Predicting the impact of CD8$^+$ T cell polyfunctionality on HIV disease progression - Supplemental Material

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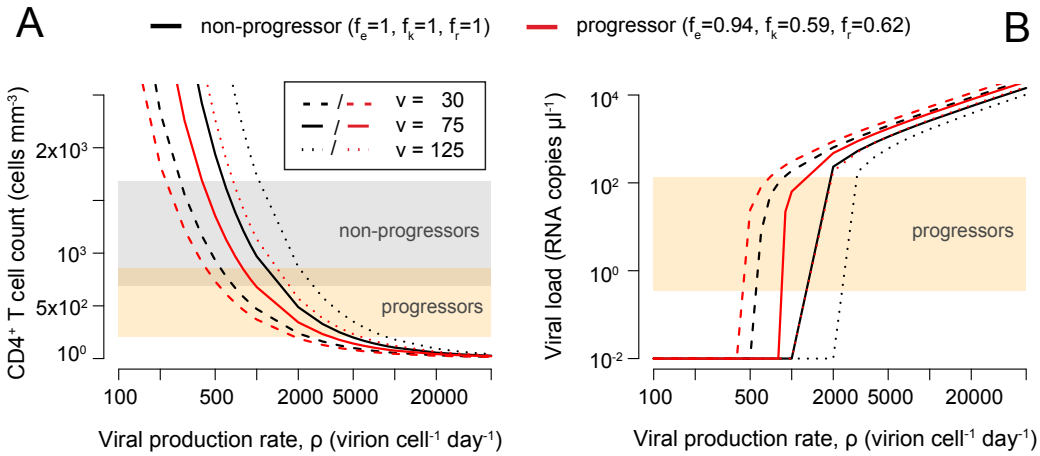

Figure S1: Development of $CD4^+$ T cell count (**A**) and plasma viral load (**B**) at steady state as described in Eqs. (2) and (3) in the main manuscript, respectively, dependent on different parameterizations of the viral production rate, ρ. The model is either parameterized with a fully functional $CD8^+$ T cell response (*black*), or with a dysfunctional $CD8^+$ T cell response as observed for HIV-progressors (*red*). The results for three different scaling factors in the estimated range of ν are shown. Grey and orange shaded areas indicate the 10%-90% percentiles of observed $CD4^+$ T cell counts and plasma viral loads in HIV progressors and non-progressors out of Betts et al. (2006) (see also Table 2 in the manuscript).

