

**Supplementary Table S1.** Systematic review of the immune response against *Treponema pallidum* subs *pallidum*.

<b>Syphilis</b>					
<b>Stage</b>	<b>Cells involved</b>	<b>Response</b>	<b>Cytokines/ Antibodies</b>	<b>Transcription Factors</b>	<b>References</b>
<b>Primary</b>	Th1	High	IFN- $\gamma$ / TNF	STAT1 / T-bet	[10,13,15]
	Th2	Low	IL-4	GATA3	[13]
	Trex	High	IL-10 / TGF- $\beta$	Foxp3	[9,13,18]
	Th17	Low	IL-17Ra	ROR- $\gamma$ t	[9,24]
	Mo	High	--	--	[5,10]
	DC	High	--	--	[5,30,36]
<b>Secondary</b>	NK	High (Skin)	IFN- $\gamma$	RORa/GATA3	[5]
	Th1	High	IFN- $\gamma$ / TNF	STAT1/T-bet	[10,13,15]
	Trex	High	IL-10 / TGF- $\beta$	Foxp3	[13,9]
	CD8	Low	IFN- $\gamma$ Granzyme B	T-bet	[5,13]
	DC	Low	--	--	[5,30]
<b>Tertiary</b>	NK	High (blood)	IFN- $\gamma$	RORa/GATA3	[5]
	Th17	High	IL-17Ra	ROR- $\gamma$ t	[18,24,30]
	B	High	IgM / IgG	NFkb	[34,35]
	CD8	High	IFN- $\gamma$	T-bet	[13]

**Supplementary Table S2.** Systematic review of the immune response in people living with HIV co-infected with *Treponema pallidum subs pallidum*.

Syphilis in persons living with HIV				
Stage	Cells	Response	Results	References
Primary	CD4	Low	Decrease of 85% and 80% in people with ART and without ART respectively. Primary co-infection was associated with an increase in IL-10. Both IL-10 and TNF decreased after syphilis treatment.	[22,23]
	T $\gamma\delta$	High	Greater number of IL-17 producing T $\gamma\delta$ cells and up to 8 times greater IFN- $\gamma$ production.	[24]
	T rex	High	Greater number of Foxp3+Helios+CD25+ T rex compared with healthy donors.	[25]
	Intermediate Monocytes	High	Higher antigen presentation HLA-DR. Higher migration with CCR2 and CX3CR1 chemokines.	[26]
Secondary	CD4	No difference <i>versus</i> healthy donors	Nine times higher concentration of IL-10 was reported.	[27]
Tertiary	CD4	Low	"Lymphopenia" as a predictor of neurosyphilis.	[28]

Supplementary Figure S1. Kinetics of the progression of Syphilis vs. HIV.

