Supplementary FIGURE 1

Supplementary FIGURE 2

Supplementary FIGURE 3

A

$R^2= 0.826$
$P<0.001$

% CD28+ in A2/Melan-A tetramer+ CD8+ T cells

% BTLA+ in A2/Melan-A tetramer+ CD8+ T cells

B

Patients vaccinated without CpG

Patients vaccinated with CpG

% BTLA+ in whole CD8 T cells

$R^2= 0.082$
NS   EM

$R^2= 0.042$
NS   EM

$R^2= 0.092$
NS   EMRA

$R^2= 0.138$
NS   EMRA

Number of vaccinations
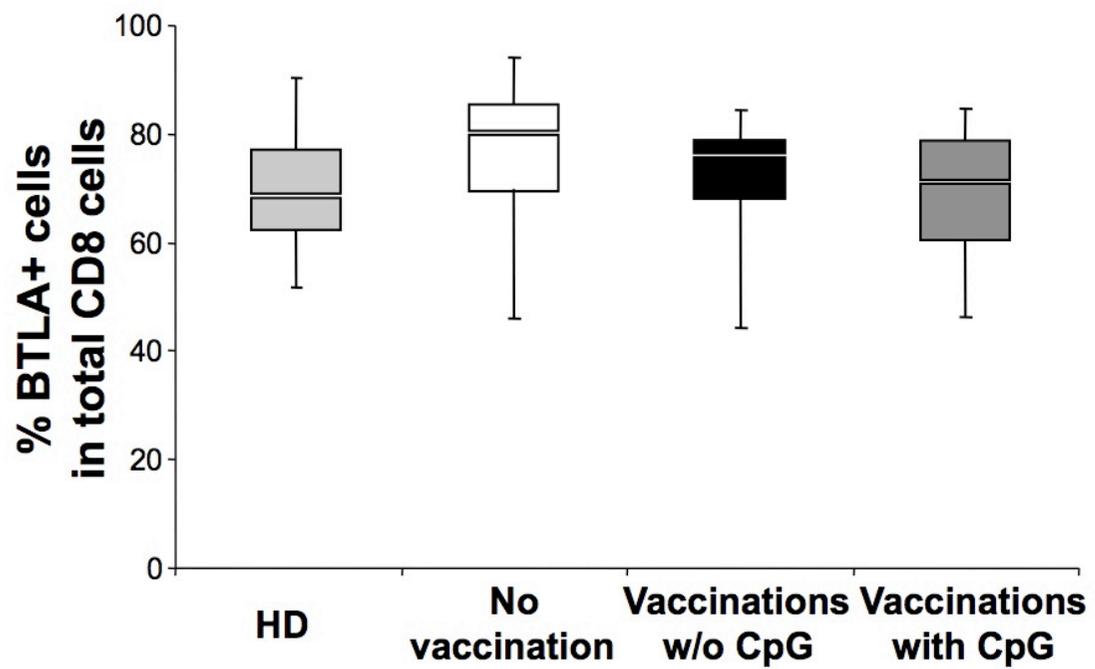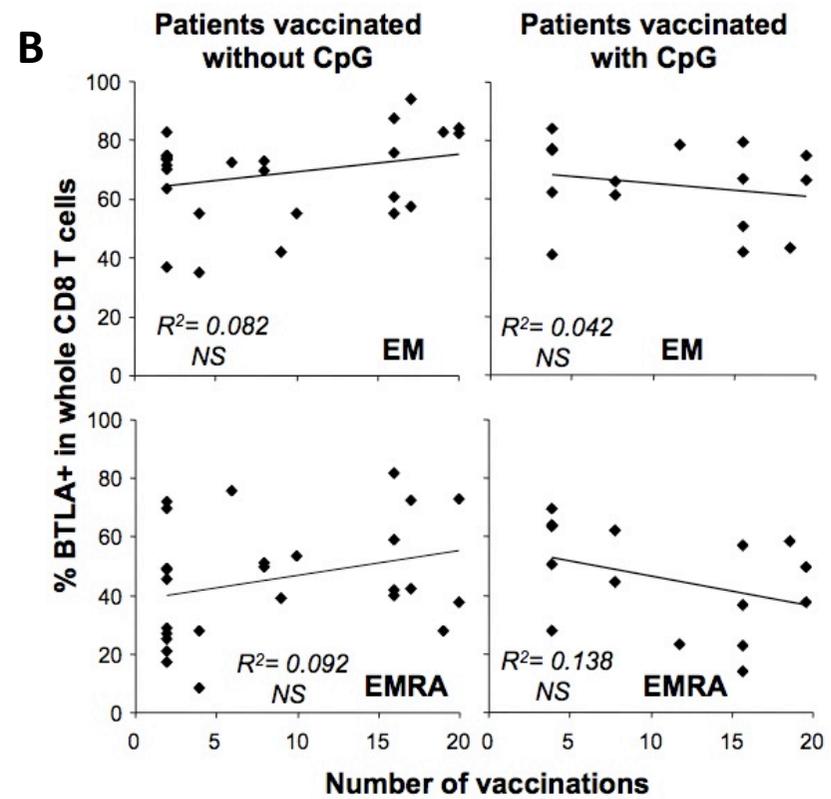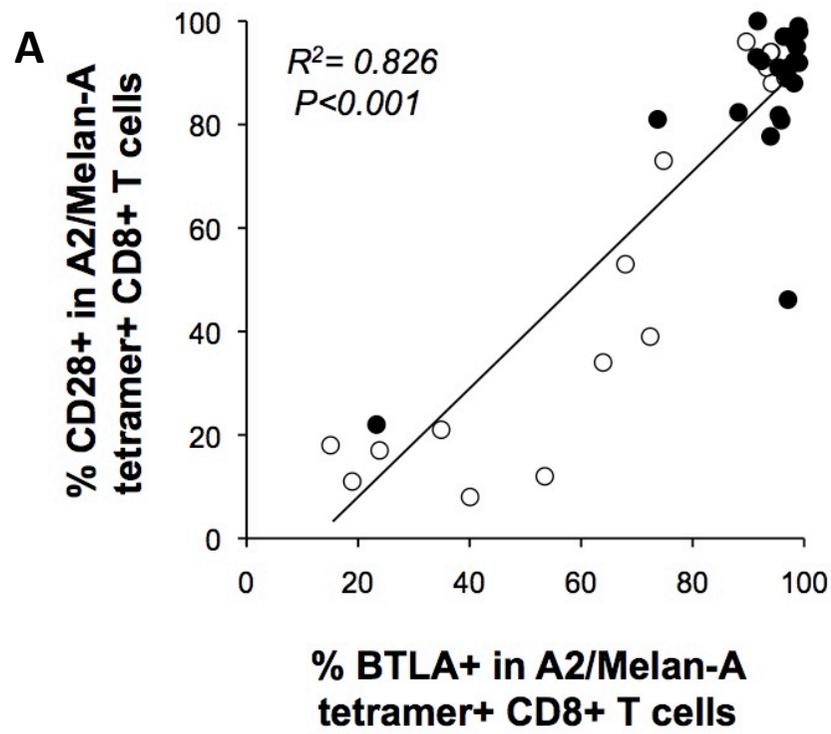
Supplementary FIGURE 4

