

**Tonsillar cytotoxic CD4 T cells are involved in the control of EBV primary infection in children**

María Eugenia Amarillo, Agustina Moyano, Natalia Ferressini Gerpe, Elena De Matteo, Maria Victoria Preciado, Paola Chabay.

Infection status by EBV	VCA IgM	VCA IgG 1/10. 1/40. 1/320	EA IgG	EBNA1 IgG
Primary infection	+	+/-	+/-	-
Healthy carrier	-	+	-	+
Reactivation	-/+	+	+	+
Non-infected	-	-	-	-

Supplementary table S1. Infection status by EBV serological profile.

Latency profiles	Viral antigen expression
0	-
I	EBERs
II	LMP1. EBERs
III	EBNA2. EBERs. LMP1

Supplementary table S2. Latency profile by EBV protein expression

Infection status by EBV	Median age (range)
Primary infection	5 (2-12)
Healthy carrier	6 (2-15)
Reactivation	5 (2-11)
Non-infected	2 (1-11)

Supplementary table S3. Age distribution of EBV infection status

Infection status by EBV	N	CD4/mm <sup>2</sup> median (IQ range)			Foxp3/mm <sup>2</sup> median (IQ range)			GZMB/mm <sup>2</sup> median (IQ range)			CD4-Foxp3/mm <sup>2</sup> median (IQ range)			CD4-GZMB/mm <sup>2</sup> median (IQ range)		
		GC	IF	Total	GC	IF	Total	GC	IF	Total	GC	IF	Total	GC	IF	Total
Primary infection	16	3063 (2253-3451)	8232 (6911-10150)	11129 (9791-13634)	58.70 (13.81-117.4)	752.7 (421.3-875.6)	808.0 (497.2-973.7)	145.0 (79.93-191.6)	542.1 (429.9-725.1)	721.7 (540.4-851.1)	51.79 (13.81-62.15)	721.7 (440.2-820.1)	759.6 (433.3-871.9)	14.50 (13.81-34.53)	217.5 (153.7-281.4)	234.8 (183.0-291.1)
Healthy carrier	21	2866 (2431-3992)	8591 (6985-9865)	11325 (10317-13228)	48.34 (20.72-107.0)	669.9 (576.6-1091)	863.2 (645.7-1205)	110.5 (54.56-200.3)	435.1 (313.9-580.1)	550.4 (424.7-688.5)	44.89 (20.72-62.15)	669.9 (531.7-1036)	787.3 (604.3-1088)	27.62 (13.81-44.89)	145.0 (103.2-193.4)	179.5 (128.1-218.2)
Reactivation	9	2592 (2565-3384)	8100 (6426-8739)	10642 (9202-12161)	34.53 (20.72-46.61)	442.0 (379.8-932.3)	469.6 (410.9-1087)	124.3 (100.1-172.6)	429.5 (317.7-628.4)	649.1 (419.2-812.1)	41.43 (17.26-51.79)	435.1 (379.8-894.3)	469.6 (407.4-949.5)	27.62 (17.75-48.34)	186.5 (158.8-224.4)	193.4 (180.0-265.9)
Non-infected	4	3391 (3128-4161)	7571 (6507-10734)	11535 (9922-14035)	31.08 (12.09-39.71)	455.4 (367.7-502.2)	489.9 (383.3-535.0)	55.25 (19.51-65.60)	300.4 (253.8-590.4)	362.6 (276.7-645.7)	31.08 (12.09-39.71)	455.4 (367.7-502.2)	489.9 (383.3-535.0)	10.36 (0.000-25.90)	176.1 (94.95-329.7)	189.9 (94.95-352.2)