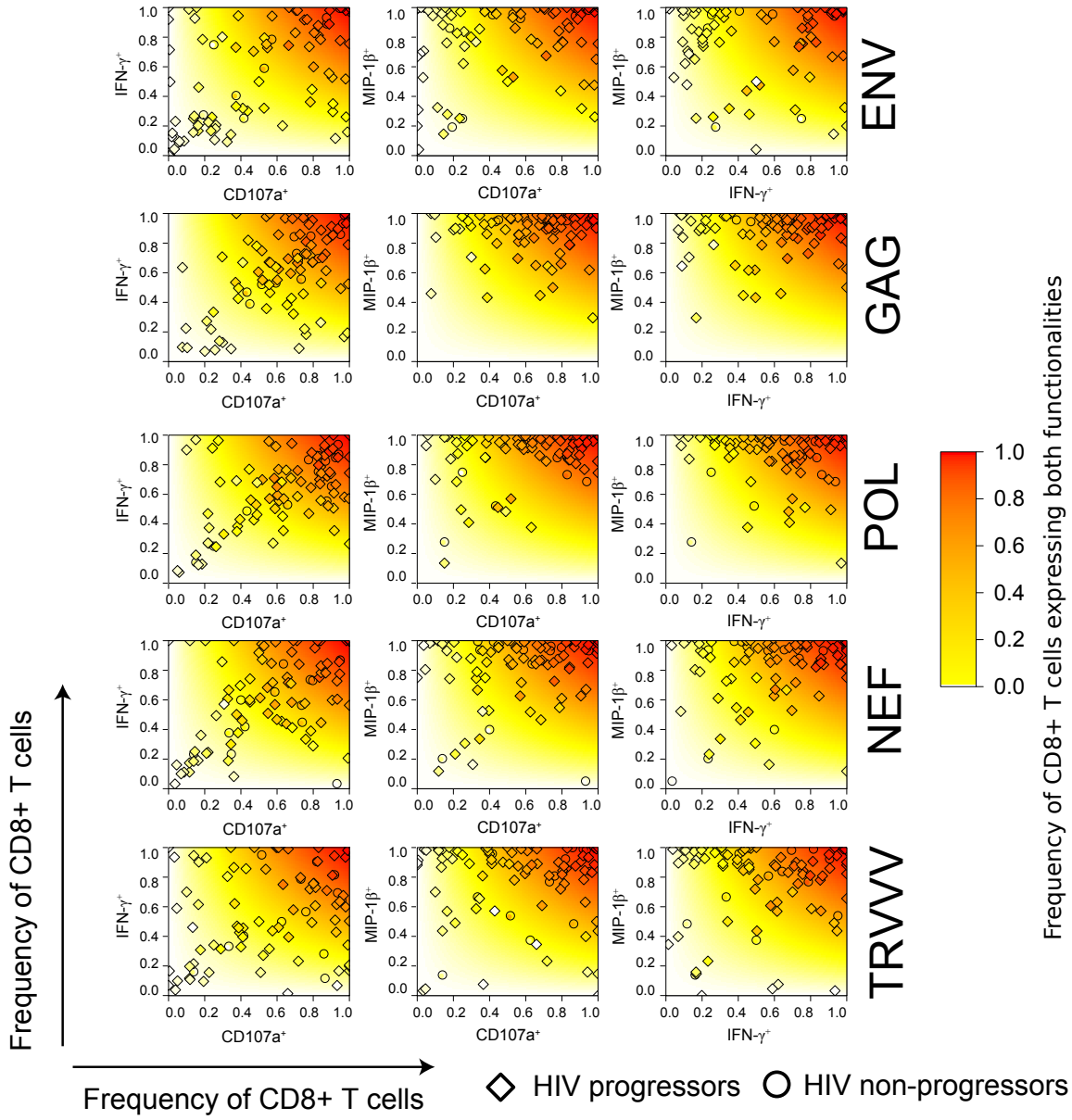

Figure S2: Correlated expression of particular functions I: For each patient, the frequency of $CD8^+$ T cells expressing two of the three functionalities indicated by CD107a, IFN-γ and MIP-1β, f_{ab}, is plotted against the total frequencies of $CD8^+$ T cells expressing the corresponding specific functionalities, i.e., f_a and f_b. The colored background indicates the profile of the expected frequency of combined expression under the assumption that the particular functionalities are expressed independently, $E[f_{ab}] = f_a \times f_b$. Observations are shown separately for each HIV specific epitope.

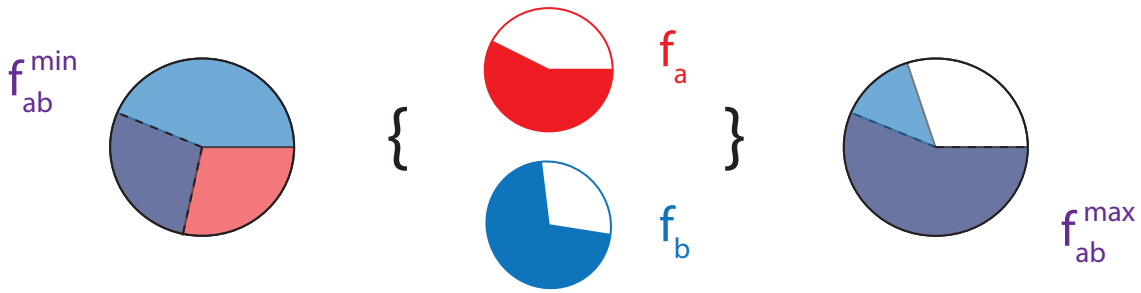

Figure S3: Range of f_{ab}: Sketch of the possible minimal, $f_{ab}^{\min}$, and maximal, $f_{ab}^{\max}$, observable values for f_{ab} given f_a and f_b.

