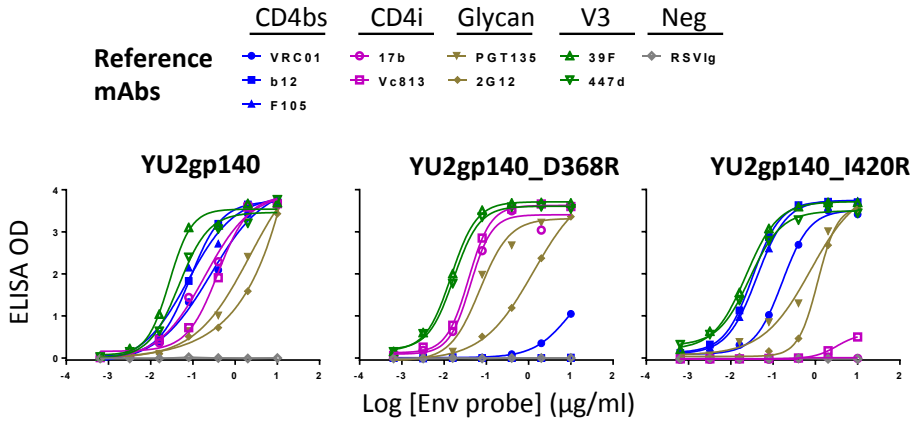
**Supplemental Table 1.** Gene array comparison of gp140-specific B cells with strong versus weak pro-resting memory profiles

| Category | Gene names | Fold change | FDR[B] | p-value |
|---|---|---|---|---|
| Inhibitory Receptors | FCRL4 | **-3.05**[A] | **0.064** | **2.60E-02** |
| | SIGLEC6 | **-3.20** | **0.020** | **4.33E-03** |
| | FCGR2B | **-3.91** | **0.020** | **2.16E-03** |
| | LILRB1 | **-2.97** | **0.064** | **2.60E-02** |
| | LILRB2 | **-4.61** | **0.031** | **8.66E-03** |
| | CD72 | **-3.38** | **0.031** | **8.66E-03** |
| | LAIR1 | -0.04 | 0.725 | 5.89E-01 |
| | CD84 | **-3.72** | **0.020** | **4.33E-03** |
| | PTGER4 | 1.10 | 0.274 | 1.80E-01 |
| Cell Activation | SLAMF7 | -1.99 | 0.115 | 6.49E-02 |
| Trafficking | ITGAX | **-4.71** | **0.020** | **2.16E-03** |
| | SELL | 1.24 | 0.274 | 1.80E-01 |
| | CCR7 | -1.01 | 0.525 | 3.94E-01 |
| Cytokine Receptors | IL13RA1 | -1.34 | 0.525 | 3.78E-01 |
| | IL4R | -1.47 | 0.349 | 2.40E-01 |
| Tyrosine Kinases | HCK | **-4.68** | **0.020** | **2.16E-03** |
| & Phosphatases | LCK | 2.19 | 0.115 | 6.49E-02 |
| | FGR | **-3.03** | **0.048** | **1.52E-02** |
| | FYN | **-2.87** | **0.064** | **2.60E-02** |
| | PTPN22 | -2.26 | 0.115 | 6.49E-02 |
| | DUSP4 | 0.69 | 0.903 | 8.18E-01 |
| Somatic Hypermutation | AICDA | **-3.55** | **0.020** | **4.33E-03** |
| Transcription Factors | PBX3 | -1.93 | 0.115 | 6.49E-02 |
| | SOX5 | **-2.74** | **0.094** | **4.11E-02** |
| | BCL11B | **-3.83** | **0.020** | **4.33E-03** |
| Cell Cycle | CCNB2 | -0.47 | 0.725 | 5.89E-01 |
| Cell-cell Signaling | SEMA4A | -0.08 | 1.000 | 1.00E+00 |
| Apoptosis | TNFRSF1B | -1.85 | 0.157 | 9.31E-02 |
| Cell Anergy | LAX1 | -0.39 | 0.799 | 6.99E-01 |

[A]Bold numbers indicate a statistical significant difference in gene expression
[B]Wilcoxon test followed by Benjamini-Hochberg FDR calculation

