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Supporting Information

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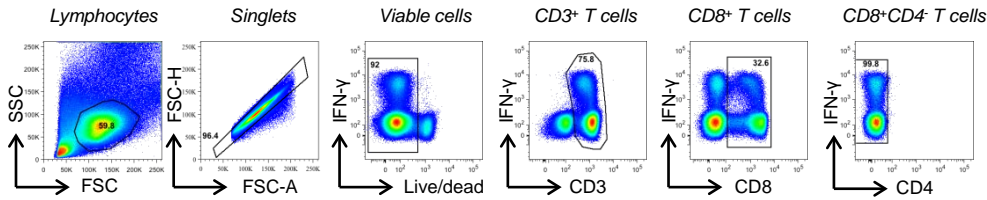
Virginie Rozot, Selena Vigano, Jesica Mazza-Stalder, Elita Idrizi, Cheryl L. Day, Matthieu Perreau, Catherine Lazor-Blanchet, Elisa Petruccioli, Willem Hanekom, Delia Goletti, Pierre-Alexandre Bart, Laurent Nicod, Giuseppe Pantaleo and Alexandre Harari

***Mycobacterium tuberculosis*-specific CD8⁺ T cells are functionally and phenotypically different between latent infection and active disease**

Supporting Information Figure 1

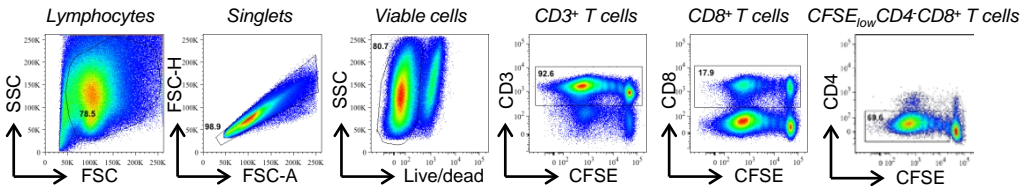
A

Gating strategy for ex vivo T-cell analysis



B

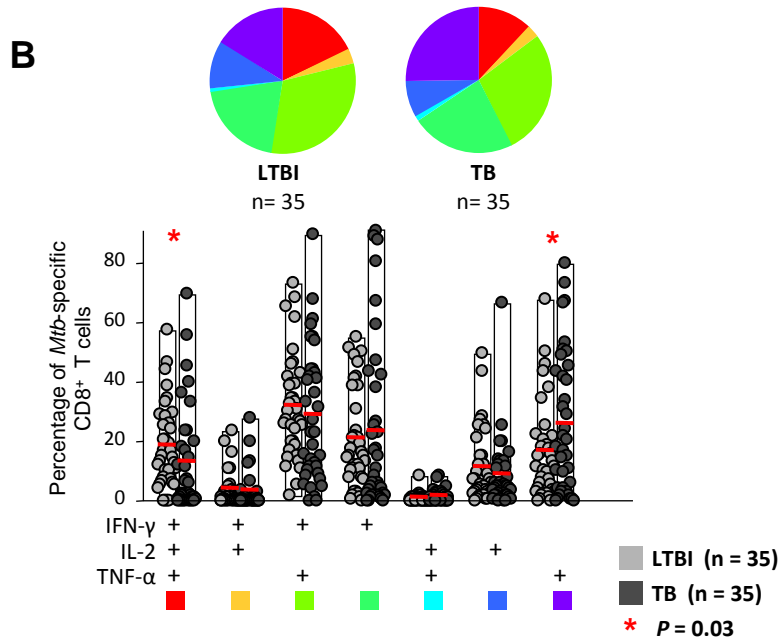
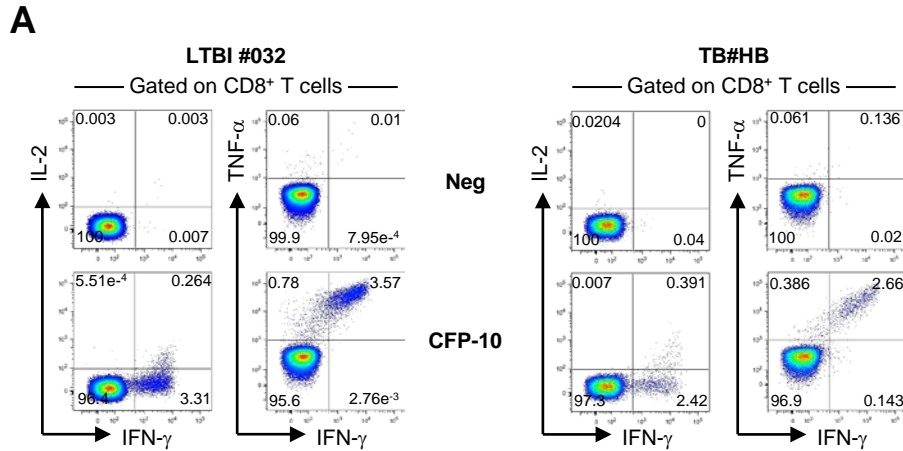
Gating strategy for in vitro expanded T-cell analysis



