

Figure S1: HLA*02:01 subtyping and gating strategies applied to human PBMCs-derived HSV-1 VP11/12₂₂₀₋₂₂₈-specific CD8⁺ T cells: (A) HLA typing: HLA-A*02 patients were first screened by flow cytometry, and subtyping subsequently performed by PCR to include only HLA-A*02:01 subtyped individual in the study. Gating strategy used for sorting and analysis of HSV-1 VP11/12₂₂₀₋₂₂₈-specific CD8⁺ T cells from PBMCs of SYMP vs. ASYMP individuals is shown.

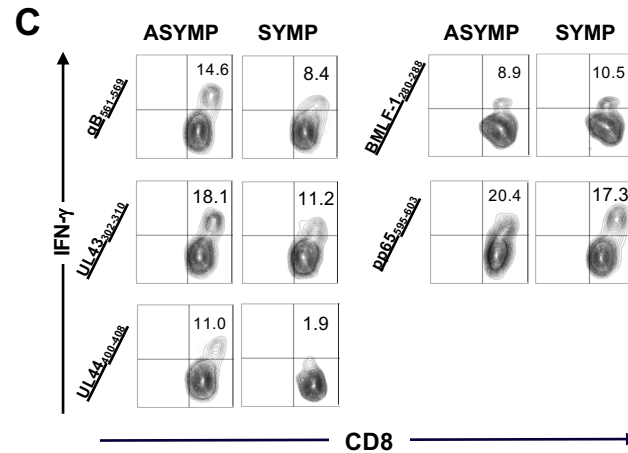
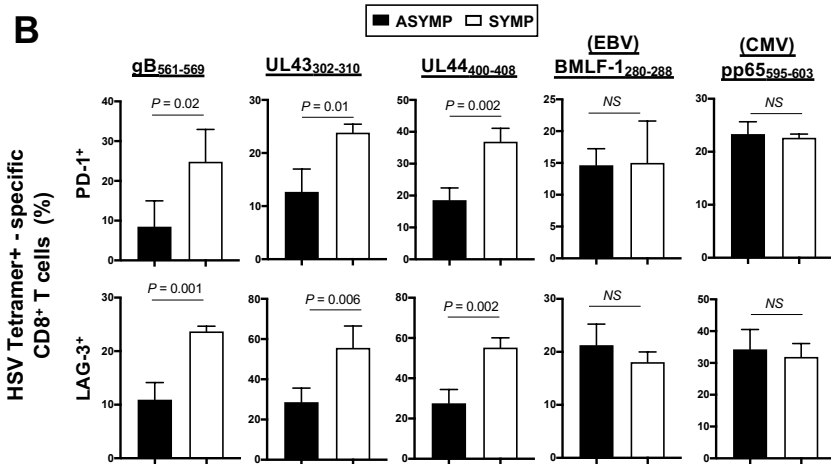
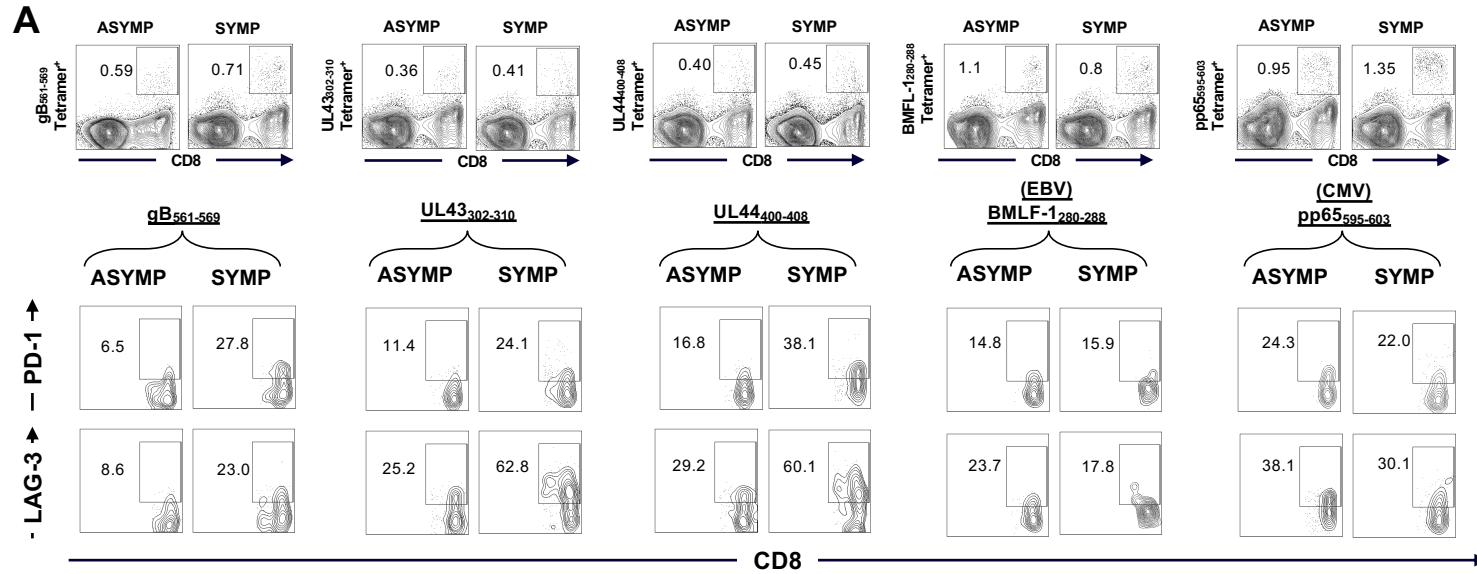