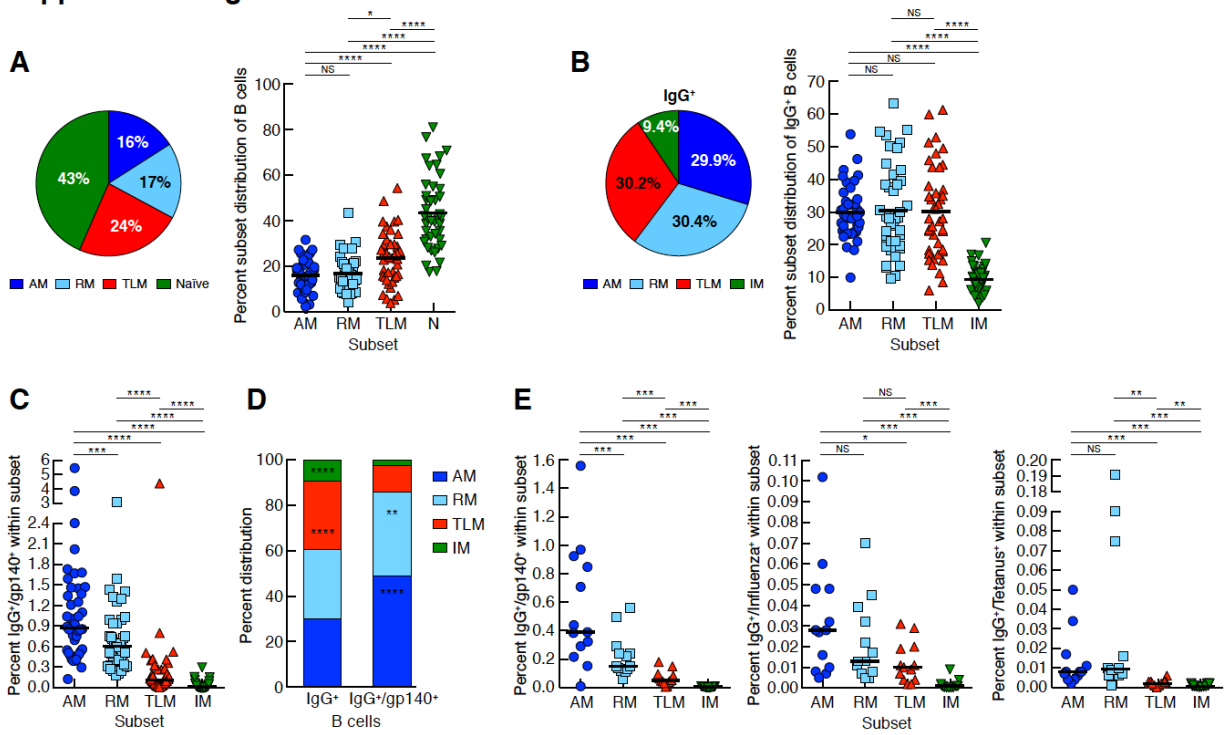
**Supplemental Figure 1**




| | Binding of YU2gp140FT-Biotin Probes to Selected Antibodies | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | CD4bs | | | CD4i | | V3 | | Glycan | | Neg. Control | | |
| | VRC01 | b12 | F105 | 17b | Vc813 | 39F | 447d | PGT135 | 2G12 | RSVIg | | |
| YU2gp140FT WT | +++ | ++++ | ++++ | +++ | +++ | ++++ | ++++ | +++ | +++ | - | | |
| YU2gp140FT D368R | + | - | - | ++++ | ++++ | ++++ | ++++ | ++++ | +++ | - | | |
| YU2gp140FT I420R | +++ | ++++ | ++++ | - | + | ++++ | ++++ | +++ | +++ | - | | |
| | | | | | | | | | | | | |
| | Relative binding of probes was based on the $OD_{450}$ values at the highest concentration of protein (10 ug/ml), and $EC_{50}$ values: | | | | | | | | | | | |
| | $OD_{450} \geq 3.0$ and $EC_{50} \leq 0.10$ = ++++; $OD_{450} \geq 3.0$ and $EC_{50} > 0.10$ = +++; $1.0 \leq OD_{450} < 3.0$ = ++; $0.2 \leq OD_{450} < 1.0$ = +; $OD_{450} < 0.2$ = - | | | | | | | | | | | |

