**Supplementary Table 1:** M&M Individual Participant Demographics

| Study Arm | Participant | Sex at birth (Male M, Female F) | Race[1] | Ethnicity[2] | HLA Protective Alleles[3] | CD4 Nadir | Enrollment data | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Age (yr) | ART (yr) | CD4 count (/mm$^3$) | CD8 count (/mm$^3$) | CD4: CD8 | VL (copies/ mL) |
| **M3** | 00836 | M | AA | NH | | | 33 | 7.83 | 758 | 794 | 0.95 | 20 |
| | 01237a | M | U | H | | | 41 | 10.17 | 642 | 766 | 0.84 | 20 |
| | 01249 | M | C | NH | | | 28 | 8.11 | 738 | 585 | 1.26 | 20 |
| | 00937 | F | AA | NH | | | 48 | 9.21 | 1235 | 976 | 1.27 | 40 |
| | 00835 | M | C | NH | | | 43 | 9.61 | 789 | 589 | 1.34 | 20 |
| | 01214 | M | C | NH | | | 57 | 16.14 | 605 | 464 | 1.3 | 20 |
| | 01009 | F | AA | NH | B*58:01 | | 60 | 11.86 | 515 | 555 | 0.93 | 20 |
| | | | | | Average | | 44.28 | 10.42 | 754.57 | 675.57 | 1.23 | |
| **M4** | 00749[4,5] | M | AA | NH | | | 30 | 5.87 | 484 | 332 | 1.46 | 20 |
| | 01262 | M | C | H | | | 55 | 12.16 | 708 | 938 | 0.75 | 20 |
| | 01264[5,6] | M | AA | NH | | | 37 | 6.03 | 1002 | 745 | 1.3 | 20[6] |
| | 01276 | M | AA | NH | | | 46 | 11.12 | 427 | 493 | 0.87 | 20 |
| | 01277[5] | M | AA | NH | B*81:01 | | 31 | 2.47 | 795 | 659 | 1.2 | 40 |
| | 01095[4] | F | C | NH | | | 58 | 10.41 | 571 | 867 | 0.66 | 20 |
| | **00115** | M | C | NH | | | 59 | 18.12 | 821 | 996 | 0.82 | 40 |
| | | | | | Average | | 45.14 | 9.45 | 686.86 | 718.57 | 1.01 | |
| **M3M4** | **00631**[5] | M | AA | NH | | | 29 | 6.44 | 944 | 648 | 1.46 | 20 |
| | **00371**[4] | M | AA | NH | B*57:03, 58:01 | | 30 | 10.72 | 566 | 538 | 1.05 | 20 |
| | 01153 | M | C | NH | | | 55 | 12.71 | 847 | 942 | 0.9 | 40 |
| | 01280 | M | C | NH | | | 54 | 6.55 | 1086 | 616 | 1.76 | 40 |
| | **01213** | M[#] | AA | NH | | | 21 | 2.45 | 463 | 406 | 1.14 | 20 |
| | 01295[5] | M | AA | NH | B*57:03 | | 41 | 9.01 | 1365 | 876 | 1.56 | 20 |
| | 01293[5] | M | AA | NH | | | 31 | 4.34 | 855 | 1219 | 0.7 | 20 |
| | | | | | Average | | 37.29 | 7.46 | 875.14 | 749.29 | 1.22 | |
| **Placebo** | 00818[5] | M | B/AA | NH | | | 24 | 6.68 | 792 | 1447 | 0.55 | 20 |
| | 01270[5] | M | C | NH | | | 28 | 4.59 | 1070 | 1322 | 0.81 | 20 |
| | 01220[5] | M | C | NH | | | 52 | 2.37 | 522 | 787 | 0.66 | 20 |
| | | | | | Average | | 34.67 | 4.55 | 794.67 | 1185.33 | 0.67 | |
| | | | | | Cohort Average (n=24) | | 41.29 | 8.54 | 775.00 | 773.33 | 1.06 | |

[1]C: White/Caucasian, AA: Black/African American, U: Did not fall in NIH categories of American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, or White
[2]H: Hispanic, NH: Non-Hispanic
[3] Participant expresses one or more of HLA I alleles, B*57:01/03, B*58:01, B*81:01
[4] T-cell response against HIV outgrowth virus/s measured
[5]Phenotyped by mass cytometry to assess post-vaccination T-cell activation detailed Figure 4D.
[6] Virus blip at Day 70 (153 copies/mL), Day 86 (86 copies/mL) detailed Figure 4B
**Bolded** Participant Identifiers: initiated ART in acute HIV-1 infection, # PID01213 is a transgender woman.

**Supplementary Table 2:** Number of all solicited[1] and reportable unsolicited adverse events (including recurrences) by treatment arm.

| | Treatment Arm | | | | |
|---|---|---|---|---|---|
| **Adverse Event** | **M3 (n=7)** | **M4 (n=7)** | **M3M4 (n=8[1])** | **Placebo (n=3)** | **Total** |
| **Solicited** | | | | | |
| Injection Site Pain and, or tenderness | 13 | 12 | 13 | 3 | 41 |
| Headache | 9 | 4 | 5 | 3 | 21 |
| Fatigue | 7 | 5 | 5 | 2 | 19 |
| Malaise | 9 | 5 | 3 | 2 | 19 |
| Myalgia | 5 | 7 | 4 | 1 | 17 |
| Influenza Like Illness | 7 | 2 | 4 | 1 | 14 |
| Chills | 4 | 4 | 3 | 0 | 11 |
| Decreased Appetite | 4 | 1 | 3 | 1 | 9 |
| Nausea | 4 | 1 | 4 | 0 | 9 |
| Arthralgia | 3 | 0 | 3 | 1 | 7 |
| Hyperhidrosis | 3 | 1 | 1 | 1 | 6 |
| Dizziness | 4 | 1 | 0 | 0 | 5 |
| Abdominal Pain | 1 | 0 | 2 | 0 | 3 |
| Body Temperature Increased | 2 | 1 | 0 | 0 | 3 |
| Injection Site Swelling | 3 | 0 | 0 | 0 | 3 |
| Injection Site Warmth | 0 | 1 | 2 | 0 | 3 |
| Vomiting | 1 | 0 | 1 | 0 | 2 |
| Diarrhea | 0 | 1 | 0 | 0 | 1 |
| Injection Site Discoloration | 0 | 1 | 0 | 0 | 1 |
| Injection Site Erythema | 0 | 0 | 1 | 0 | 1 |
| Injection Site Induration | 0 | 0 | 1 | 0 | 1 |
| **Unsolicited** | | | | | |
| Procedural Hypertension | 12 | 13 | 15 | 5 | 45 |
| Blood Pressure Increased | 0 | 3 | 1 | 0 | 4 |
| Tissue Infiltration | 0 | 1 | 3 | 0 | 4 |
| Citrate Toxicity | 1 | 0 | 2 | 0 | 3 |
| Presyncope | 1 | 0 | 0 | 1 | 2 |
| Blood Creatinine Increased | 1 | 0 | 0 | 0 | 1 |
| Blood HIV RNA Increased | 0 | 1 | 0 | 0 | 1 |
| Erythema | 0 | 1 | 0 | 0 | 1 |
| Hyperhidrosis | 1 | 0 | 0 | 0 | 1 |
| Post Procedural Contusion | 1 | 0 | 0 | 0 | 1 |
| Post Procedural Hematoma | 0 | 1 | 0 | 0 | 1 |
| Procedural Dizziness | 0 | 0 | 0 | 1 | 1 |
| Procedural Pain | 0 | 0 | 1 | 0 | 1 |
| Pyrexia | 0 | 0 | 0 | 1 | 1 |
| Vessel Puncture Site Hemorrhage | 0 | 0 | 0 | 1 | 1 |
| Vessel Puncture Site Pain | 0 | 0 | 0 | 1 | 1 |
| **Total** | 96 | 67 | 77 | 25 | 265 |

[1] In the M3M4 group, one participant was vaccinated with M3M4 and completed study visits but had received a COVID-19 vaccination within two weeks of enrollment. This participant was subsequently replaced.