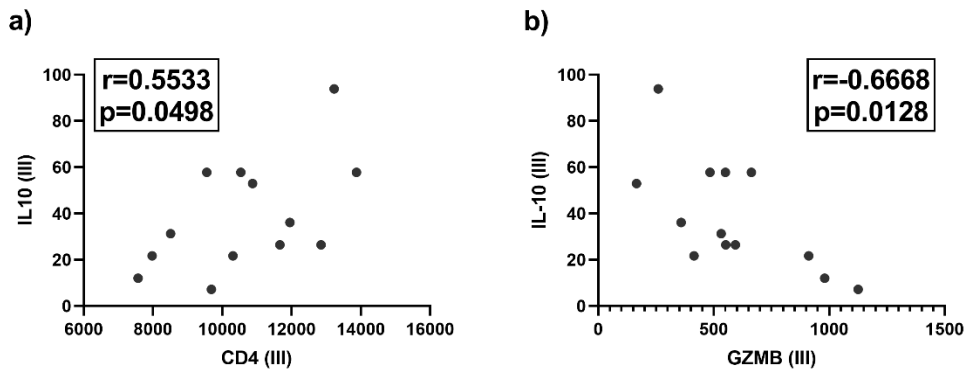
Supplementary table S4. Median and Interquartile (IQ) range according to EBV infection status. GC: germinal center; IF: interfollicular region.

EBV Latency profile	N	CD4/mm <sup>2</sup> median (IQ range)			Foxp3/mm <sup>2</sup> median (IQ range)			GZMB/mm <sup>2</sup> median (IQ range)			CD4-Foxp3/mm <sup>2</sup> median (IQ range)			CD4-GZMB/mm <sup>2</sup> median (IQ range)		
		GC	IF	Total	GC	IF	Total	GC	IF	Total	GC	IF	Total	GC	IF	Total
0	7	2728 (2445-3529)	9316 (8826-10241)	12707 (11760-13729)	48.34 (20.72-103.6)	966.8 (738.9-1084)	987.5 (787.2-1146)	78.73 (41.43-207.2)	448.9 (400.5-614.6)	566.3 (435.1-711.3)	48.34 (20.72-103.6)	745.8 (656.0-1036)	870.1 (704.4-1095)	13.81 (6.906-48.34)	158.8 (124.3-207.2)	186.5 (131.2-221.0)
I	12	2679 (2327-3190)	8100 (7921-10676)	10642 (10324-14509)	55.25 (34.53-96.68)	875.6 (607.7-1153)	972.3 (628.4-1264)	186.5 (118.8-226.2)	488.2 (367.2-623.2)	657.4 (500.8-839.0)	55.25 (27.62-89.77)	794.2 (524.8-1057)	864.6 (545.6-1119)	34.53 (27.62-34.53)	181.3 (116.5-240.0)	221.7 (148.5-269.3)
II	14	2842 (2374-3373)	7804 (6075-9483)	10977 (8772-12507)	48.34 (13.81-75.96)	587.4 (366.0-820.1)	794.2 (386.7-904.7)	113.9 (65.60-202.0)	504.1 (324.6-711.3)	656.0 (481.7-799.3)	43.85 (20.72-54.38)	483.4 (352.2-783.8)	787.3 (386.7-866.7)	17.95 (13.81-50.07)	217.5 (150.2-293.5)	249.0 (177.8-311.8)
III	13	3232 (2439-3719)	7603 (6056-8649)	10534 (9029-12403)	41.43 (13.81-200.3)	607.7 (366.0-766.5)	663.0 (379.8-991.0)	107.0 (86.32-136.4)	442.0 (265.9-663.0)	550.4 (386.7-787.3)	41.43 (10.36-55.25)	607.7 (366.0-759.6)	663.0 (376.4-814.9)	20.72 (10.36-87.62)	158.8 (91.50-183)	184.0 (102.4-208.9)

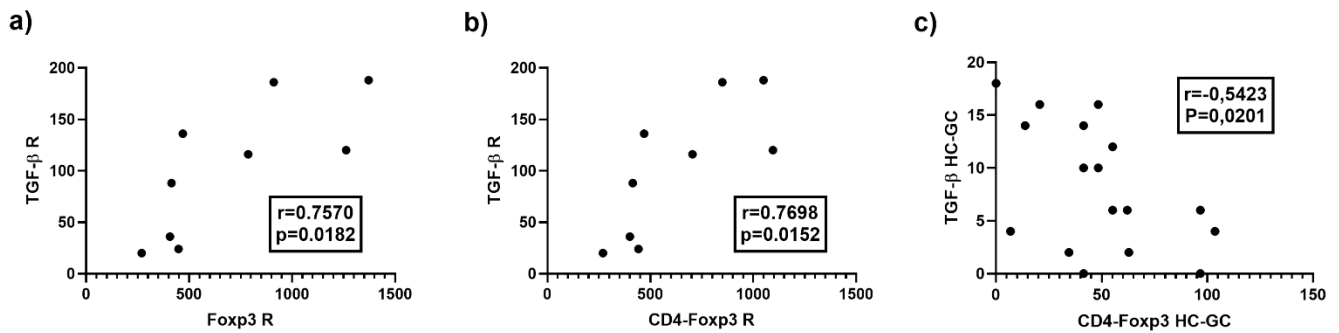
Supplementary table S5. Median and Interquartile (IQ) range according to latency profiles. GC: germinal center; IF: interfollicular region.

