Supplementary Table 1. Demographic and clinical characteristics of study participants

Subject	Age	Gender	Location of HSV lesion	HSV1/2	Site of control biopsy
1	46.8	F	Perineal	HSV-1&2	Contra
2	63	F	Buttock	HSV-1&2	Contra
3	60.9	F	Buttock	HSV-2	Arm
4	46	F	Labia	HSV-2	Arm
5	26.2	М	Mons	HSV-1&2	Arm
6	32.3	F	Labia	HSV-2	Contra
7	56.7	F	Buttock	HSV-1&2	Contra
8	51.2	F	Buttock	HSV-2	Contra
9	48.5	F	Buttock	HSV-2	Arm
10	47	F	Buttock	HSV-1&2	Contra
11	58.5	F	Buttock	HSV-2	Arm
12	57.7	F	Perianal	HSV-2	Arm
13	52.9	М	Buttock	HSV-2	Contra
14	18.5	F	Mons	HSV-2	Contra
15	66.3	F	Buttock	HSV-1&2	Arm
16	33.1	F	Buttock	HSV-2	Contra

Supplementary Figure 1. Comparison of the relative expression of CXCL12 (A) and CXCR4 (B) in genital skin biopsies using arraybased gene expression data from Gene Expression Omnibus. Dataset GSE18527.







Supplementary Figure 2. RMCorr graphs showing correlation over multiple participants of transformed data. Lack of correlation between IgG+ and T cell subsets. Participants are labeled by color, Biopsies from genital and control areas from each participant are included in each graph. Results from pooled Spearman signed-rank analysis is shown for comparison.



16

CD20 + cells per mm<sup>2</sup> (log10)

CD20 + cells per mm<sup>2</sup> (log10)

CD4 + cells per mm<sup>2</sup> (log10)

16

 $CD20 + cells per mm^2 (log10)$ 

Supplementary Figure 3. Isotype control (A) and isolated primary antibody (B, no secondary antibody) for IgG IFA and additional images of *IGHG* co-expression by FISH with *PRDM1* (C), *CXCR4* (D), and *IRF4* (E).













Supplementary Figure 4. Reactivity of patient sera collected during HSV-2 reactivation in genital skin to HSV-2 and control antigens. All measurements were performed in duplicates in one experiment using GCLP-qualified Luminex HSV-2 binding antibody assay. Values from these dilution curves were used to calculate the area under the curve (AUC) summarized in Supplementary Table 2.



Supplementary Table 2. Area under the binding curve for titration of serum samples collected concurrently with genital skin biopsies (Supplementary Figure 4).

	Lesion/ Control	Healing	2 wph	4 wph	8 wph
Participant 1					
gB2	32797	34319	33089	33492	33103
gD2	23328	25318	23833	23665	23532
Flu-HA	9890	10731	9931	9890	9321
EBV gp350	654.1	744.1	656.9	637.4	582.4
Participant 6					
gB2	26953	26821	24505	26847	26046
gD2	25590	25790	23541	25383	24838
Flu-HA	18527	18100	16195	17926	17512
EBV gp350	19714	19340	17472	19159	19110

All measurements were performed in duplicate in one experiment using GCLPqualified Luminex HSV2 binding antibody assay. Supplementary Figure 5. Reactivity of patient sera collected at the time point closest to the biopsy analyzed to HSV2 and control antigens. All measurements were performed in duplicates in one experiment using GCLP-qualified Luminex HSV2 binding antibody assay. Values from the dilution curves were used to determine the area under the curve (AUC) summarized in Supplementary Table 2.



Supplementary Table 3. Area under the binding curve for serum antibody titration presented on the Supplementary Figure 5. All measurements were performed in duplicates in one experiment using GCLP-qualified Luminex HSV-2 binding antibody assay.

	AUC					
Participant	gB2	gD2	EBV gp350	Flu-HA		
1	40503	34094	1155	16752		
2	ND	ND	ND	ND		
3	32816	35684	4006	6269		
4	28339	34379	22671	3270		
5	25076	37211	3230	575.8		
6	37948	36046	30478	28894		
7	26804	30027	3213	2690		
8	21202	29135	33278	12150		
9	16567	33321	9956	3171		
10	22263	18853	3285	5567		
11	24454	33078	4209	4296		
12	26532	34902	9999	6974		
13	28964	36371	28316	5154		
14	30898	31376	17674	6670		
15	18793	33526	5413	4332		
16	13068	8913	12417	1467		