**Supplementary Table 3:** Fold-change in Mos-1- and Mos-2-specific T-cell frequencies following vaccination measured by IFN-γ ex vivo ELISpot

| Study Arm | Participant | Sex[1] | Age[2] | Years on ART[3] | Protective HLA Alleles[4] | Fold change from Baseline[5] | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Day 7 | | Day 14 | | Day 70 | |
| | | | | | | Mos-1 | Mos-2 | Mos-1 | Mos-2 | Mos-1 | Mos-2 |
| **M3** | 00836 | M | 33 | 7.83 | | 8.877 | 6.364 | 8.282 | 6.277 | 7.835 | 5.885 |
| | 01237a | M | 41 | 10.17 | | 2.789 | 2.657 | 2.770 | 3.053 | 1.434 | 1.197 |
| | 01249 | M | 28 | 8.11 | | 9.849 | 2.908 | 24.590 | 6.916 | 20.966 | 6.543 |
| | 00937 | F | 48 | 9.21 | | 4.959 | 3.681 | 6.727 | 4.993 | 3.031 | 2.204 |
| | 00835 | M | 43 | 9.61 | | 2.848 | 2.129 | 4.857 | 5.169 | 2.868 | 2.114 |
| | 01214 | M | 57 | 16.14 | | 2.000 | 1.495 | 1.444 | 1.021 | 1.275 | 1.027 |
| | 01009 | F | 60 | 11.86 | B*58:01 | 1.537 | 1.028 | 1.434 | 1.057 | 1.357 | 1.102 |
| **M4** | 00749 | M | 30 | 5.87 | | 5.242 | 5.856 | 4.959 | 5.736 | 3.605 | 3.482 |
| | 01262 | M | 55 | 12.16 | | 2.114 | 2.219 | 2.828 | 3.182 | 2.888 | 2.497 |
| | 01264 | M | 37 | 6.03 | | 1.007 | 2.282 | 1.266 | 4.347 | 1.079 | 2.694 |
| | 01276 | M | 46 | 11.12 | | 1.569 | 1.892 | 1.395 | 1.778 | 1.125 | 1.310 |
| | 01277 | M | 31 | 2.47 | B*81:01 | 1.516 | 9.190 | 2.000 | 13.929 | ND[6] | ND |
| | 01095 | F | 58 | 10.41 | | 1.181 | 1.602 | 0.993 | 1.181 | ND | ND |
| | **00115** | M | 59 | 18.12 | | 3.272 | 1.905 | 7.311 | 4.500 | 1.932 | 1.516 |
| **M3M4** | **00631** | M | 29 | 6.44 | | 11.472 | 3.138 | 8.340 | 2.000 | 4.287 | 1.357 |
| | **00371** | M | 30 | 10.72 | B*57:03, 58:01 | 7.674 | 3.364 | 3.864 | 2.549 | 2.189 | 1.892 |
| | 01153 | M | 55 | 12.71 | | 3.364 | 5.897 | 3.482 | 7.062 | 2.532 | 4.627 |
| | 01280 | M | 54 | 6.55 | | ND | ND | 0.722 | 0.883 | 0.993 | 1.165 |
| | **01213** | M# | 21 | 2.45 | | 6.021 | 6.589 | 8.340 | 9.781 | 7.062 | 8.225 |
| | 01295 | M | 41 | 9.01 | B*57:03 | 1.625 | 2.657 | 1.892 | 3.117 | 1.395 | 1.548 |
| | 01293 | M | 31 | 4.34 | | 2.000 | 2.585 | 2.770 | 4.228 | 2.732 | 4.112 |
| **Placebo** | 00818 | M | 24 | 6.68 | | 0.889 | 0.847 | 1.102 | 1.102 | 1.395 | 0.883 |
| | 01270 | M | 28 | 4.59 | | 1.057 | 1.064 | 0.737 | 0.920 | 0.920 | 0.514 |
| | 01220 | M | 52 | 2.37 | | 1.050 | 0.973 | 1.464 | 1.414 | 0.883 | 1.028 |
| | | M3, M4, M3M4 Vaccinees only: Median (IQR) | | | | 2.819 (3.579) | 2.657 (1.848) | 2.828 (3.987) | 4.228 (4.013) | 2.532 (1.721) | 2.114 (2.121) |
| | | Vaccinees with Non-Protective Alleles: Median (IQR) | | | | 3.060 (1.824) | 2.621 (1.687) | 3.482 (2.956) | 4.347 (3.596) | 2.800 (1.593) | 2.350 (1.530) |
| | | Vaccinees with Protective Alleles: Median (IQR) | | | | 1.581 (1.842) | 3.010 (1.587) | 1.946 (2.526) | 2.833 (3.068) | 1.395 (1.525) | 1.548 (1.530) |

[1] Sex at birth, M = male, F = female
[2] age (years) enrollment
[3] years from antiretroviral therapy (ART) initiation to enrollment
[4] Participant expresses one or more of the following HLA I alleles, B*57:01/03, B*58:01, B*81:01
[5] Fold-change from the average of two pre-vaccination timepoints to indicated visit (see Methods)
[6] ND – not done. No sample available for testing.
**Bolded** Participant Identifiers: initiated ART in acute HIV-1 infection # PID01213 is a transgender woman.

