397-05	Fluarix	167	7	7	100.0	4.2
397-09	Fluarix	50	5	1	20.0	2.0
397-22	Fluarix	37	1	0	0.0	0.0
				Median	20.0	2.0

Numbers of mAbs expressed from mRNA-1010 and Fluarix participants determined to be HA-binding by ELISA with BCRs found in sorted PB clones at 1 week post vaccination and GC B cell clones.