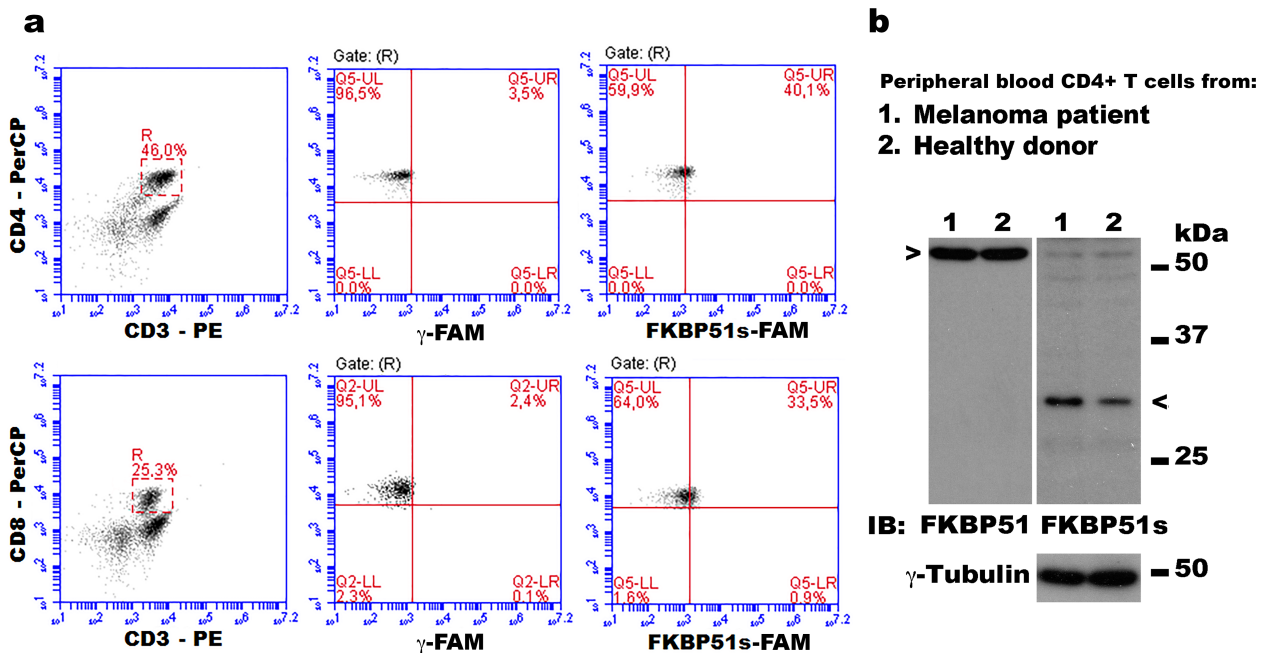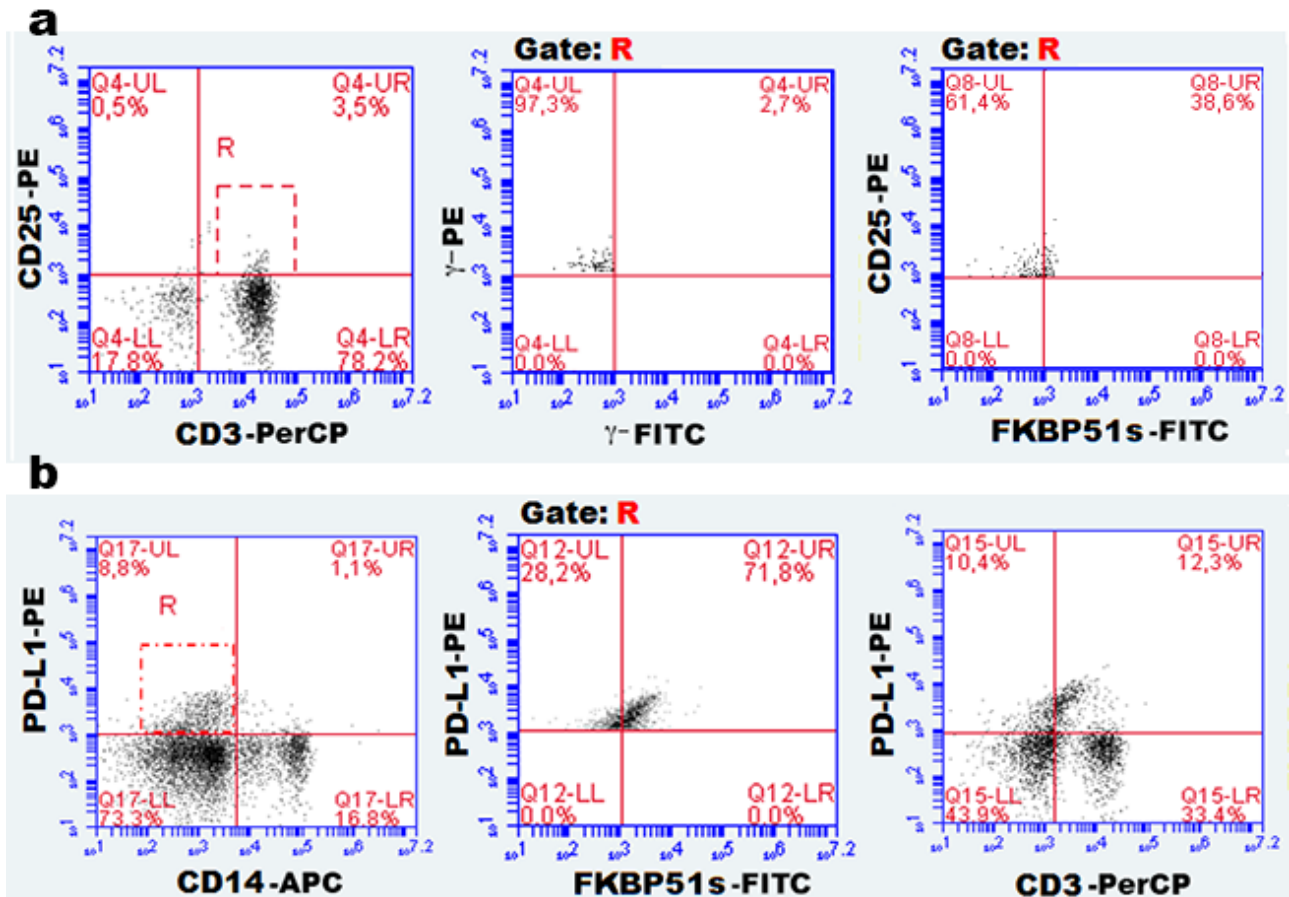