**Supplementary Table 4:** Detection of baseline HIVconsvX-specific T-cells following *in vitro* culture.

| | | Ex vivo ELISpot | | | Short term cell lines (STCL) then ELISpot | | | |
|---|---|---|---|---|---|---|---|---|
| Participant | Study Group | Sub-pool tested by ELISpot | Baseline (SFU/$10^6$ PBMC)[1] | Post-vaccination (SFU/$10^6$ PBMC)[2] | Stimulating Peptide Pool | Sub-pool tested by ELISpot | Day -28 (SFU/$10^6$ STCL) | Fold-expansion relative to baseline ex vivo frequency[3] |
| **836** | **M3** | A (G1) | 225 | 1180 | Mos-1 | **A (G1)** | **2200** | **9.8** |
| | | C (P3-A) | ≤20 | 69 | | C (P3-A) | ≤20 | - |
| | | E (P6) | ≤20 | 71 | | E (P6) | ≤20 | - |
| | | | | | Mos-2 | **A (G1)** | **2460** | **11** |
| | | | | | | **C (P3-A)** | **469** | **23.4** |
| | | | | | | E (P6) | ≤20 | - |
| 1237a | M3 | A (G1) | 106 | 300 | Mos-1 | A (G1) | 329 | 3.1 |
| | | C (P3-A) | ≤20 | 27 | | C (P3-A) | ≤20 | - |
| | | | | | Mos-2 | A (G1) | ≤20 | - |
| | | | | | | C (P3-A) | ≤20 | - |
| **1249** | **M3** | A (G1) | 45 | 209 | Mos-1 | **A (G1)** | **700** | **15.5** |
| | | C (P3-A) | ≤20 | 61 | | C (P3-A) | ≤20 | - |
| | | D (P3-B) | ≤20 | 105 | | D (P3-B) | ≤20 | - |
| | | E (P6) | ≤20 | 143 | | **E (P6)** | **794** | **39.7** |
| | | | | | Mos-2 | **A (G1)** | **1065** | **24** |
| | | | | | | C (P3-A) | ≤20 | - |
| | | | | | | **D (P3-B)** | **300** | **15** |
| | | | | | | E (P6) | ≤20 | - |
| 937 | M3 | A (G1) | 76 | 451 | Mos-1 | A (G1) | ≤20 | - |
| | | C (P3-A) | ≤20 | 280 | | C (P3-A) | ≤20 | - |
| | | E (P6) | ≤20 | 178 | | E (P6) | ≤20 | - |
| | | | | | Mos-2 | A (G1) | ≤20 | - |
| | | | | | | C (P3-A) | ≤20 | - |
| | | | | | | E (P6) | ≤20 | - |
| **835** | **M3** | A (G1) | 219 | 513 | Mos-1 | **A (G1)** | **3983** | **18.2** |
| | | E (P6) | ≤20 | 160 | | **E (P6)** | **794** | **39.7** |
| | | | | | Mos-2 | **A (G1)** | **1827** | **8.3** |
| | | | | | | **E (P6)** | **725** | **36.3** |
| **1214** | **M3** | A (G1) | 388 | 612 | Mos-1 | **A (G1)** | **8700** | **22.4** |
| | | C (P3-A) | ≤20 | 22 | | C (P3-A) | ≤20 | - |
| | | | | | Mos-2 | **A (G1)** | **8508** | **22** |
| | | | | | | C (P3-A) | 150 | 7.5 |
| 1009 | M3 | A (G1) | 1682 | 1731 | Mos-1 | A (G1) | 1208 | - |
| | | C (P3-A) | ≤20 | 45 | | C (P3-A) | ≤20 | - |
| | | E (P6) | ≤20 | 71 | | E (P6) | ≤20 | - |
| | | | | | Mos-2 | A (G1) | 1894 | 1.1 |
| | | | | | | C (P3-A) | ≤20 | - |
| | | | | | | E (P6) | ≤20 | - |
| **749** | **M4** | A (G1) | | 288 | Mos-1 | A (G1) | ≤20 | - |
| | | C (P3-A) | | 85 | | C (P3-A) | ≤20 | - |
| | | D (P3-B) | | 212 | | D (P3-B) | ≤20 | - |
| | | | | | Mos-2 | **A (G1)** | **200** | **8.7** |
| | | | | | | C (P3-A) | ≤20 | - |
| | | | | | | D (P3-B) | 142 | 7.1 |
| **1262** | **M4** | A (G1) | 150 | 304 | Mos-1 | **A (G1)** | **1529** | **10.2** |
| | | D (P3-B) | ≤20 | 32 | | **D (P3-B)** | **644** | **32.2** |
| | | | | | Mos-2 | **A (G1)** | **1479** | **9.9** |
| | | | | | | **D (P3-B)** | **300** | **15.0** |
| **1264** | **M4** | A (G1) | 296 | 374 | Mos-1 | A (G1) | ≤20 | - |
| | | C (P3-A) | ≤20 | 78 | | C (P3-A) | ≤20 | - |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | D (P3-B) | ≤20 | 105 | | D (P3-B) | ≤20 | - |
| | | | | | Mos-2 | **A (G1)** | **3225** | **10.9** |
| | | | | | | C (P3-A) | ≤20 | - |
| | | | | | | D (P3-B) | ≤20 | - |
| 1277 | M4 | A (G1) | 859 | 1295 | Mos-1 | A (G1) | ≤20 | - |
| | | D (P3-B) | ≤20[1] | 275 | | D (P3-B) | ≤20 | - |
| | | E (P6) | ≤20[1] | 164 | | E (P6) | ≤20 | - |
| | | | | | Mos-2 | A (G1) | ≤20 | - |
| | | | | | | D (P3-B) | ≤20 | - |
| | | | | | | E (P6) | ≤20 | - |
| **1095** | **M4** | A (G1)[1] | 348 | 759 | Mos-1 | **A (G1)** | **2771** | **8.0** |
| | | C (P3-A) | ≤20 | 118 | | C (P3-A) | ≤20 | - |
| | | E (P6) | ≤20 | 198 | | **E (P6)** | **1113** | **55.6** |
| | | | | | Mos-2 | **A (G1)** | **2260** | **6.5** |
| | | | | | | C (P3-A) | ≤20 | - |
| | | | | | | **E (P6)** | **1760** | **88.0** |
| **631** | **M3M4** | A (G1) | 91 | 645 | Mos-1 | A (G1) | ≤20 | - |
| | | B (G2+P4+P5) | ≤20 | 263 | | B (G2+P4+P5) | ≤20 | - |
| | | C (P3-A) | ≤20 | 67 | | C (P3-A) | ≤20 | - |
| | | D (P3-B) | ≤20 | 116 | | D (P3-B) | ≤20 | - |
| | | E (P6) | ≤20 | 125 | | E (P6) | ≤20 | - |
| | | | | | Mos-2 | **A (G1)** | **1656** | **18.2** |
| | | | | | | B (G2+P4+P5) | ≤20 | - |
| | | | | | | C (P3-A) | ≤20 | - |
| | | | | | | D (P3-B) | ≤20 | - |
| | | | | | | E (P6) | ≤20 | - |
| **371** | **M3M4** | A (G1) | 759 | 2498 | Mos-1 | A (G1) | 2331 | 3.1 |
| | | B (G2+P4+P5) | ≤20 | 144 | | B (G2+P4+P5) | ≤20 | - |
| | | | | | **Mos-2** | **A (G1)** | **2929** | **3.9** |
| | | | | | | B (G2+P4+P5) | ≤20 | - |
| **1153** | **M3M4** | A (G1) | 46 | 192 | Mos-1 | **A (G1)** | **250** | **5.4** |
| | | E (P6) | ≤20 | 50 | | **E (P6)** | **213** | **10.6** |
| | | | | | Mos-2 | **A (G1)** | **310** | **6.7** |
| | | | | | | E (P6) | ≤20 | - |
| **1213** | **M3M4** | A (G1) | 81 | 414 | Mos-1 | **A (G1)** | **1581** | **19.5** |
| | | C (P3-A) | ≤20 | 92 | | C (P3-A) | ≤20 | - |
| | | | | | Mos-2 | **A (G1)** | **1825** | **22.5** |
| | | | | | | C (P3-A) | ≤20 | - |
| **1295** | **M3M4** | A (G1) | 153 | 401 (D14) | Mos-1 | **A (G1)** | **3135** | **20.5** |
| | | B (G2+P4+P5) | ≤20 | 48 (D14) | | B (G2+P4+P5) | ≤20 | - |
| | | D (P3-B) | ≤20 | 27 (D14)[6] | | D (P3-B) | ≤20 | - |
| | | | | | Mos-2 | **A (G1)** | **3129** | **20.5** |
| | | | | | | B (G2+P4+P5) | ≤20 | - |
| | | | | | | D (P3-B) | ≤20 | - |
| **1293** | **M3M4** | A (G1) | 645 | 2113 (D14) | Mos-1 | **A (G1)** | **11223** | **17.4** |
| | | C (P3-A) | ≤20 | 73 (D14)[5] | | C (P3-A) | 94 | 4.7 |
| | | | | | Mos-2 | **A (G1)** | **12567** | **19.5** |
| | | | | | | **C (P3-A)** | **369** | **18.4** |

[1] Baseline T-cell frequency is the average of two pre-vaccination visits. [2] Day 7 post-MVA.HIVconsvX visit unless otherwise specified in parentheses. Note: A HIVconsvX sub-pool was assigned positive post-vaccination only if positivity criteria for ex vivo ELISpot (Methods) were met at 2 or more post-vaccination visits. [3] Fold-change calculated from baseline T-cell frequency (the average of two pre-vaccination visits, details Methods). For sub-pools <20 SFU/$10^6$ PBMC and/or had a replicate value of '0', a value of 20 SFU was assigned to calculate fold change. [4] In all participants, a positive ex vivo T-cell response (details Methods) was detected against sub-pool A, G1. [5] PID1293, T-cell response in ex vivo ELISpot to sub-pool C was negative at Day 7 but positive at Day 14 (shown) [6] PID1295, T-cell response in ex vivo ELISpot to sub-pool D was negative at Day 7 but positive at Day 14 (shown). **Bold** = Positive HIV-specific T-cell response to HIVconsvX in cultured ELISpot. Criteria: > 200 SFU/$10^6$ cells, > 3-fold above mock-stimulated cells. For sub-pools B-E, a > 3.5-fold expansion to sub-pool A (G1) in the same parent STCL was required as a positive control for HIV-specific expansion of T-cells.