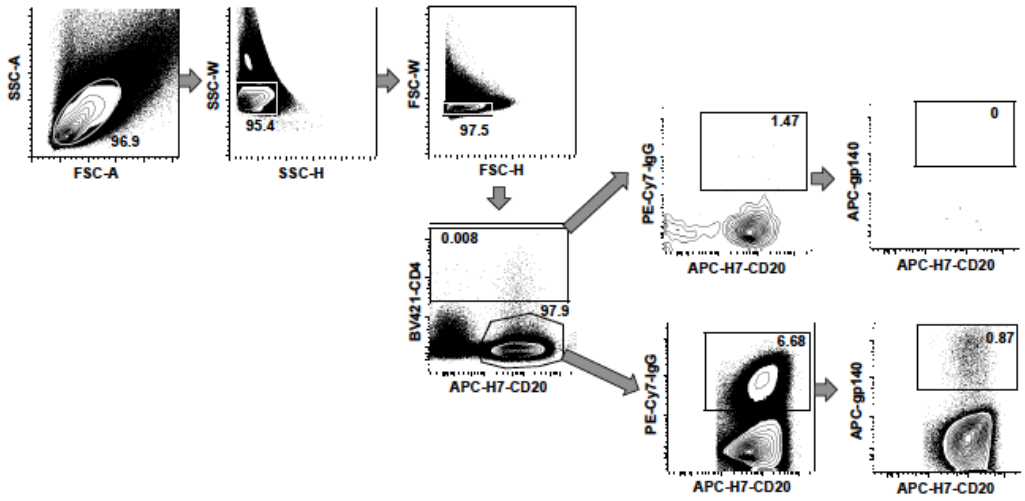
Validation of specificity of YU2-biotin probes by ELISA. ELISA (96-well) plates were coated with 100 µl of HIV-1 Env –specific reference mAbs at 2 µg/ml, followed by addition of five-fold serial dilutions of biotin-labeled YU2gp140 and derivative probes, starting at 10 µg/ml. Bound probe was detected with streptavidin-HRP conjugate (Sigma) and TMB substrate (Invitrogen). Reference mAbs included CD4bs-, CD4-induced (CD4i)-, glycan-, and V3-specific mAbs. The non-HIV mAb RSVIg was used as negative (Neg) control.

## Supplemental Figure 2




Frequencies of total, $IgG^+$, $IgG^+/gp140^+$, $IgG^+/influenza^+$ and $IgG^+/tetanus^+$ B-cell subsets. Mature ($CD10^-$) B cells isolated from the peripheral blood of HIV-infected untreated individuals and stained for CD3, CD20, IgG, CD21, CD27 and probes for gp140, influenza and tetanus. Gates were set on (**A**) $CD20^+$ and (**B**) $IgG^+$ B cells, followed by determination of the distribution of each subset using markers CD21 and CD27. Pie chart analysis of $CD20^+$ and $IgG^+$ B cells by subset and comparison between subsets are shown for the same 42 HIV-viremic individuals as in Figure 3. (**C**) Comparison between B-cell subsets of gp140-binding within each subset for the same 42 HIV-viremic individuals. (D) Comparison of mean percent distribution among subsets between $IgG^+$ and $IgG^+/gp140^+$ B cells. (**E**) Comparison between B-cell subsets of gp140-, influenza- or tetanus-binding within each subset for the same 12 HIV-viremic individuals shown in Figure 5.Horizontal bars show mean (**A, B**) and median (**C, E**) values and asterisk are for following p-values: * < 0.05; ** < 0.01; *** < 0.001; **** < 0.0001.

**Supplemental Figure 3**




Purity of B cells and absence of CD4-mediated binding to gp140 among $IgG^+$ B cells. Mature ($CD10^-$) B cells isolated from the peripheral blood of a representative HIV-infected individual were stained for CD4, CD20, IgG and the gp140-WT probe. Live cells and singlets were established by forward (FSC) and side (SSC) scatter gating, followed by gating on $CD4^+$ and $CD20^+$ cells and determination of percent gp140 binding among IgG/CD20-expressing cells from each gate.