SKMEL37
+ empty vector

SKMEL37
+ HVEM

90%
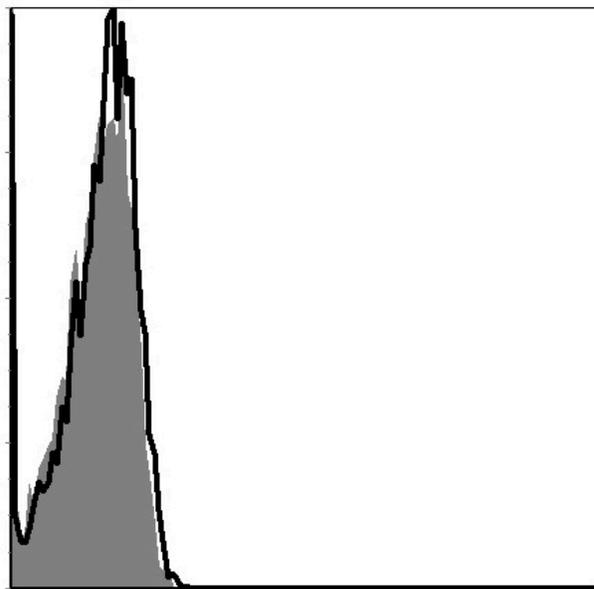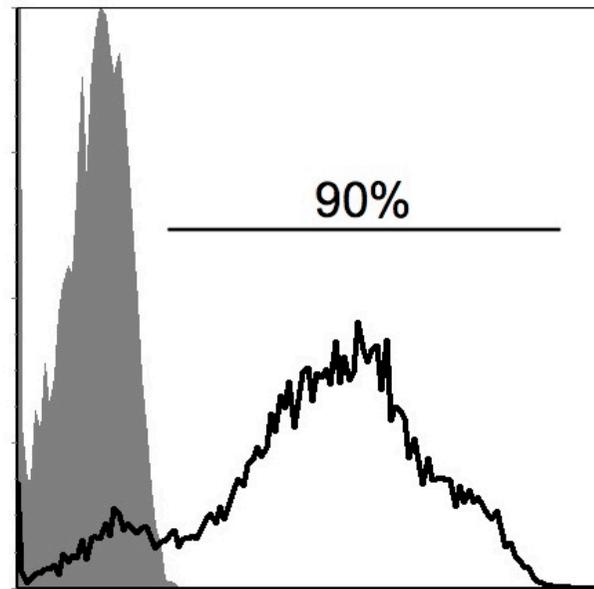
HVEM

Supplementary FIGURE 5

Patient LAU 618

No peptide   1 μM Melan-A