**Supplementary Table 5:** T-cell frequencies measured by ex vivo IFN-γ ELISpot against autologous HIV sequences.

| Participant - group | HXB2 Region | Autologous Virus Sequence (predicted HLA restriction) [1] | # autologous viruses in which sequence occurs | Sequence in HIVCONSX immunogen[2] (Y/N) | %Seq. Identity with Mos-1 peptide[2] | %Seq. Identity with Mos-2 peptide[2] | %Seq. Identity with Clade B peptide[3] | **Ex vivo ELISpot SFU/10⁶, (SEM)** [4] | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Pre-vaccination Visit 3 - Baseline | Post-MVA.HIVconsvX Vaccination Visit 8 - Day 28 |
| 00371-M3M4 | Gag 240→249 | TSTLQEQIGW[4] (HLA-B*57:03, B*58:01) | 3/3 | Y | 90.00% | 100.00% | 100.00% | 321 (21) | 882 (10) |
| | Gag 244→261 | QEQIGWMTNNPPIPVGEI | 3/3 | Y | 88.88% | 100.00% | 100.00% | 276 15) | 875 (31) |
| | Gag 300→317 | FYKTLRAEQASQDVKNWM | 3/3 | Y | 94.44% | 83.33% | 94.44% | 23 (3) | 13 (5) |
| | Gag 196→213 | AAMQMLKETINEEAAEWD | 3/3 | Y | 94.44% | 100.00% | 100.00% | 21 (4) | 12 (3) |
| | Pol 873→890 | LKKIIGQVRDQAEHLKTA | 3/3 | Y | 94.44% | 100.00% | 100.00% | 38 (8) | 75 (3) |
| 00749-M4 | Pol 481→498 | IAEIQKQGQGQWTYQIYQ | 15/15 | Y | 94.44% | 100.00% | 100.00% | 146 (15) | 395 (23) |
| | Pol 929→946 | QKQISKIQNFRVYYRDNR | 15/15 | Y | 88.88% | 88.88% | 88.88% | 60 (9) | 183 (12) |
| | Pol 969→986 | NSEIKVVPRRKAKIIRDY | 15/15 | Y | 88.88% | 100.00% | 94.44% | 53 (4) | 183 (10) |
| | Vif 32→40,$_{36K}$ | SKKC**K**GWFY[4] | 14/16 | N | N/A | N/A | 77.77% | 44 (8) | 146 (4) |
| | Vif 32→40,$_{36N}$ | SKKC**N**GWFY[4] (HLA-B*15:03) | 2/16 | N | N/A | N/A | 66.66% | 0 | 4 (2) |
| 01095-M4 | Pol 313→321,$_{320T}$ | AIFQSSM**T**K[4] | 32/35 | Y | 100.00% | 88.88% | 100.00% | 559 (20) | 795 (12) |
| | Pol 313→321,$_{320I}$ | AIFQSSM**I**K[4] (HLA-A*03:01, A*11:01) | 3/35 | Y | 88.88% | 77.77% | 88.88% | 411 (32) | 593 (27) |
| | Pol 273→290 | VPLDKDFRKYTAFTIPSI | 35/35 | Y | 88.88% | 94.44% | 100.00% | 393 (15) | 498 (19) |
| | Gag 397→414,$_{406K,411K}$ | REGHIAKNC**K**APRK**K**GCW | 8/35 | Y | 83.33% | 77.77% | 88.88% | 68 (15) | 52 (7) |
| | Gag 397→414,$_{406R,411R}$ | REGHIAKNC**R**APRK**R**GCW | 5/35 | Y | 94.44% | 77.77% | 88.88% | 77 (10) | 61 (14) |
| | Gag 397→414,$_{406R,411K}$ | REGHIAKNC**R**APRK**K**GCW | 19/35 | Y | 88.88% | 83.33% | 94.44% | 55 (4) | 58(7) |
| | Pol 353→370,$_{355A,359E,366K}$ | HR**A**KIE**E**LRQHLL**K**WGFT | 11/35 | Y | 94.44% | 88.88% | 88.88% | 76 (14) | 105 (7) |
| | Pol 353→370,$_{355I,359E,366K}$ | HR**I**KIE**E**LRQHLL**K**WGFT | 6/35 | Y | 88.88% | 88.88% | 88.88% | 76 (14) | 108 (8) |
| | Pol 353→370,$_{355I,359E,366R}$ | HR**I**KIE**E**LRQHLL**R**WGFT | 2/35 | Y | 83.33% | 94.44% | 94.44% | 89 (10) | 103 (7) |
| | Pol 353→370,$_{355A,359K,366K}$ | HR**A**KIE**K**LRQHLL**K**WGFT | 1/35 | Y | 88.88% | 83.33% | 83.33% | 4 (SEM) | 5 (SEM) |
| | Pol 353→370,$_{355A,359E,366R}$ | HR**A**KIE**E**LRQHLL**R**WGFT | 15/35 | Y | 88.88% | 94.44% | 94.44% | 84 (5) | 82 (9) |

[1] HIV outgrowth assays were performed at limiting dilution in each participant prior to vaccination. Near full-length virus sequences were produced using PacBio sequencing (see Methods). 00749 and 01095 sequences were previously published in (42). Sequences deposited GenBank.[2] HIVconsvX sequences published in (7) [3] Clade B sequence (www.lanl.gov) [4] Each participant was first mapped against overlapping peptides spanning HIV Clade B. The corresponding 18-mer autologous outgrowth reservoir virus peptide/s for all previously defined reactive 18-mers from the initial mapping ELISpot were also synthesized. In addition, optimal CD8 T-cell peptides predicted through LANL's epitope location finder ('ELF') software based on HLA-prediction software (https://www.hiv.lanl.gov/content/sequence/ELF/epitope_analyzer.html), and 18-mer peptides spanning regions where > 40% of the sequences contain non-synonymous mutations in the same position were synthesized. These autologous sequences were then tested in ex vivo ELISpot pre- and post-vaccination to produce the final list of reactive autologous epitopes within each participant. 'Negative' data to variant sequences are also shown.
[5] Empirically confirmed optimal CD8 T-cell epitope (restricting HLA allele).

**Supplementary Table 6:** Mos-1- and Mos-2-specific CD4+ and CD8+ T cells detected by intracellular cytokine staining (ICS) measured post-vaccination.

| Study Arm | Participant | Set at birth | Raace[1] | Ethnicity[2] | Days from vaccination[3] | ICS (background -subtracted frequency) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | CD4 T cells | | | | CD8 T cells | | | |
| | | | | | | IFN-g + | | IFN-g+CD107a+ | | IFN-g+ | | IFN-g+CD107a+ | |
| | | | | | | Mos-1 | Mos-2 | Mos-1 | Mos-2 | Mos-1 | Mos-2 | Mos-1 | Mos-2 |
| **M3** | 00836 | M | AA | NH | 7 | **0.158%** | **0.174%** | **0.074%** | **0.089%** | *0.021%* | *0.016%* | **0.026%** | **0.017%** |
| | 01237a | M | U | H | 56 | **0.045%** | **0.128%** | *0.012%* | *0.016%* | **0.160%** | **0.123%** | **0.150%** | **0.093%** |
| | 01249 | M | C | NH | 14 | **0.258%** | **0.252%** | **0.033%** | **0.036%** | **0.024%** | **0.034%** | *0.011%* | *0.007%* |
| | 00937 | F | AA | NH | 56 | **0.106%** | **0.058%** | **0.017%** | *0.009%* | **0.203%** | **0.118%** | **0.209%** | **0.119%** |
| | 00835 | M | C | NH | 7 | **0.104%** | **0.064%** | **0.015%** | **0.015%** | **0.100%** | **0.026%** | **0.098%** | **0.028%** |
| | 01214 | M | C | NH | 7 | **0.086%** | *0.051%* | *0.022%* | *0.016%* | *0.0%* | *0.005%* | *0.006%* | *0.020%* |
| | 01009[1] | F | AA | NH | 7 | **0.041%** | *0.027%* | **0.007%** | *0.005%* | **0.100%** | **0.100%** | **0.098%** | **0.108%** |
| **M4** | 00749 | M | AA | NH | 7 | *0.043%* | *0.037%* | *0.003%* | *0.004%* | **0.123%** | **0.477%** | **0.065%** | **0.246%** |
| | 01262 | M | C | H | 56 | **0.045%** | **0.047%** | *0.014%* | *0.015%* | *0.023%* | *0.008%* | **0.056%** | **0.036%** |
| | 01264 | M | AA | NH | 56 | **0.088%** | **0.126%** | *0.001%* | *0.000%* | **0.432%** | **0.081%** | **0.278%** | **0.056%** |
| | 01276 | M | AA | NH | 7 | **0.015%** | **0.026%** | *0.006%* | *0.011%* | **0.182%** | **0.217%** | **0.186%** | **0.216%** |
| | 01277[1] | M | AA | NH | 14 | **0.264%** | **0.298%** | **0.017%** | **0.019%** | **0.369%** | **0.272%** | **0.368%** | **0.268%** |
| | 01095 | F | C | NH | 14 | **0.113%** | **0.085%** | **0.012%** | **0.018%** | **0.622%** | **0.058%** | **0.621%** | **0.061%** |
| | 00115 | M | C | NH | 7 | **0.165%** | **0.139%** | **0.040%** | **0.039%** | *0.0%* | **0.133%** | **0.018%** | **0.127%** |
| **M3M4** | 00631 | M | AA | NH | 7 | **0.068%** | **0.092%** | **0.039%** | **0.050%** | **0.049%** | **0.096%** | **0.050%** | **0.085%** |
| | 00371[1] | M | AA | NH | 7 | **0.082%** | **0.095%** | *0.0%* | *0.000%* | **0.050%** | **0.424%** | *0.013%* | **0.180%** |
| | 01153[2] | M | C | NH | 7 | *0.037%* | *0.049%* | *0.004%* | *0.008%* | *0.011%* | *0.005%* | *0.003%* | *0.003%* |
| | 01280 | M | C | NH | 56 | **0.081%** | **0.088%** | **0.030%** | **0.024%** | *0.0%* | *0.0%* | *0.003%* | *0.005%* |
| | 01213 | F | AA | NH | 14 | **0.090%** | **0.086%** | *0.006%* | *0.007%* | *0.008%* | *0.009%* | *0.0%* | **0.009%** |
| | 01295[1] | M | AA | NH | 14 | *0.021%* | **0.055%** | *0.001%* | *0.000%* | **0.049%** | **0.065%** | **0.058%** | **0.055%** |
| | 01293 | M | AA | NH | 56 | **0.438%** | **0.427%** | *0.013%* | *0.010%* | **0.642%** | **0.378%** | **0.460%** | **0.290%** |

