

Figure legends.

Figure 1. (A) Phenotype breakdown of the NVP HSR patients (n=19) together with the significant HLA alleles associated with each phenotype.

Figure 2. (A) NVP induced $\text{INF}\gamma$ response as detected by ELISpot (SFU/million cells) plotted against days since the NVP HSR for patients 1, 2, 3 and 4. (B) Time line of NVP HSR for *Patient 4* showing $\text{INF}\gamma$ responses SFU /million cells (blue triangles and line), eosinophils per 10^9 cells/L (red squares and line) and ALT levels in U/L (grey circles and line). NVP start and stop dates are shown, with days since NVP stop on the x-axis. (C) Regulatory T cells expressed as a % of CD4 T cells are shown in the plot where clear symbols indicates samples from *Patient 4* and filled in symbols indicate samples from controls (black, blue) and an HIV patient not on medication (red symbol).

Figure 3 (A) $\text{INF}\gamma$ ELISpot images showing NVP stimulation in whole PBMC, CD4+ T-cell depleted PBMC and CD8+ T cell depleted PBMC for *Patient 4* (a-c) and *Patient 1* (g-i). Dot plots showing CD4+ and CD8+ T-cell subsets for *Patient 4* confirming the absence of depleted populations for each cell population dispensed in the ELISpot is shown in (d-f). (B) Dot plots of NVP-stimulated PBMC isolated from *Patient 3* (day 2 post NVP HSR) showing $\text{INF}\gamma$ production by CD4 and CD8 T cells (a) forward and side scatter (b) CD4 and CD8 expression on gated lymphocytes (c) CD4 T cell production of $\text{INF}\gamma$ in Unstimulated cells, (d) CD4 T cell production of $\text{INF}\gamma$ after NVP stimulation, (e) CD8 T cell production of $\text{INF}\gamma$ in Unstimulated cells, (f) CD8 T cell production of $\text{INF}\gamma$ in NVP-stimulated cells. (C) Dot plots showing expression of (I) CD3/CD4, (II) CCR7/CD45Ra, (III) and CD3/IL-2 in lymphocytes after overnight culture of PBMC from *Patient 4* with $40\mu\text{m}$ NVP shows that NVP induced IL-2 production originates from CD4+ T cells and backgating of IL-2

producing cells shows CD4+IL-2 producing T cells express CCR7 or CCR7+/CD45Ra+. The black dots represent IL-2 producing cells in the three plots. **(D)** NVP stimulated IFN γ producing cells are primarily single cytokine producing cells whereas TNF α producing cells also produce IL-2 after NVP stimulation. Dot plots display CD3+ T cells on the Y axis expressing either IFN γ (image 1, 4 and 7), TNF α (image 2, 5 and 8) or IL-2 (image 3, 6 and 9) on the x axis. Back gating on IFN γ positive cells (colored black cells) in images 1, 2 and 3 indicate IFN γ producing cells are primarily single cytokine producing cells. TNF α producing cells (colored black cells) in image 4, 5 and 7 show TNF α producing cells can also produce IL-2 but not IFN γ . IL-2 producing cells (black colour cells) in image 7, 8 and 9 are capable of producing TNF α but not IFN γ .

Figure S1. CBA kit cytokine data for serum samples from *Patient 4* **(A)** compared to healthy control samples. **(B)** The x-axis for *Patient 4* shows the days since the NVP HSR (NVP stop date). The Y axis shows pg/ml of cytokine detected. Blue bars - IL-2, orange bars - IL-4, grey bars - IL-6, dark blue bars - TNF, green bars - IFN γ , IL-17a - navy blue bars.