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**Supplemental Figure 1.** Functional avidity defined as the peptide concentration needed to elicit half maximal response rates in the luminex assay was assessed to determine optimal peptide concentrations for the studies. (A) Serial 10-fold dilutions of the epitopic peptides ranging from 100 to 0.0001 µg/ml and was calculated as a non-linear regression dose response curve fit using GraphPad Prism software. As shown in these representative examples, most responses reached a plateau for concentrations  $\geq$ 10 µg/ml. (B) Summary data of epitope-specific EC50s in a group of controllers (HC) and a group of progressors (CP). The horizontal bars represent the median EC50s in the two cohorts.



**Supplemental Figure 2.** Proliferative responses to a pool of 66 HIV-1 Gag peptides were measured 7 days after stimulation of CD4-depleted PBMCs. The CD4 depletion was performed to avoid the impact of cytokine secretion, in particular IL-2, by HIV-1 Gag-specific CD4 T cells. The columns represent the mean proliferative responses (+/- SEM) in a group of 10 controllers (HC) and 9 progressors (CP). Vertical interval bars correspond to the Standard Error to the Mean (SEM)



**Supplemental Figure 3. Analysis of early TNF-** $\alpha$  secretion by HIV-1-specific CD8 T cells. Summary data of the mean magnitude of TNF- $\alpha$  secretion by HIV-1-specific CD8 T cells after a 6h stimulation with panels of individual HLA Class I-matched HIV-1 epitopes. **(a)** Statistical analysis of mean TNF- $\alpha$  secretion amongst the three groups of HIV-1-infected subjects of the discovery cohort (n= 64). **(b)** Statistical analysis of early TNF- $\alpha$  responses stratified by protective versus non-protective HLA-I alleles in controller (HC), progressor (CP) and ART-treated (ARTC) subjects. Color codes: Throughout the figure, controller data is represented in blue; CP, red; ARTC, green. Statistical tests: All comparisons of adjusted means were done using GLM controlling for clustering within individuals. Vertical interval bars correspond to the Standard Error to the Mean (SEM).



**Supplemental Figure 4.** Kinetics of cytokine responses to a pool of 66 HIV-1 Gag peptides was measured 6, 24 and 72 hours after stimulation of CD4-depleted PBMCs. The CD4 depletion was performed to avoid the impact of cytokine secretion by HIV-1 Gag-specific CD4 T cells. The graphs illustrate summary data for a group of 10 controllers (HC) and 9 progressors (CP), this for A) IFN- $\gamma$ ; B) IL-2; C) TNF- $\alpha$ . Vertical interval bars correspond to the Standard Error to the Mean (SEM).