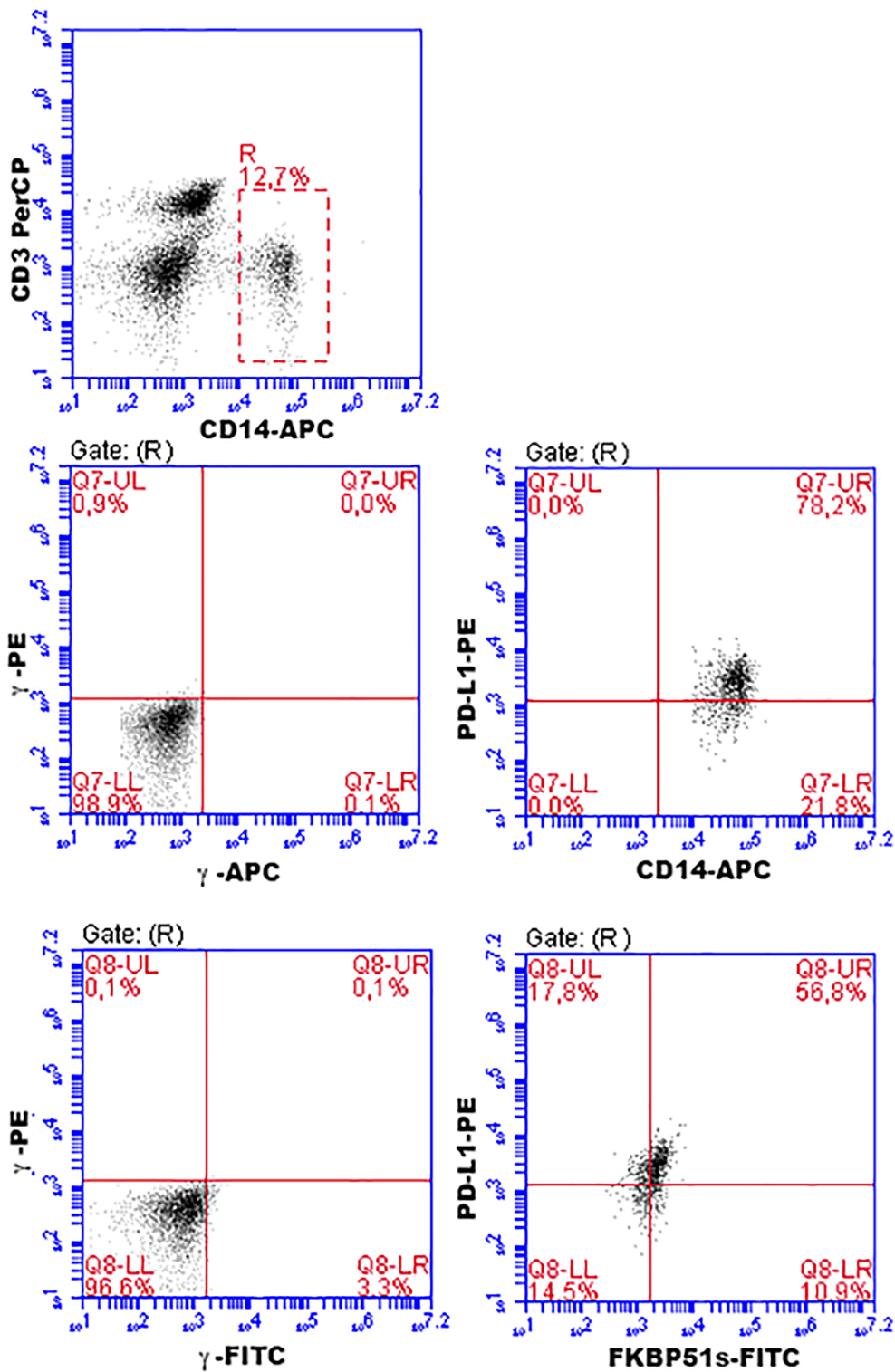**Supplementary Data**