[1] Participant expresses one or more of the following HLA I alleles, B*57:01/03, B*58:01, B*81:01 (detailed Supplementary Table 1)

[2] 001153 ICS performed on Day 7 post-vaccination. Average T-cell responses measured by IFN-γ ELISpot at baseline (average two pre-vaccination visits) was Mos-1 105 SFU/$10^6$ and Mos-2 39 SFU/$10^6$ and average on Day 7 for Mos-1 was 354 SFU/$10^6$ and Mos-2 was 221 SFU/$10^6$

[3] To maximize assay sensitivity, ICS was performed at or near the peak measured HIVconsvX-specific T cell response by IFN-γ ELISpot.

**Bold** = Mos-1- or Mos-2-specific T-cell response defined by ≥2×mock-stimulated cells and functional gate of Mos-1- or Mos-2-stimulated cells had ≥25 events than corresponding functional gate of mock stimulated cells. Negative measurements indicated in *gray italic.*

**Supplementary Table 7:** The association of age at enrollment on T-cell response to MVA.HIVconsvX vaccination in PWH on ART[1] estimated from simple linear regression

| | Age | Mos-1 | Mos-2 |
|---|---|---|---|
| Fold-change per 10 person years from baseline to D14 post-vaccination | 20 | 7.30 | 7.64 |
| | 30 | 5.06 | 5.32 |
| | 40 | 3.50 | 3.70 |
| | 50 | 2.43 | 2.58 |
| | 60 | 1.68 | 1.79 |
| Fold-change per 10 person years from baseline to D70 post-vaccination | 20 | 5.95 | 4.61 |
| | 30 | 4.05 | 3.37 |
| | 40 | 3.50 | 2.46 |
| | 50 | 1.88 | 1.80 |
| | 60 | 1.68 | 1.31 |

**Supplementary Table 8:** Age at enrollment and years on ART predict post-vaccination T-cell response following MVA.HIVconsvX vaccination

| Antigen | log2FC from baseline to day | Predictors | Slope Estimate[1] | p-value[2] | Multiple R2 |
|---|---|---|---|---|---|
| Mos-1 | 7 | Age | -0.046 | 1.74 ×10-2 | 0.28 |
| | 14 | Age | -0.053 | 1.64 ×10-2 | 0.27 |
| | 70 | Age | -0.056 | 6.90 ×10 -3 | 0.36 |
| | 7 | Age<br>Years on ART | -0.109<br>0.236 | 5.03 ×10-4<br>7.63 ×10-3 | 0.53 |
| | 14 | Age<br>Years on ART | -0.110<br>0.233 | 6.24 ×10-4<br>1.15 ×10-2 | 0.49 |
| | 70 | Age<br>Years on ART | -0.075<br>0.082 | 1.79 ×10-2<br>ns | 0.39 |
| | 7 | Age<br>Pre-vax logIPDA | -0.030<br>-0.501 | ns<br>ns | 0.39 |
| | 14 | Age<br>Pre-vax logIPDA | -0.034<br>-0.526 | ns<br>ns | 0.35 |
| | 70 | Age<br>Pre-vax logIPDA | -0.047<br>-0.381 | ns<br>ns | 0.42 |
| Mos-2 | 7 | Age | -0.042 | 2.54 ×10-3 | 0.41 |
| | 14 | Age | -0.052 | 5.52 ×10-3 | 0.34 |
| | 70 | Age | -0.045 | 8.13 ×10-3 | 0.35 |
| | 7 | Age<br>Years on ART | -0.028<br>-0.052 | ns<br>ns | 0.43 |
| | 14 | Age<br>Years on ART | -0.055 0.011 | ns<br>ns | 0.34 |
| | 70 | Age<br>Years on ART | -0.038<br>-0.030 | ns<br>ns | 0.35 |
| | 7 | Age<br>Pre-vax logIPDA | -0.040<br>0.035 | 0.018<br>ns | 0.36 |
| | 14 | Age<br>Pre-vax logIPDA | -0.050<br>0.142 | 0.024<br>ns | 0.32 |
| | 70 | Age<br>Pre-vax logIPDA | -0.043<br>-0.067 | ns<br>ns | 0.31 |

[1] Models are simple or multiple linear regression estimates
[2] ns - non-significant p>0.05
FC=fold change, ART antiviral therapy