BMRF1 expression	N	CD4/mm <sup>2</sup> median (IQ range)			Foxp3/mm <sup>2</sup> median (IQ range)			GZMB/mm <sup>2</sup> median (IQ range)			CD4-Foxp3/mm <sup>2</sup> median (IQ range)			CD4-GZMB/mm <sup>2</sup> median (IQ range)		
		GC	IF	Total	GC	IF	Total	GC	IF	Total	GC	IF	Total	GC	IF	Total
BMRF1+	10	3049 (2466-3617)	7728 (6424-8836)	10612 (9654-11483)	48.34 (17.26-145.0)	642.2 (417.8-915.0)	745.8 (424.7-1042)	96.68 (65.60-134.7)	421.3 (272.8-490.3)	490.3 (386.7-574.9)	41.43 (13.81-55.25)	635.3 (412.6-911.6)	742.4 (419.5-961.6)	20.72 (13.81-27.62)	165.7 (155.4-202.0)	189.9 (177.8-215.8)
BMRF1-	40	3004 (2445-3487)	8524 (6733-9875)	11506 (9951-13231)	44.89 (20.72-96.68)	635.3 (421.3-918.5)	752.7 (459.2-1126)	113.9 (69.06-191.6)	455.8 (333.0-664.7)	625.0 (457.0-787.3)	41.43 (20.72-56.97)	621.5 (414.3-870.1)	687.1 (459.2-935.7)	27.62 (13.81-41.43)	177.8 (124.3-252.1)	210.6 (138.1-279.7)

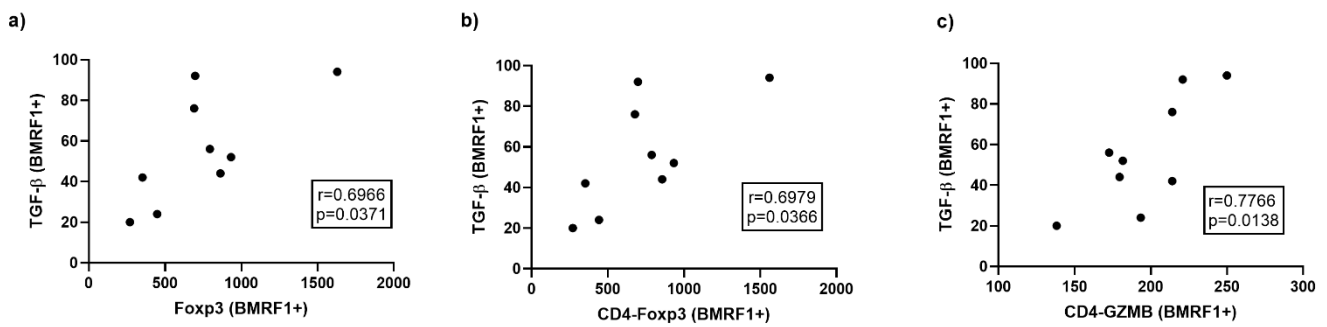
Supplementary table S6. Median and Interquartile (IQ) range according to BMRF1 expression. GC: germinal center; IF: interfollicular region.



Supplementary figure 1. Correlation of IL-10+ cells with CD4 (a) and GZMB (b) in latency III.



Supplementary figure 2. Correlation of TGF $\beta$ + cells with Foxp3 (a) and CD4-Foxp3 (b) in reactivation, and with CD4-Foxp3 at the GC (c).



Supplementary figure 3. Correlation of TGF $\beta$ + cells with Foxp3 (a), CD4-Foxp3 (b) and with CD4-GZMB (c) in BMRF1+ cases.