Supplementary figure 1

Supplementary figure 1a. *Lymphocyte CD3/CD4/FKBP51s and CD3/CD8/FKBP51s measurements.* FSC/SSC-gated lymphocytes were plotted on CD3/CD4 or CD3/CD8 axes to determine the percentage of CD4 and CD8 T lymphocytes (R value, CD3 plot). Then, R gated cells was plotted to measure the proportion of FKBP51s^{pos} cells (value in UR quadrant, FKBP51s plot). Finally, the percentage of CD3/CD4/FKBP51s and CD3/CD8/FKBP51s cells were calculated as follows: R-value (CD3 plot) × UR value (FKBP51s plot) / 100). **b**, *Western Blot assay of FKBP51s in CD4 lymphocytes*. CD4+ lymphocytes were sorted from the PBMCs of a melanoma patient (1) and a control donor (2) (CD4+>98%). Then, total lysates were obtained and subjected to Western blotting. The anti-FKBP51s antibody recognizes a band at ~30 kDa but not the canonical FKBP51.
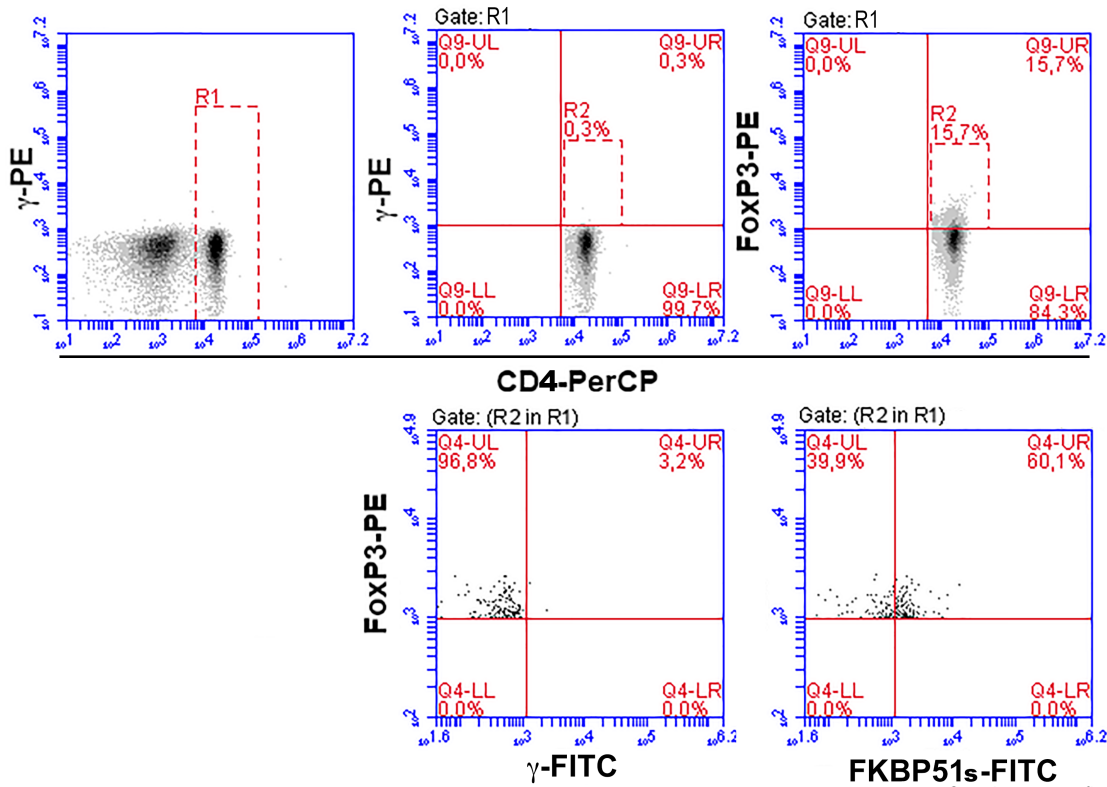