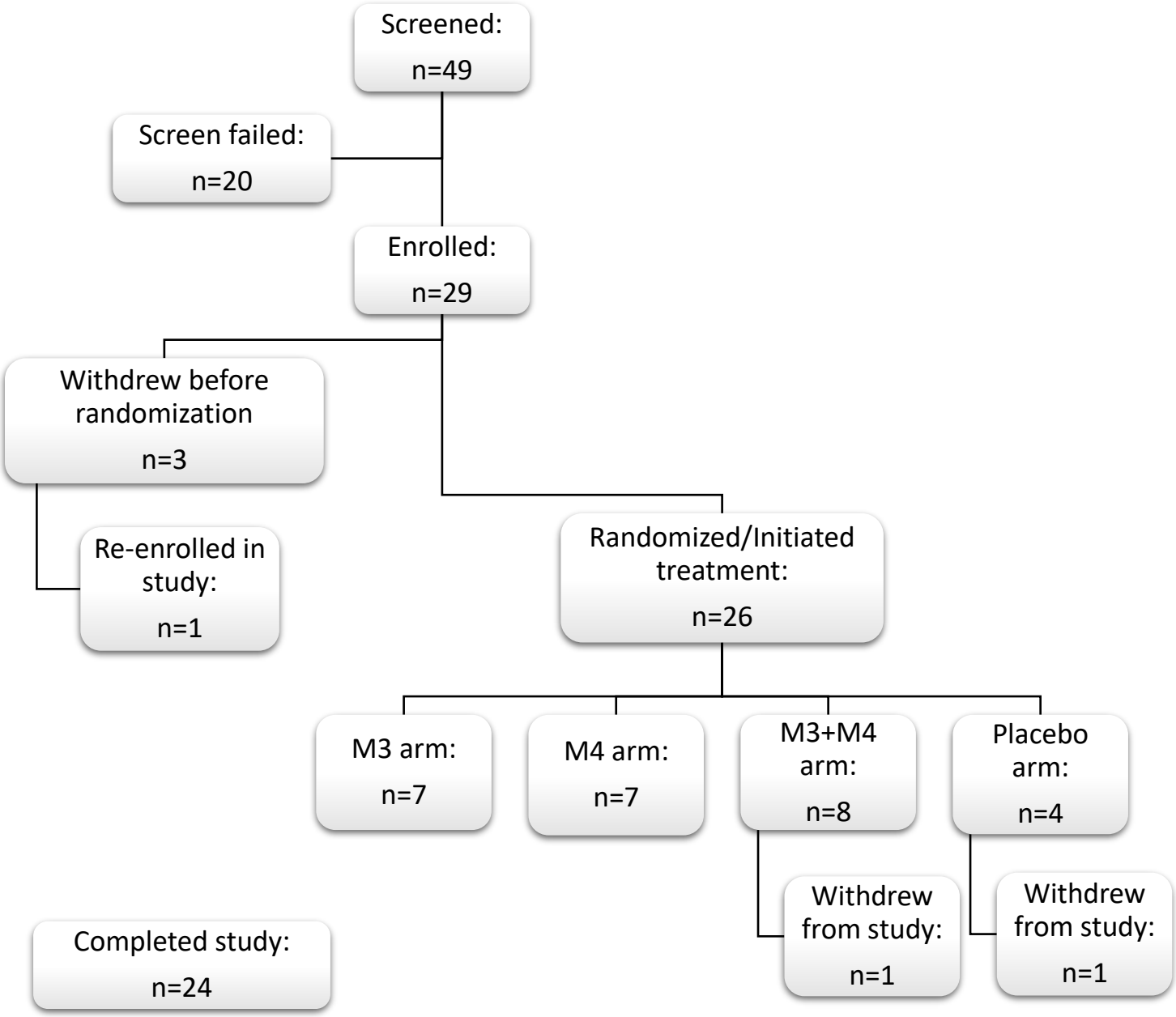
**Supplementary Table 9:** Key Reagents and Resources

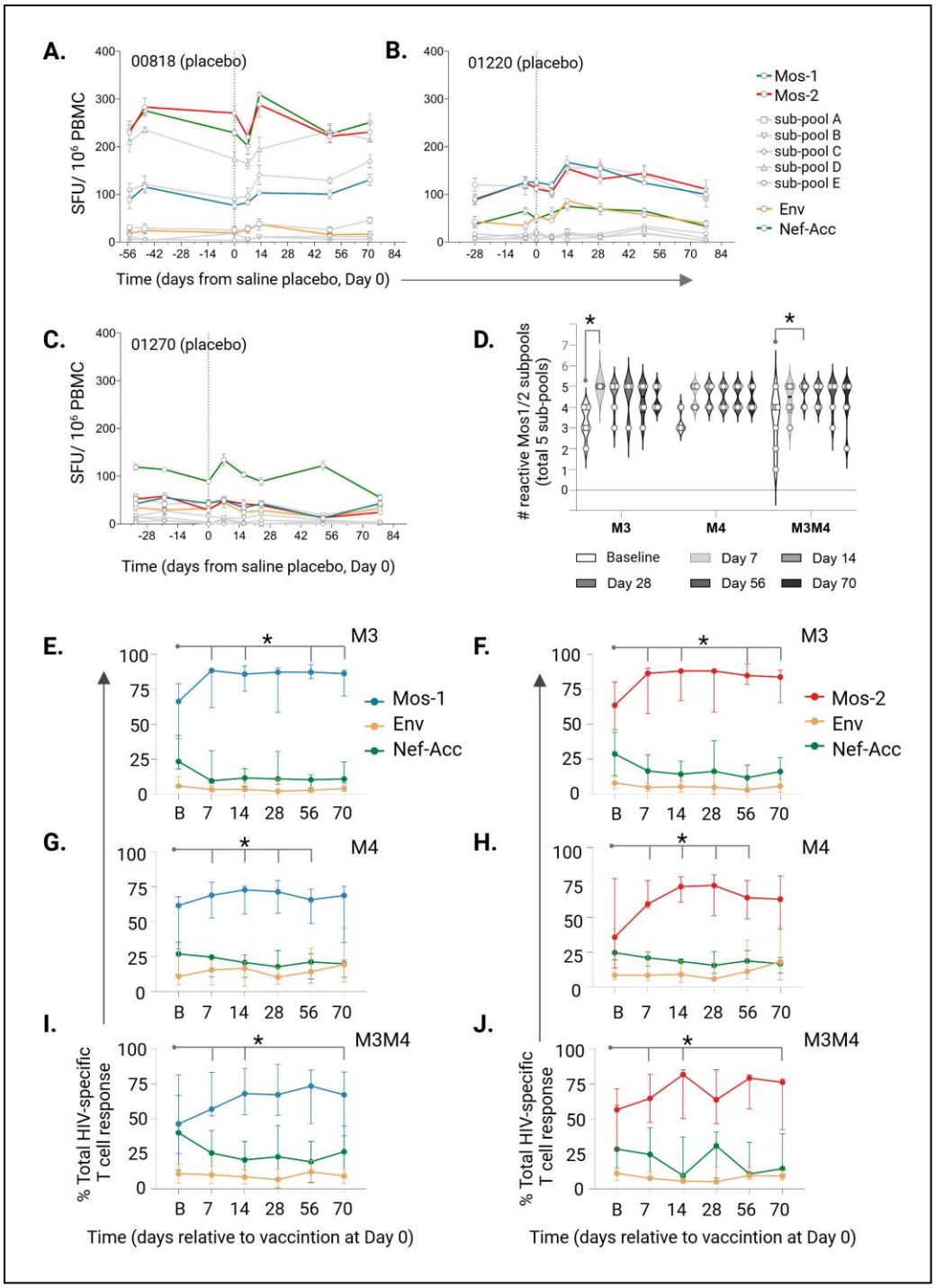
| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---|---|---|
| Antibodies – flow cytometry | | |
| CD107a-APC | Biolegend | Cat# 328620, RRID:AB_1279055 |
| CD3-PerCP-Cy5.5 | Biolegend | Cat# 300430, RRID:AB_893299 |
| CD4-PE-Cy5 | Biolegend | Cat# 317412, RRID:AB_571957 |
| CD8-BV510 | Biolegend | Cat# 344732, RRID:AB_2564624 |
| CD14-BV650 | Biolegend | Cat# 301836, RRID:AB_2563799 |
| CD16-BV650 | Biolegend | Cat# 302042, RRID:AB_2563801 |
| CD19-BV650 | Biolegend | Cat# 302238, RRID:AB_2562097 |
| CD56-BV650 | Biolegend | Cat# 318344, RRID:AB_2563838 |
| CD45RO-BV605 | Biolegend | Cat# 304238, RRID:AB_2562153 |
| IFN-γ-PE | Biolegend | Cat# 502509, RRID:AB_315234 |
| TNFα-PE-Dazzle 594 | Biolegend | Cat# 502946, RRID:AB_2564173 |
| MIP-1β-PE-Cy7 | BD Biosciences | Cat# 560687, RRID:AB_1727566 |
| Perforin-BV421 | Biolegend | Cat# 353307, RRID:AB_11149688 |
| Granzyme B-FITC | Biolegend | Cat# 372206, RRID:AB_2687030 |
| Zombie NIR | Biolegend | Cat# 423106 |
| Antibodies – mass cytometry | | |
| CD45 HI30 111Cd | Standard BioTools | Cat# 3111001B |
| CCR6 11A9 141Pr | Standard BioTools | Cat# 3141014A |
| CD19 HB19 142Nd | Standard BioTools | Cat# 3142001B |
| CD45RA HI100 143Nd | Standard BioTools | Cat# 3143006B |
| CD4 RPA-T4 145Nd | Standard BioTools | Cat# 3145001B |
| CCR4 L291H4 149Sm | Standard BioTools | Cat# 3149029A |
| CD14 M5E2 151Eu | Standard BioTools | Cat# 3151009B |
| CXCR5 RF8B2 153Eu | Standard BioTools | Cat# 3153020B |
| PD-1 EH12.2H7 155Gd | Standard BioTools | Cat# 3155009B |
| CXCR3 G025H7 156Gd | Standard BioTools | Cat# 3156004B |
| CD27 L128 158Gd | Standard BioTools | Cat# 3158010B |
| FoxP3 259D/C7 159Tb | Standard BioTools | Cat# 3159028A |
| CD28 CD28.2 160Gd | Standard BioTools | Cat# 3160003B |
| Ki-67 B56 162Dy | Standard BioTools | Cat# 3162012B |
| CD95 DX2 164Dy | Standard BioTools | Cat# 3164008B |
| CD127 A019D5 165Ho | Standard BioTools | Cat# 3165008B |
| CCR7 G043H7 167Er | Standard BioTools | Cat# 3167009A |
| CD8 SK1 168Er | Standard BioTools | Cat# 3168002B |
| CD25 2A3 169Tm | Standard BioTools | Cat# 3169003B |
| HLA-DR L243 170Er | Standard BioTools | Cat# 3170013B |
| CCR5 NP-6G4 171Yb | Standard BioTools | Cat# 3171017A |
| CD38 HIT2 172Yb | Standard BioTools | Cat# 3172007B |
| CD56 N901 176Yb | Standard BioTools | Cat# 3172007B |
| CD16 3G8 209Bi | Standard BioTools | Cat# 3209002B |
| CD45 HI30 89Y | Standard BioTools | Cat# 3089003B |
| CD31 WM59 144Nd | Standard BioTools | Cat# 3144023B |
| CD3 UCHT1 | Biolegend | Cat# 300443 |
| CD99 3B2/TA8 | Biolegend | Cat# 371302 |
| Bcl-2 100 | Biolegend | Cat# 658702 |
| TCRγδ B1 | Biolegend | Cat# 331202 |
| CD57 HCD57 | Biolegend | Cat# 359602 |