Supporting Information Figure 1.

Gating strategies for the flow cytometric analyses. (A) Gating strategy for ex vivo analyses **(B)** Gating strategy for the analyses of in vitro T-cell expansion.

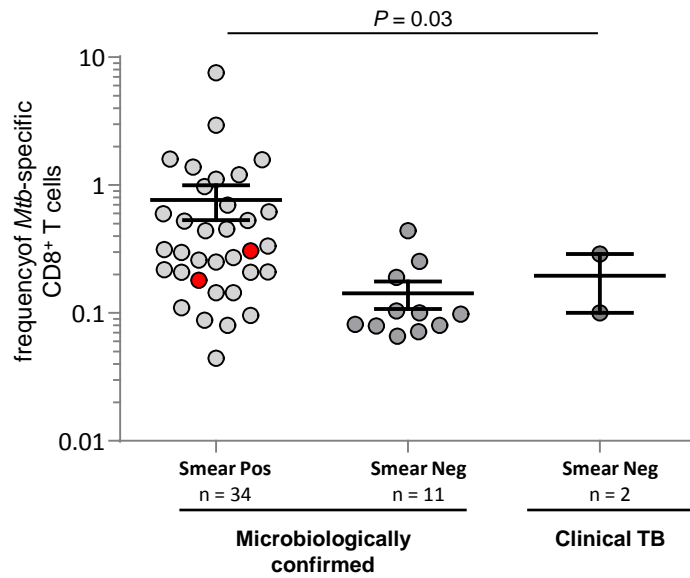
Supporting Information Figure 2



Supporting Information Figure 2.

Representative flow cytometric profiles of LTBI subject and TB patients (A) and cumulative analyses (B) showing IFN- γ , IL-2 and TNF- α expression on *Mtb*-specific CD8⁺ T cells. Flow cytometry profiles are gated on live CD3⁺CD4⁻CD8⁺ T cells. (B) All the possible combinations of the different markers are shown on the x axis whereas the percentages of the distinct T-cell subsets within *Mtb*-specific CD8⁺ T cells are shown on the y axis.