Figure S2: Cell surface expression of exhaustion receptors by various HSV-specific CD8⁺ T cells from symptomatic vs. asymptomatic individuals.

The experimental design is similar to that in Fig. 2A with a focus on CD8⁺ T cells specific to three different epitopes derived from HSV-1 envelope and tegument proteins (gB₅₆₁₋₅₆₇, UL43₃₀₂₋₃₁₀ or UL44₄₀₀₋₄₀₈). **(A)** PBMCs from 10 SYMP and 10 ASYMP individuals were stained for CD3/CD8 followed by tetramers specific for either gB₅₆₁₋₅₆₇, UL43₃₀₂₋₃₁₀ or UL44₄₀₀₋₄₀₈ epitopes and LAG-3/PD-1 exhaustion markers. In parallel, CD8⁺ T cells specific to control epitopes were stained for CD3/CD8 followed by tetramers specific for either EBV (BMLF-1₂₈₀₋₂₈₈) or CMV (pp65₅₉₅₋₆₀₃). Representative dot plots represent the exhaustion status of the five epitope-specific CD8⁺ T cells from the same ASYMP/SYMP subjects. **(B)** Average frequencies of HSV-1-specific CD8⁺ T cells (gB₅₆₁₋₅₆₇, UL43₃₀₂₋₃₁₀ or UL44₄₀₀₋₄₀₈) and EBV or CMV-specific CD8⁺ T cells expressing PD-1 and LAG-3 receptors, detected from SYMP vs. ASYMP individuals. **(C)** Representative FACS plots of functional HSV-1 gB₅₆₁₋₅₆₇⁺, UL43₃₀₂₋₃₁₀⁺ and UL44₄₀₀₋₄₀₈⁺-specific CD8⁺ T or EBV- and CMV- specific CD8⁺ T cells expressing IFN- γ in SYMP vs. ASYMP individuals. Data are expressed as means \pm the standard deviations (SD). The indicated *P* values were determined using unpaired *t* test.

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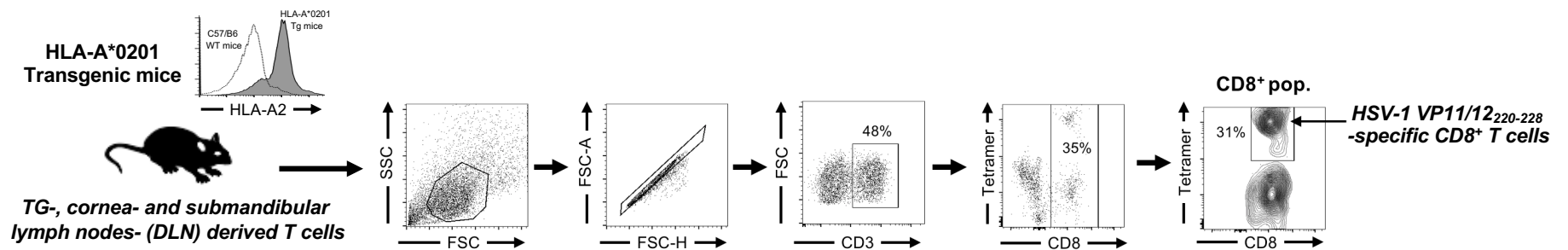


Figure S3: HLA*02:01 expression and gating strategies applied to HLA transgenic-derived HSV-1 VP11/12₂₂₀₋₂₂₈-specific CD8⁺ T cells: HLA typing: HLA-A*02:01 Transgenic mice were screened by flow cytometry to include only mice that express high level of HLA-A2 molecules. Gating strategy used for sorting and analysis of HSV-1 VP11/12₂₂₀₋₂₂₈-specific CD8⁺ T cells in DLN of HLA-A*02:01 Transgenic mice is shown.