| | | |
|---|---|---|
| CCR10 314305 | R&D systems | Cat# MAB3478 |
| CD3 UCHT1 AF488 | Biolegend | Cat# 300415, RRID: AB_389310 |
| CD4 OKT4 BV650 | Biolegend | Cat# 317436, RRID: AB_2563050 |
| CD8 SK1 BV510 | Biolegend | Cat# 344732, RRID: AB_2564624 |
| CD14 M5E2 PerCP Cy5.5 | Biolegend | Cat# 325622, RRID: AB_893250 |
| CD19 HIB19 PerCP Cy5.5 | Biolegend | Cat# 302230, RRID: AB_2073119 |
| CD56 HCD56 PerCP Cy5.5 | Biolegend | Cat# 318322, RRID: AB_893389 |
| CD16 3G8 PerCP Cy5.5 | Biolegend | Cat# 302028, RRID: AB_893262 |
| Biological samples | | |
| Human PBMCs | Human | Assigned de-identifying code |
| Buffy Coats | Human | Not applicable |
| Tissue Culture | | |
| Fetal Calf Serum (ex vivo studies) | Corning | Cat# 35-079-CV |
| Human AB serum (short term cell lines) | GemCell™ | SKU# 100-512-100 |
| IL-2 | PeproTech | Cat# 200-02-50UG |
| RPMI-1640 | Gibco | Cat# 61870036 |
| L-Glutamine | VWR | Cat # 97068-088 |
| Sodium Pyruvate | Gibco | Cat# 11360070 |
| Chemicals, peptides, and recombinant proteins | | |
| Phytohemagglutinin | Thermofisher | Cat# 10576015 |
| Cell-ID Intercalator-Ir | Standard BioTools | Cat# 201192A |
| Cell Stimulation Cocktail (500X) (PMA / Ionomycin) | eBioscience™ | 00497093 |
| Peptides | Sigma-Aldrich | VC80023 |
| Cell-ID Cisplatin-195Pt | Standard BioTools | Cat# 201195 |
| Critical commercial reagents | | |
| Maxpar X8 Antibody Labeling 147Sm | Standard BioTools | Cat# 201147A |
| Maxpar X8 Antibody Labeling 152Sm | Standard BioTools | Cat# 201152A |
| Maxpar X8 Antibody Labeling 173Yb | Standard BioTools | Cat# 201173A |
| Maxpar X8 Antibody Labeling 175Lu | Standard BioTools | Cat# 201175A |
| Maxpar X8 Antibody Labeling 166Er | Standard BioTools | Cat# 201166A |
| $Ca^{2+}$ $Mg^{2+}$ free PBS | Rockland | Cat# MB008 |
| Maxpar Cell Staining Buffer | Standard BioTools | Cat# 201068 |
| Human TruStain FcX | Biolegend | Cat# 422301 |
| FoxP3 Fixation/Permeabilization kit | Thermofisher | Cat# 00-5523-00 |
| Zombie NIR Fixable Viability Kit | Biolegend | Cat# 423106 |
| CD3/28 Human Dynabeads | Gibco™ | Cat# 11131D |
| CD4+ T cell isolation kit | Miltenyi Biotec | Cat# 130-096-533 |
| Deposited data | | |
| Preprocessed mass cytometry data | Goonetilleke Group, UNC | Cytobank Premium, Beckman Coulter |
| GenBank Sequencing data | Swanstrom /Zhou Groups, UNC. | Gen Bank under PRJNA666896, MT307344-MT308415 and MW054719-MW054856 All data generated (raw) |
| Software and Algorithms | | |
| Prism v9 | Graphpad | https://www.graphpad.com/ |
| FlowJo v10.8.1 | BD Biosciences | https://www.flowjo.com/ |

| | | |
|---|---|---|
| Python v3.6 | Python Software Foundation | https://www.python.org/ |
| Mixcr v2.1.9.6 | Bolotin et al. (43, 44) | https://github.com/milaboratory/mixcr/tree/v2.1.9 |
| R v4.2.2 | R Core Team | https://cran.r-project.org/ |
| Cytobank v9.3 | Cytobank | https://unc.cytobank.org/cytobank |
| Muscle v5.1 | (45) | https://github.com/rcedgar/muscle/releases |
| Ninja v1.2.2 | https://wheelerlab.org/software/ninja/files/NINJA_preprint.pdf | https://github.com/ninja-build/ninja/releases |