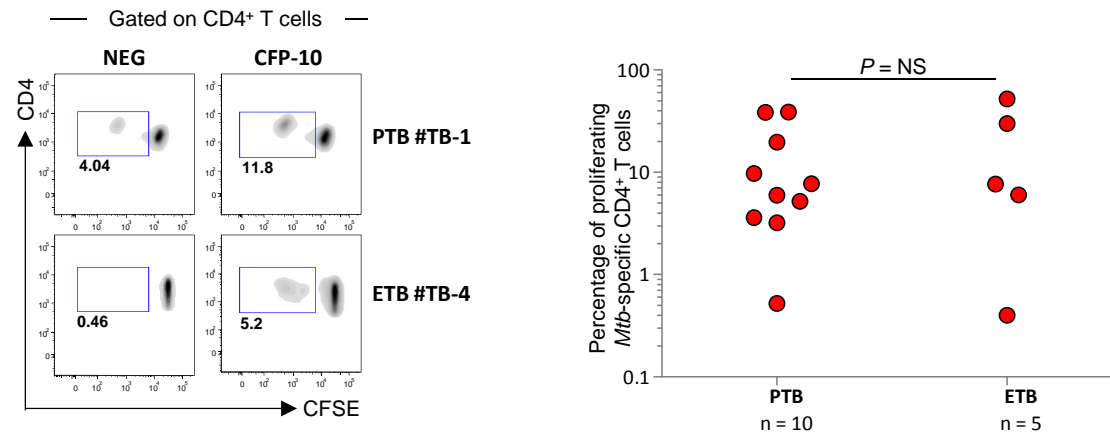
Supporting Information Figure 3



Supporting Information Figure 3.

Frequency (mean \pm SEM) of *Mtb*-specific IFN- γ -producing CD8⁺ T cells in microbiologically-confirmed and clinical PTB subdivided into smear-positive and smear-negative patients. An unpaired two-tailed student's t test was performed. Red points identify *Mtb*-specific CD8⁺ T-cell responses from HIV-coinfected subjects.

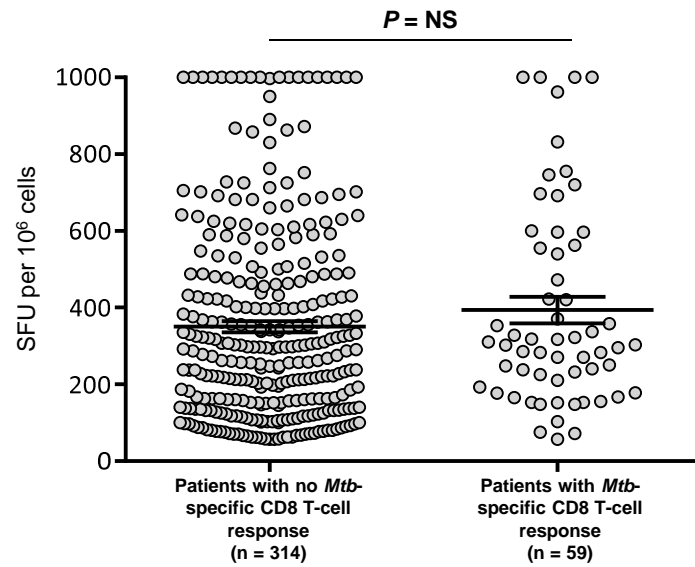
Supporting Information Figure 4



Supporting Information Figure 4.

Proliferation capacity of *Mtb*-specific CD4⁺ T-cell responses from the PTB and ETB patients shown in figure 4E.

Supporting Information Figure 5



Supporting Information Figure 5.

Mtb-specific IFN- γ ELISpot responses in the 240 subjects with latent *Mtb* infection. Shown are the T-cell responses against ESAT-6 and/or CFP-10 peptide pools in the 203 subjects with no detectable *Mtb*-specific CD8 T-cell responses (left) and in the 37 subjects with detectable *Mtb*-specific CD8 T-cell responses (right). Bars represent mean \pm SEM. An IFN- γ ELISpot result was defined as positive if the number of SFUs was > 55 SFU/10⁶ cells and > 4-fold the negative control. Statistical significance (P values) of the results was calculated by unpaired two-tailed student's t test using GraphPad Prism 5.

Supporting Information Table 1

Demographic and clinical description of the 52 TB patients with *Mtb*-specific CD8+ T-cell responses

