

Supplementary Material

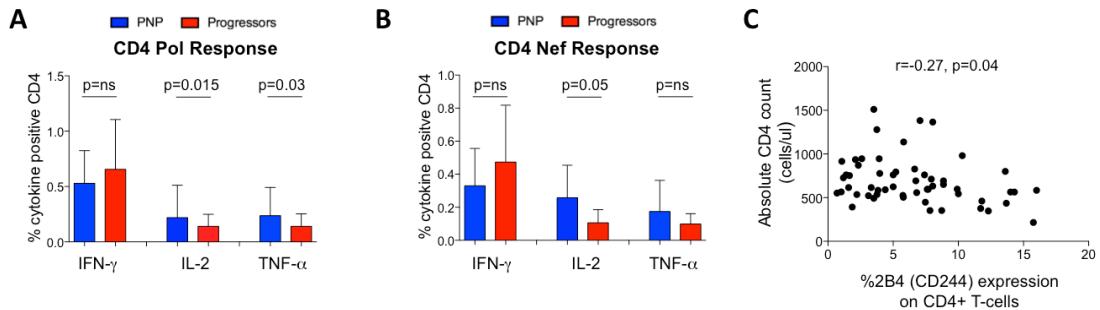


Fig. S1. Decreased CD4 T-cell function and increased expression of exhaustion markers in pediatric progressors. **a-b:** IFN- γ , IL-2 and TNF- α intracellular cytokine staining (ICS) responses to Pol and Nef peptide pools in progressors (red bars, n=8) and non-progressors (blue bars, n=18). Mann-Whitney test. **c.** Increased expression of 2B4 (CD244) on CD4 T-cells in pediatric progressors. Spearman rank correlation test (n=58).

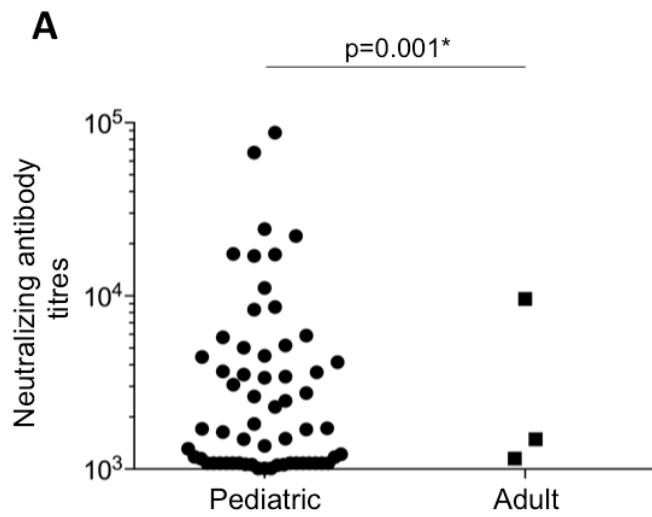


Fig. S2. Neutralizing antibody potency in pediatric and adult subjects. a. Among neutralizing antibody responses made to all 16 viruses by 85 pediatric and 19 adult subjects, neutralizing antibody titers of >1:1000 were observed in 4.4% versus 0.9% of tests involving pediatric versus adult samples respectively ($p=0.001$, Fisher's Exact test comparing frequency of neutralizing antibody titers of >1:1000 across 16 viruses).

| Generalized linear model | | | | |
|-----------------------------|------------------|-------------------------|-------|---------|
| Variable | Beta-coefficient | 95% Confidence Interval | | p-value |
| | | Lower | Upper | |
| Log Viral load | 3.9 | 0.676 | 7.122 | 0.018 |
| Total breadth OLP responses | 0.81 | 0.008 | 1.62 | 0.048 |
| Age at visit | 1.28 | -1.03 | 2.653 | 0.07 |
| CD4 count | 0.001 | -0.006 | 0.009 | 0.749 |

Table S1. CD8+ T-cell activation is independently associated with total breadth of HIV-specific CTL responses and viral load. Results are shown for a generalized linear model with CD8 T-cell activation (%CD38+HLADR+ CD8 T-cells) as the dependent variable and log viral load, overlapping peptide (OLP) breadth, age and absolute CD4 count as independent variables (n=30).

| Pseudoviruses tested for neutralizing sera activity | | |
|---|-----------|-----------|
| Subtype A | Subtype B | Subtype C |
| Q23.17 | PVO.4 | Du156.2 |
| Q168.a2 | 6535.3 | Du172.17 |
| Q842.d12 | TR0.11 | CAP45.G3 |
| Q461.e2 | WITO.4160 | ZM197M |
| | AC10.0.29 | CAP239.G3 |
| | QH0692.42 | ZM214M |

Table S2. List of pseudoviruses tested for neutralizing sera activity by HIV-1 subtype.