3.2   72.9   SKMEL37

2.7   69.4   SKMEL37 HVEM+

CD107a
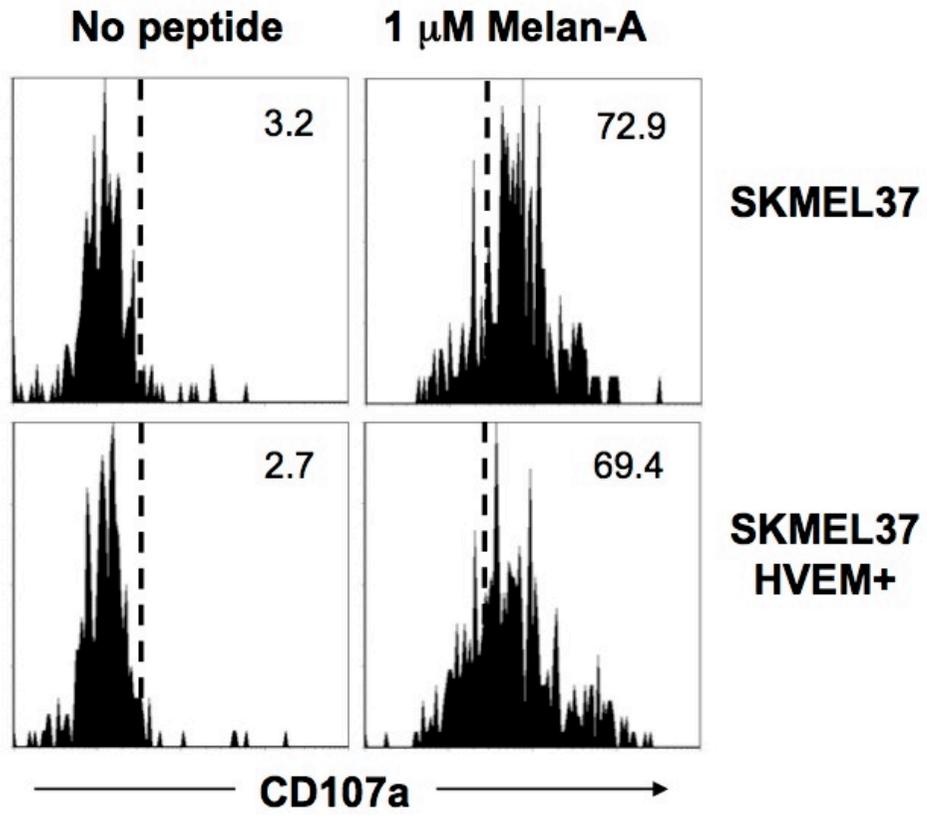
Supplementary FIGURE 6
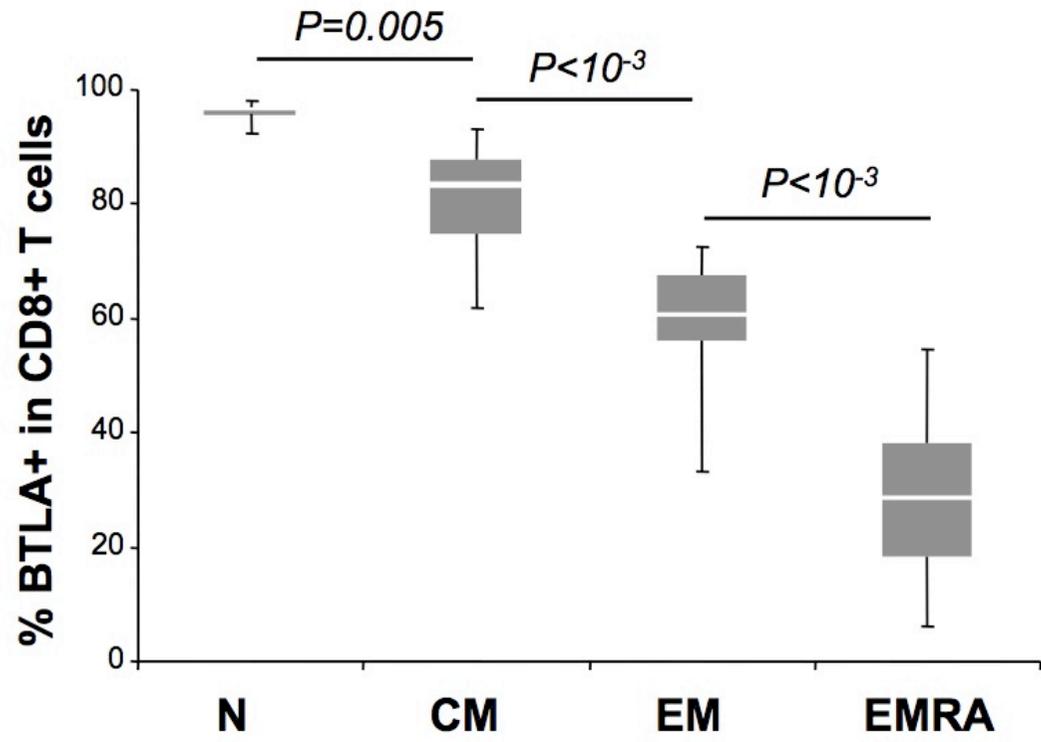
Supplementary FIGURE 7