**Supplementary Figure 1: M&M Study Flowchart of participants enrollment**

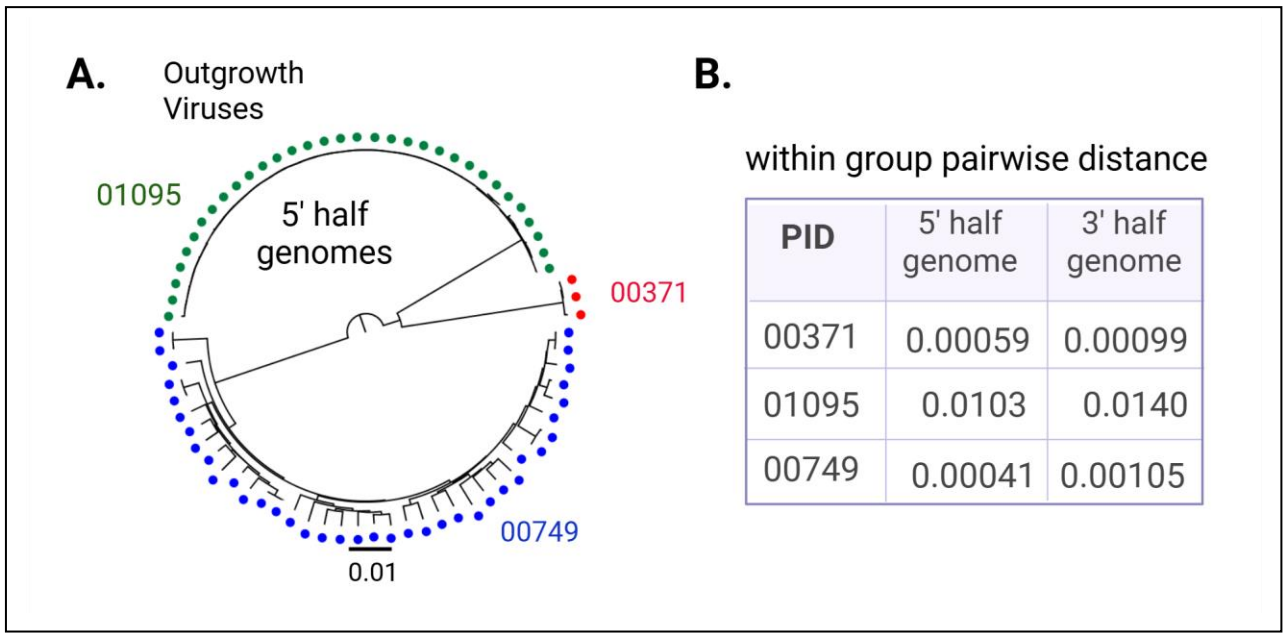




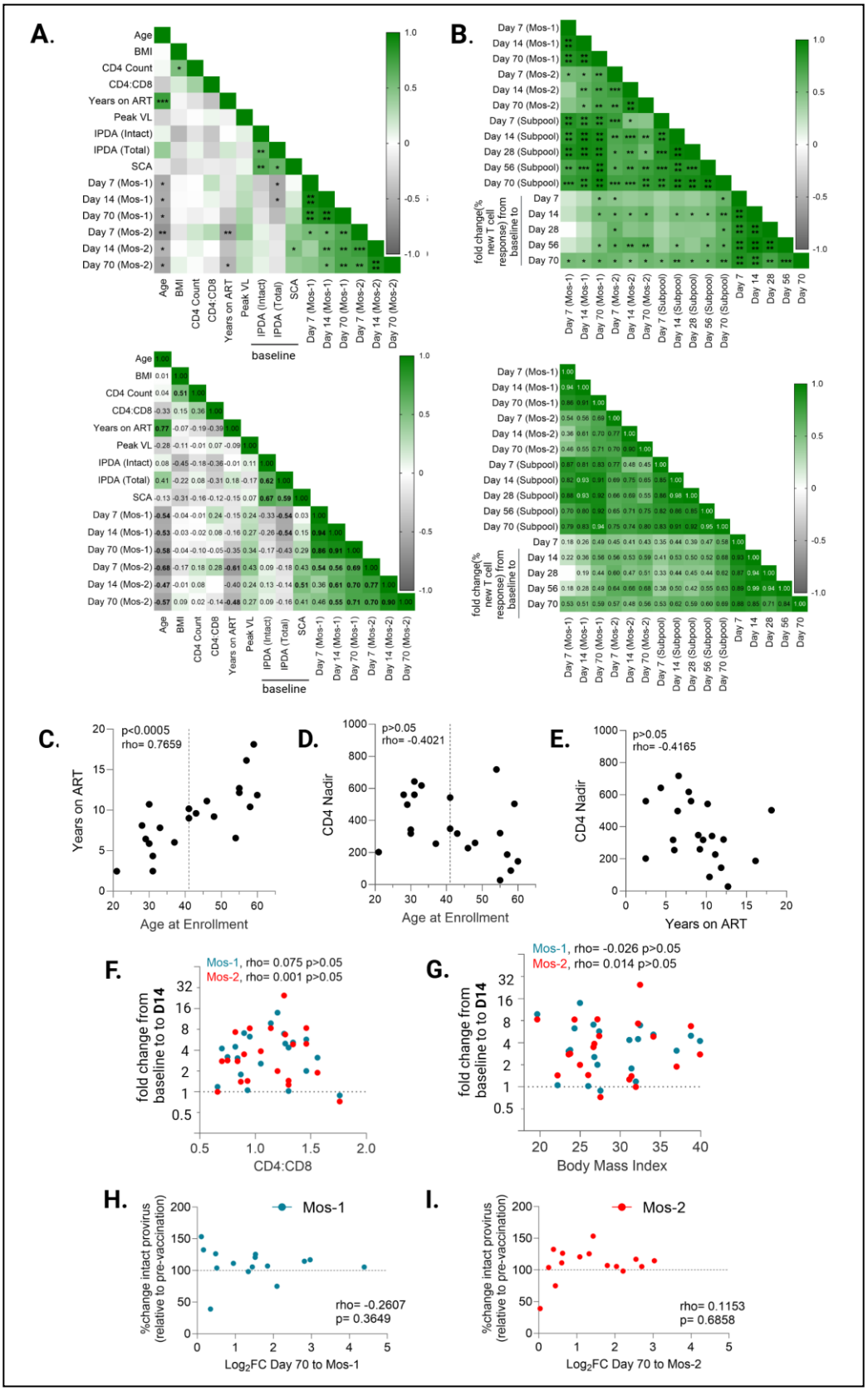

**Supplementary Figure 2**: **Vaccination with MVA-vectored HIVconsvX immunogens produce significant increases in the frequency of HIV-1-specific T-cells**. (**A-C**) Frequency of HIV-1-specific T-cells (mean +/- SEM) measured by ex vivo IFN-γ ELISpot in participants (**A**) 00818, (**B**) 01220 and (**C**) 01270 receiving saline placebo at day 0. (**D**) Within vaccine arm (n=7/group) changes in T-cell breadth from baseline. Average and 95% CI. (**E-J**) Median and IQR of %Mos-1 (left, E, G, I) and %Mos-2 (right, F, H, J) T-cell frequencies relative to total measured HIV-1-specific T-cell frequency in each vaccine group (n=7/group). %Env and %NEF-ACC also shown. Total frequency = sum of (Mos-1 or 2), Env, NEF and ACC.

Baseline was defined as the average of two pre-vaccination visits, at Day 0 and a previous visit mostly occurring between days -28 to -7. ACC in NEF/ACC peptide pool spans clade B Rev, Tat, Vif, Vpu, Vpr. (D-J) Statistically significant comparisons (*) between baseline (B) and post-vaccination visits are identified with downward ticks, Wilcoxon signed-ranked test. * = $p < 0.05$

**Supplementary Figure 3**: (**A**) Phylogenetic trees displaying 5' half genome sequences for 00749 (blue), 01905 (green) and 00371 (red). The genetic distance is shown by scale bar (indicated with an asterisk), 1 substitution out of 1000 bp. Trees are midpoint-rooted. (**B**) Group pairwise distance for 5' and 3' genomes.




| PID | 5' half genome | 3' half genome |
|---|---|---|
| 00371 | 0.00059 | 0.00099 |
| 01095 | 0.0103 | 0.0140 |
| 00749 | 0.00041 | 0.00105 |




**Supplementary Figure 4**: **Demographic and clinical data, particularly age, were associated with T-cell response to vaccination with MVA.HIVconsvX vaccines**. (**A-I**) All associations Spearman Rank, two-tailed. (**A**) Correlation matrix between fold-change in T-cell response to Mos-1 and Mos-2 from baseline (average of two pre-vaccination visits) to indicated post-vaccination visit, demographic data and baseline measurements of persistent viremia. Upper panel shows significance levels, lower panel rho values. Age = age at enrolment, BMI = body mass index, SCA = single copy assay, IPDA = integrated proviral DNA assay. CD4 count and CD4:CD8 = values at enrolment (**B**) Correlation matrix between fold-change in T-cell response to Mos-1 and -2, Mos-1/2 sub-pools and %new T cells detected following vaccination across all vaccinees (n=21). Upper panel shows significance levels, lower panel rho values. New T-cells were defined by T-cell response to Mos1/2 sub-pools not detected at baseline timepoints but detected at two or more post-vaccination timepoints. (**C-G**) Associations between selected clinical and or demographic data in vaccinees (n=21). (**H-I**) %Change in intact IPDA® from pre-vaccination (median day -7) to post-vaccination (median day 28) versus log2FC in frequency of Mos-1 (**H**) and Mos-2 (**I**) T-cell frequency for vaccinees (n=17). * = p < 0.05, ** = p < 0.005, *** p < 0.0005, **** p < 0.00005

**Supplementary Figure 5**: Gating strategy for intracellular cytokine staining. Fluorescence minus one (FMO) controls were used to inform gates for functional markers.