Supplementary figure 2. *Lymphocytes CD25/FKBP51s and PD-L1/FKBP51s measurements.* **a**, FSC/SSC-gated lymphocytes were plotted according to CD3/CD25 to determine the percentage of CD25 T lymphocytes (R-value, CD3 plot). Then, R gated cells were plotted to measure the proportion of FKBP51s^{pos} cells. The percentage of CD25/FKBP51s cells was calculated as follows: R-value (CD3 plot) × UR value (FKBP51s plot) / 100. **b**, PBMCs were plotted according to CD14/PD-L1 to determine the percentage of PD-L1[pos] lymphocytes (R value, CD14 plot). Then, R gated cells were plotted to measure the proportion of FKBP51s^{pos} cells. The percentage of PD-L1/FKBP51s cells was calculated as follows: R-value (CD14 plot) × UR value (FKBP51s) / 100. The PD-L1^{pos} lymphocyte count was calculated using a CD14 negative population because of low CD3 expression (CD3[Dim]).
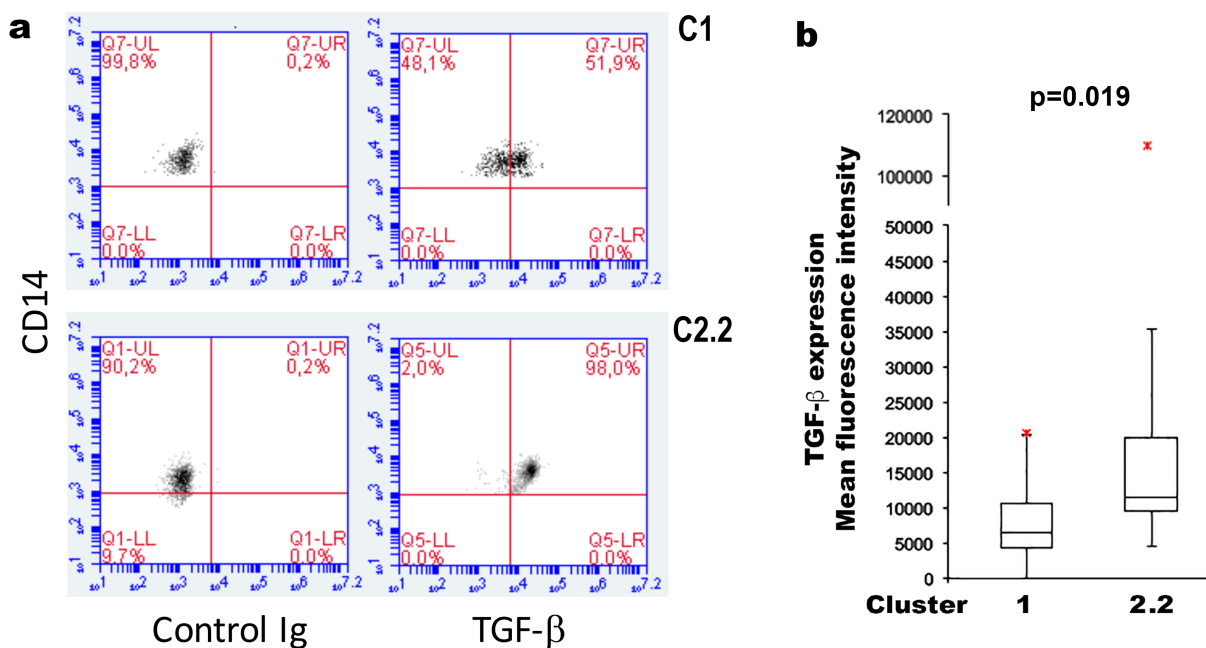
Supplementary figure 3