Supplementary Figure 1: Representative example of BTLA expression by Melan-A^{MART-1} tetramer positive cells from a healthy individual.

Supplementary Figure 2: (A,B) The blocking activity of titrated BTLA-8.2 (A) and BTLA-7.1 mAb (B) was assessed in a competition assay based on the inhibition of HVEM-Fc binding to BTLA transiently expressed on COS cells. Anti-PD1 mAb (PD1-3.1) was used to determine specificity.

Supplementary Figure 3: Percentages of BTLA+ cells among total CD8 T-cells from healthy donors, unvaccinated patients, and patients vaccinated without CpG or with CpG.

Supplementary Figure 4: (A) Correlation between CD28 and BTLA expression by Melan-A^{MART-1}-specific CD8 T-cells from patients vaccinated without CpG (black circles) or with CpG (open circles). (B) Percentages of BTLA+ CD8 T-cells from patients vaccinated without or with CpG, and numbers of monthly booster vaccinations (EM, effector-memory cells; EMRA, CD45RA+ effector-memory cells).

Supplementary Figure 5: HVEM expression by SKMEL37 cells transfected with PCR3 empty vector or full-length human HVEM inserted in PCR3 expression vector. Cells were stained with IgG1^{APC} isotypic control (gray histogram), or with anti-HVEM^{APC} (bold line).

Supplementary Figure 6: CD107a upregulation by A2/Melan-A^{MART-1} tetramer positive T-cells after 4 hours of stimulation by SKMEL37 cells expressing or not HVEM, loaded or not with Melan-A^{MART-1} peptide.

Supplementary Figure 7: Cell surface expression of BTLA in subsets of CD8 T-cells of PBMC from healthy individuals (n =9), assessed by staining with BTLA specific mAb BTLA-7.1.