Source data for Fig 1i, 1j, 2b, 2c, 2g, 6c, 6d

Fig 1i. sCD14 (pg/uL)

| HIV-ve | PNP | Progressors |
|---------|---------|-------------|
| 1920000 | 1570000 | 2720000 |
| 2160000 | 1820000 | 2470000 |
| 2020000 | 1490000 | 2940000 |
| 3200000 | 1040000 | 4230000 |
| 4500000 | 1820000 | 4300000 |
| 1970000 | 2110000 | 4050000 |
| 2650000 | 3040000 | 2840000 |
| 1340000 | 2300000 | 1800000 |
| 2120000 | 2810000 | 2950000 |
| 912000 | 3210000 | 3110000 |
| 2000000 | 2370000 | 2930000 |
| 1220000 | 1500000 | 4650000 |
| 4620000 | 1100000 | 5360000 |
| 1700000 | 2090000 | 3530000 |
| 1590000 | | 1730000 |
| 1530000 | | 2530000 |
| 2360000 | | |
| 2260000 | | |
| 1810000 | | |
| 1960000 | | |
| 2320000 | | |

Fig 1j. iFABP (pg/uL)

| HIV-ve | PNP | Progressors |
|--------|------|-------------|
| 1890 | 2067 | 671 |
| 1393 | 1256 | 4969 |
| 1689 | 3482 | 2872 |
| 2082 | 2753 | 1004 |
| 3168 | 860 | 3778 |
| 1275 | 1375 | 1391 |
| 3838 | 2448 | 2744 |
| 3067 | 1092 | 990 |
| 5286 | 1481 | 1002 |
| 3199 | 1327 | 1491 |
| 925 | 721 | 2418 |
| 710 | 933 | 1463 |
| 2253 | 681 | 3471 |
| 2691 | 754 | 3665 |
| 2953 | | 3603 |
| 2313 | | 3452 |
| 1519 | | 1888 |
| 2198 | | 2521 |
| 1366 | | 3097 |
| 2191 | | |
| 649 | | |

Fig 2b, SEB response (%cytokine positive CD4 T-cells)

| non-Progressors | | | | Progressors | | | | HIV-negative | | |
|-----------------|-------|-----------|--|-------------|------|-----------|--|--------------|-------|-----------|
| IFN-gamma | IL-2 | TNF-alpha | | IFN-gamma | IL-2 | TNF-alpha | | IFN-gamma | IL-2 | TNF-alpha |
| 1.25 | 7.72 | 6.68 | | 2.62 | 9.35 | 7.74 | | 1.53 | 8.60 | 2.79 |
| 1.88 | 10.32 | 4.06 | | 1.51 | 2.65 | 1.37 | | 0.91 | 6.10 | 0.26 |
| 2.25 | 10.48 | 1.44 | | 1.21 | 2.17 | 2.44 | | 1.23 | 5.06 | 3.22 |
| | 9.11 | 6.58 | | 2.62 | 2.54 | 0.70 | | 1.63 | 5.46 | 3.07 |
| 0.74 | 4.16 | 2.90 | | 3.58 | 0.81 | 1.80 | | 1.48 | 4.56 | 2.02 |
| 1.78 | 3.88 | 2.47 | | 2.16 | 6.12 | 3.72 | | 1.20 | 9.11 | 3.35 |
| 2.53 | 6.40 | 1.31 | | 5.53 | 5.31 | 9.56 | | 1.88 | 7.04 | 3.21 |
| 1.92 | 11.77 | 3.58 | | 2.04 | 7.55 | 2.24 | | 1.69 | 7.61 | 2.19 |
| 6.13 | 5.53 | 5.60 | | 2.20 | 9.98 | 6.40 | | 0.98 | 6.45 | 2.41 |
| 1.03 | 6.51 | 2.29 | | 3.03 | 8.32 | 10.32 | | 1.86 | 8.53 | 2.80 |
| 1.21 | 4.15 | 2.60 | | 1.50 | 4.59 | 4.63 | | 2.51 | 4.64 | 3.62 |
| 0.66 | 6.93 | 3.25 | | 2.07 | 4.23 | 3.39 | | 0.77 | 3.38 | 1.17 |
| 0.50 | 8.38 | 2.46 | | 1.42 | 3.82 | 2.84 | | 0.94 | 5.68 | 1.09 |
| | | | | 7.67 | 2.91 | 4.50 | | 0.59 | 4.94 | 0.85 |
| | | | | 12.92 | 4.47 | 12.90 | | 2.63 | 7.79 | 3.05 |
| | | | | 1.68 | 5.82 | 3.89 | | 2.55 | 5.90 | 1.60 |
| | | | | 15.71 | 6.35 | 14.36 | | 4.64 | 16.50 | 7.28 |
| | | | | 10.36 | 7.15 | 12.85 | | 2.63 | 9.82 | 4.14 |
| | | | | 8.68 | 0.32 | 1.49 | | 3.11 | 6.81 | 6.86 |
| | | | | 15.54 | 9.91 | 16.56 | | | | |
| | | | | 4.76 | 7.56 | 8.43 | | | | |
| | | | | 2.69 | 4.07 | 3.85 | | | | |
| | | | | 2.07 | 2.80 | 1.83 | | | | |
| | | | | 1.51 | 2.06 | 0.93 | | | | |
| | | | | 1.36 | 3.39 | 1.69 | | | | |
| | | | | 6.83 | 3.47 | 8.10 | | | | |
| | | | | 3.95 | 6.92 | 6.77 | | | | |
| | | | | 5.77 | 4.77 | 4.02 | | | | |
| | | | | 7.80 | 0.53 | 0.48 | | | | |
| | | | | 1.52 | 3.27 | 5.83 | | | | |
| | | | | 1.30 | 5.58 | 4.89 | | | | |
| | | | | 1.36 | 4.27 | 2.61 | | | | |