Supplementary figure 3. *PD-L1/FKBP51s monocyte measurements.* PBMCs were CD14/CD3 plotted and a gate was placed on CD14 monocytes. The percentage of PD-L1/FKBP51s cells was calculated on gated monocytes (UR value of FKBP51s plot).

Supplementary figure 4. *FKBP51s Treg measurements.* CD4 gated lymphocytes (R1) were plotted as CD4 versus Foxp3 and the CD4/Foxp3 percentage (R2 value) calculated. Then, R2 gated cells were plotted to measure the proportion of FKBP51s^{pos} cells (value in UR quadrant, FKBP51s/Foxp3 plot). The percentage of *FKBP51s Treg*s was calculated as follows: R2 value (CD4/Foxp3 plot) × UR value (FKBP51s plot) / 100.

Supplementary figure 5

Supplementary figure 5. *Increased levels of TGF-β in cases clustered in C2.2*. Expression of TGF-β was measured by flow cytometry in cases clustered as C1 (n = 20) and cases clustered as C2.2 (n = 10). **a**, Representative flow cytometry histograms are shown. **b**, Box plots of the mean fluorescence intensity values of TGF-β expression.

Supplementary table 1. Patient profiles.

Sex		Age (y)		Primary lesion		Mutation		Sites of metastasis		Stage	
F	49	Mean	56	Cutaneous	101	BRAF	35	Lung	58	IIIc	2
M	69	Range	31-84	Ocular	9	NRAS	3	Liver	33	IV	116
				Mucosal	6	GNAQ	1	Lymph node	29		
				Unknown	2			Cutis and Subcutis	29		
								Brain	27		
								Bone	9		
								Stomach	2		
								Gut	2		
								Spleen	1		
								Kidney	1		

Supplementary table 2. Cluster distribution of NR and R, with reference to FKBP51sTreg status.

C1 n=**33**			
High n=**17**		**Low** n=**16**	
NR n=**7**	**R** n=**10**	**NR** n=**15**	**R** n=**1**
C2.1 n=**4**			
High n=**4**		**Low** n=**0**	
NR n=**2**	**R** n=**2**	**NR** n=**0**	**R** n=**0**
C2.2 n=**10**			
High n=**6**		**Low** n=**4**	
NR n=**6**	**R** n=**0**	**NR** n=**3**	**R** n=**1**
C3 n=**17**			

High n=10		Low n=7	
NR n=6	R n=4	NR n=7	R n=0
Total n=64			
High n=37		Low n=27	
NR n=21	R n=16	NR n=25	R n=2

*High: FKBP51s Treg >1.02
**Low: FKBP51s Treg <=1.02

Supplementary table 3. Response to nivolumab (n = 16 patients).

	*High n=7		**Low n=9	
	NR	R	NR	R
C1 n=8	1	2	5	0
C2.2 n=4	0	2	1	1
C3 n=4	1	1	2	0
TOTAL n=16	2	5	8	1

*High: FKBP51s Treg >1.02
**Low: FKBP51s Treg ≤ 1.02