Patient ID	Gender	Age	TSR ^a	IGRA ^b	PCR	AFB ^c	Culture ^e	Clinics	Origin	Comments
A4 ^d	F	78	/ ^e	+	+	+	+	+	/	ETB ^f /
A5 ^d	M	35	/	+	+	+	+	+	/	ETB
A8 ^d	F	48	/	+	+	+	+	+	/	PTB ^g / HIV positive
CH-3 ^d	M	76	/	+	+	+	+	+	Switzerland	PTB
CH-4 ^d	M	29	+	+	+	-	+	+	Somalia	PTB
CH-5 ^d	M	54	/	+	+	+	+	+	Somalia	PTB
RSA-1 ^d	M	41	/	+	+	+	+	+	South Africa	PTB
RSA-2 ^d	M	59	/	+	+	-	+	+	South Africa	PTB
RSA-3 ^d	M	38	/	+	+	-	+	+	South Africa	PTB
RSA-4 ^d	M	31	/	+	+	+	+	+	South Africa	PTB
RSA-5 ^d	M	47	/	+	+	-	+	+	South Africa	PTB
RSA-7 ^d	M	54	/	+	+	+	+	+	South Africa	PTB
RSA-8 ^d	M	50	/	+	+	-	+	+	South Africa	PTB
RSA-9 ^d	M	38	/	+	+	+	+	+	South Africa	PTB
RSA-10 ^d	M	51	/	+	+	-	+	+	South Africa	PTB
RSA-11 ^d	M	23	/	+	+	+	+	+	South Africa	PTB
TB-1	F	39	/	+	-	+	+	+	/	PTB
TB-2	H	83	/	/	/	+	+	+	Switzerland	PTB
TB-3	M	27	/	+	/	+	+	+	/	PTB
TB-4	H	24	/	+	-	-	+	+	Somalia	ETB
TB-5	M	56	/	+	-	-	+	+	Switzerland	ETB
TB-6	F	9	/	/	/	-	+	+	Portugal	ETB
TB-7	F	31	/	+	-	-	+	+	Portugal	ETB
TB-8	M	18	/	+	+	-	+	+	/	ETB
TB-9	M	37	/	+	+	-	+	+	/	ETB
TB-10	F	41	+	/	+	-	+	+	Peru	PTB
TB-11	F	51	/	/	/	-	+	+	Italy	PTB
TB-12	M	24	/	+	+	-	+	+	South Africa	PTB
TB-13	M	26	+	/	/	-	+	+	Romania	PTB
TB-14	M	37	/	+	/	-	+	+	South Africa	PTB
TB-15	M	67	/	/	+	-	+	+	Italy	PTB
TB-16	M	75	+	/	/	-	+	+	Italy	PTB
TB-17	F	84	/	+	/	+	+	+	Switzerland	ETB
TB-18	M	49	/	+	+	+	+	+	Romania	ETB
TB-19	M	/	/	+	/	+	+	+	/	ETB
TB-20	F	30	/	/	/	+	+	+	/	PTB
TB-21	F	33	-	+	+	+	+	+	Poland	PTB
TB-22	F	39	/	+	+	+	+	+	/	PTB
TB-23	F	46	/	/	/	+	+	+	/	PTB
TB-24	F	52	/	+	/	+	+	+	/	PTB
TB-25	M	21	+	+	+	+	+	+	Romania	PTB
TB-26	M	29	+	/	+	+	+	+	India	PTB
TB-27	M	33	-	+	+	+	+	+	Romania	PTB
TB-28	M	33	/	+	/	+	+	+	South Africa	PTB
TB-29	M	35	/	/	+	+	+	+	Romania	PTB
TB-30	M	36	+	/	+	+	+	+	Romania	PTB
TB-31	M	36	+	+	+	+	+	+	Romania	PTB
TB-32	M	37	/	+	+	+	+	+	South Africa	PTB
TB-33	M	47	+	/	+	+	+	+	Romania	PTB
TB-34	M	52	+	/	+	+	+	+	Romania	PTB
TB-35	M	63	/	-	+	+	+	+	Italy	PTB
TB-36	/	/	/	+	/	+	/	+	South Africa	PTB

^a Tuberculin Skin test. ^b IFN- γ Release assay (IFN- γ ELISpot or Quantiferon). ^c AFB (acid-fast bacilli) and culture performed according to Murray *et al*, Manual of Clinical Microbiology, American Society of Microbiology. ^d Previously described patients (Hatari *et al*, Nature medicine 2011;17:372-6). ^e Not done/Missing data. ^f Extrapulmonary TB and ^g Pulmonary TB (according to WHO guidelines (www.who.int)).