Fig 2c, Gag response (%cytokine positive CD4 T-cells)

| PNP | | | | Progressors | | |
|-----------|------|-----------|--|-------------|------|-----------|
| IFN-gamma | IL-2 | TNF-alpha | | IFN-gamma | IL-2 | TNF-alpha |
| 0.43 | 0.03 | 0.02 | | 0.55 | 0.03 | 0.01 |
| 0.76 | 0.03 | 0.03 | | 0.33 | 0.02 | 0.03 |
| 0.04 | 0.01 | 0.53 | | 0.30 | 0.03 | 0.02 |
| 0.03 | 0.52 | 0.45 | | 0.03 | 0.23 | 0.03 |
| 0.56 | 0.03 | 0.01 | | 0.03 | 0.03 | 0.28 |
| 0.45 | 0.03 | 0.61 | | 1.90 | 0.03 | 0.10 |
| 0.63 | 0.03 | 0.03 | | 0.84 | 0.03 | 0.02 |
| 0.00 | 0.63 | 0.54 | | 1.12 | 0.02 | 0.12 |
| 0.34 | 1.20 | 0.88 | | 0.57 | 0.46 | 0.02 |
| 0.54 | 0.00 | 0.18 | | 0.95 | 0.00 | 0.03 |
| 0.65 | 0.03 | 0.30 | | 0.62 | 0.13 | 0.03 |
| 0.63 | 0.45 | 0.03 | | | | |
| 0.02 | 0.86 | 0.02 | | | | |
| 0.07 | 0.46 | 0.63 | | | | |
| 0.74 | 0.43 | 0.03 | | | | |
| 0.34 | 0.56 | 0.03 | | | | |
| 0.88 | 0.01 | 0.04 | | | | |
| 0.43 | 0.02 | 0.34 | | | | |
| 0.56 | 0.34 | 0.56 | | | | |
| 0.04 | 0.99 | 0.45 | | | | |
| 0.44 | 0.58 | 0.03 | | | | |
| 1.07 | 0.03 | 0.03 | | | | |
| 0.04 | 0.53 | 0.05 | | | | |
| 0.35 | 0.85 | 0.45 | | | | |
| 0.02 | 0.66 | 0.35 | | | | |
| 0.44 | 0.74 | 0.02 | | | | |