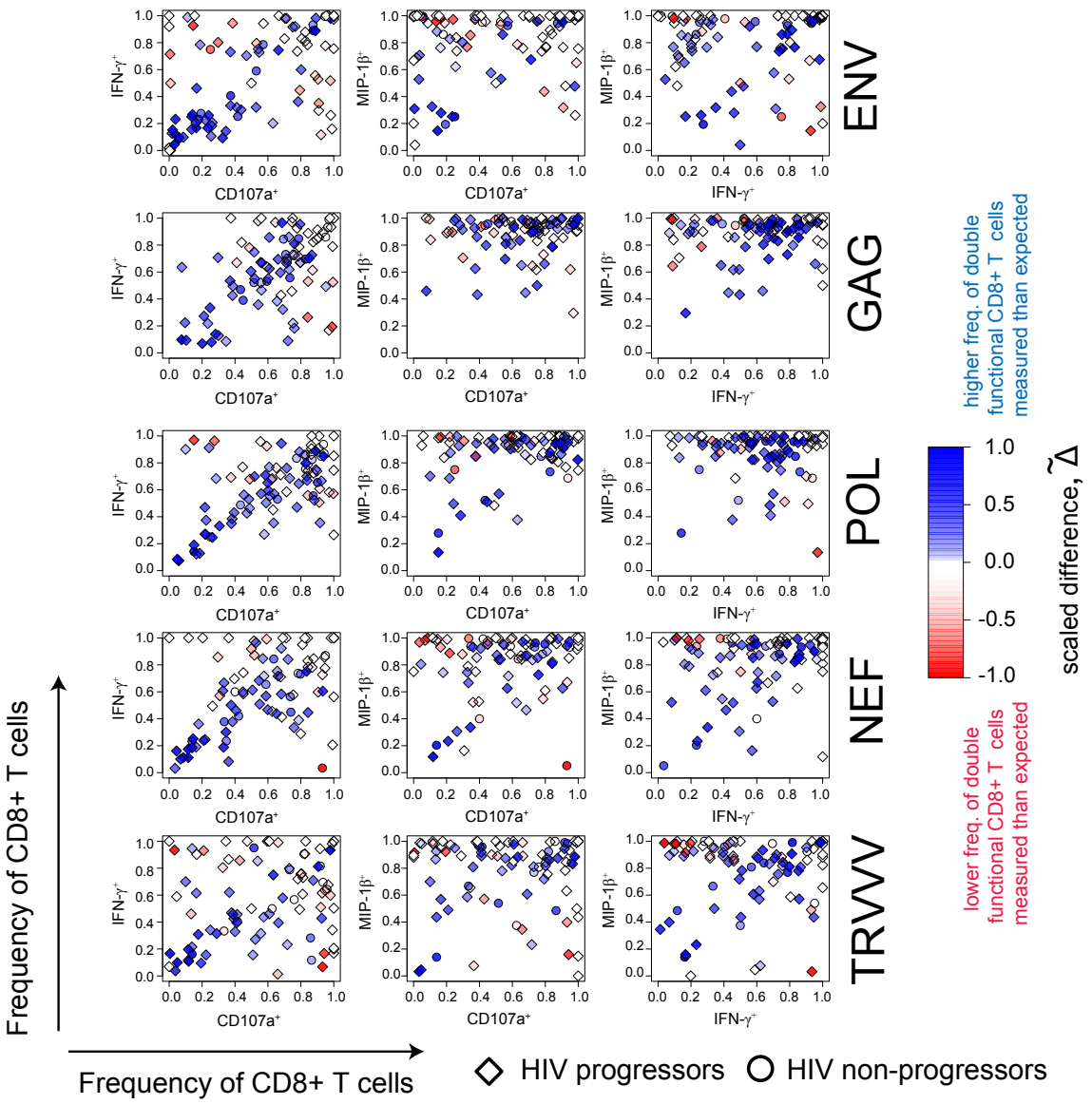

Figure S4: Correlated expression of particular functionalities II: Corresponding to Figure S2, for each patient we show the scaled difference, $\tilde{\Delta}$ between the observed frequency of $CD8^+$ T cells expressing a particular combination of functionalities, f_{ab}, and the expected frequency based on the the total frequencies of $CD8^+$ T cells expressing the corresponding specific functionalities, i.e., f_a and f_b assuming independent expression, hence, $\Delta = f_{ab} - (f_a \times f_b)$ scaled by the possible range of values for f_{ab} (see *Materials & Methods*). Blue colors indicate the observation of higher frequencies of $CD8^+$ T cells expressing both functionalities, red colors lower frequencies than expected. On average, we observe a higher expression of double functional $CD8^+$ T cells than expected by independent expression of these functionalities. The corresponding p-values (Wilcoxon-Test, not corrected for multiple comparisons) are shown in Table S1.

Table S1: Independent expression of specific functionalities: If two functionalities, a and b, are independent of each other, then the measured frequency of $CD8^+$ T cells expressing both functions, f_{ab}, should be the product of the frequencies of $CD8^+$ T cells expressing the one or the other functionality, hence, $f_{ab} = f_a \times f_b$. To test for independence, the scaled difference $\tilde{\Delta} = (f_{ab} - (f_a \times f_b))/(f_{ab}^{\max} - f_{ab}^{\min})$ was calculated for each patient of Betts et al., *Blood* 2006 (see *Materials & Methods*). The table shows the p-values corrected for multiple comparisons for comparing $\tilde{\Delta}$ to 0 (Wilcoxon-test). For p-values larger than 0.05, the null-hypothesis that the two functionalities are expressed independently cannot be rejected.

	CD107a	**IFN-γ**	**MIP-1β**	**IL-2**	**TNF-α**
ENV					
CD107a	-	0.06	1	1	<0.005
IFN-γ	0.06	-	0.19	1	<0.01
MIP-1β			-	<0.003	1
IL-2				-	1
TNF-α					-
GAG					
CD107a	-	0.015	1	1	<0.001
IFN-γ		-	<0.004	<0.006	<0.001
MIP-1β			-	0.03	1
IL-2				-	<0.001
TNF-α					-
NEF					
CD107a	-	<0.005	1	1	0.02
IFN-γ		-	0.02	1	<0.001
MIP-1β			-	0.61	1
IL-2				-	0.01
TNF-α					-
POL					
CD107a	-	0.09	1	1	<0.001
IFN-γ		-	<0.003	0.67	<0.001
MIP-1β			-	1	1
IL-2				-	<0.001
TNF-α					-
TRVVV					
CD107a	-	1	1	1	0.12
IFN-γ		-	0.1	1	<0.002
MIP-1β			-	0.52	1
IL-2				-	0.08
TNF-α					-