Fig 2g. The proportion of cells producing each cytokine to the total CD4 T-cell SEB response was determined (% of cells responding with each cytokine of total SEB response)

| Tn | | | Tcm | | | Tem | | | Temra | | |
|------|-----------|-----------|------|-----------|-----------|------|-----------|-----------|-------|-----------|-----------|
| IL-2 | IFN-gamma | TNF-alpha | IL-2 | IFN-gamma | TNF-alpha | IL-2 | IFN-gamma | TNF-alpha | IL-2 | IFN-gamma | TNF-alpha |
| 83.3 | 0.0 | 0.0 | 94.0 | 10.0 | 6.0 | 72.0 | 36.0 | 36.0 | 65.0 | 95.0 | 75.1 |
| 84.2 | 2.6 | 0.0 | 88.0 | 5.0 | 10.0 | 71.0 | 28.0 | 36.0 | 49.0 | 93.0 | 78.2 |
| 94.9 | 10.2 | 5.1 | 90.4 | 22.0 | 29.0 | 59.0 | 43.0 | 45.0 | 40.0 | 100.0 | 30.0 |
| 64.7 | 21.2 | 7.1 | 78.6 | 20.0 | 17.0 | 55.0 | 51.0 | 37.0 | 43.0 | 95.0 | 69.6 |
| 93.7 | 6.3 | 0.0 | 95.2 | 11.0 | 10.0 | 81.0 | 18.0 | 44.0 | 65.0 | 75.0 | 50.1 |
| 80.6 | 0.0 | 0.0 | 85.4 | 11.0 | 22.0 | 66.0 | 37.0 | 53.0 | 71.0 | 79.0 | 71.4 |
| 74.2 | 8.4 | 0.0 | 80.3 | 22.0 | 12.0 | 79.0 | 25.0 | 49.0 | 80.0 | 74.0 | 59.6 |
| 85.2 | 0.0 | 2.4 | 88.0 | 5.0 | 16.0 | 85.0 | 11.0 | 37.0 | 31.0 | 77.0 | 62.0 |
| 66.7 | 11.2 | 11.2 | 79.9 | 15.0 | 19.0 | 65.0 | 30.0 | 44.0 | 37.0 | 87.0 | 66.6 |
| 100 | 0.0 | 0.0 | 86.3 | 10.0 | 11.0 | 65.0 | 45.0 | 41.0 | 50.0 | 100.0 | 75.5 |
| 100 | 0.0 | 0.0 | 94.7 | 5.0 | 5.0 | 66.0 | 36.0 | 51.0 | 32.0 | 79.0 | 63.2 |

Fig 6c. Viral load (c/ml)

| PNP | FP |
|--------|--------|
| 76000 | 34000 |
| 25374 | 21000 |
| 12132 | 160000 |
| 8124 | 140000 |
| 13422 | 440000 |
| 175876 | 29000 |
| 13611 | 58000 |
| 41291 | 16000 |
| 144429 | 10000 |
| 18776 | 36000 |
| | 19000 |
| | 15000 |

Fig 6c. CD4 T-cell count CD4 count (/mm³)

| PNP | FP |
|------|------|
| 1057 | 694 |
| 1289 | 799 |
| 1223 | 1123 |
| 1646 | 576 |
| 1151 | 846 |
| 1058 | 1595 |
| 1279 | 1234 |
| 1071 | 1077 |
| 3181 | 1088 |
| 2087 | 1289 |
| | 1604 |
| | 1268 |

Fig 6d. log HIV copies per million cells

| Tn | | Tscm | | Tcm | | Tem | |
|-------|-------|-------|--------|-------|-------|-------|-------|
| PNP | FP | PNP | FP | PNP | FP | PNP | FP |
| 0.19 | 0.52 | 2 | 2.22 | 2.3 | 3.9 | 3.44 | 2.4 |
| 0.74 | 0.68 | 1.18 | 2.32 | 1.53 | 2.35 | 2.75 | 0.27 |
| 0.53 | 0.74 | 1.47 | 3.06 | 0.74 | 2.6 | 2.5 | 3.52 |
| 0.3 | 0.41 | 0.25 | 2.07 | 0.53 | 1.52 | 1.6 | 1.38 |
| 0.375 | 0.38 | 1.56 | 4.81 | 1.144 | 1.9 | 2.745 | 2.54 |
| 0.355 | 0.465 | 1.962 | 2.355 | 1.288 | 1.223 | 2.44 | 2.14 |
| 0.27 | 0.412 | 1.8 | 1.887 | 2.07 | 2.565 | 3.784 | 2.565 |
| 0.171 | 0.468 | 2.062 | 1.972 | 1.377 | 4.29 | 3.025 | 2.16 |
| 0.666 | 0.612 | 1.323 | 2.601 | 1.666 | 2.585 | 2.75 | 0.243 |
| 0.477 | 0.666 | 0.225 | 1.7595 | 2.477 | 2.86 | 1.76 | 3.168 |
| | 0.369 | | 4.0885 | | 1.672 | | 1.242 |
| | 0.342 | | 1.344 | | 2.09 | | 2.286 |