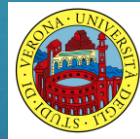


RICCIONE, 28-30 novembre 2019

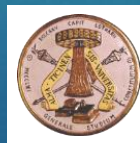


HUMAN CYTOMEGALOVIRUS AND EPSTEIN-BARR VIRUS-SPECIFIC T-CELL IMMUNITY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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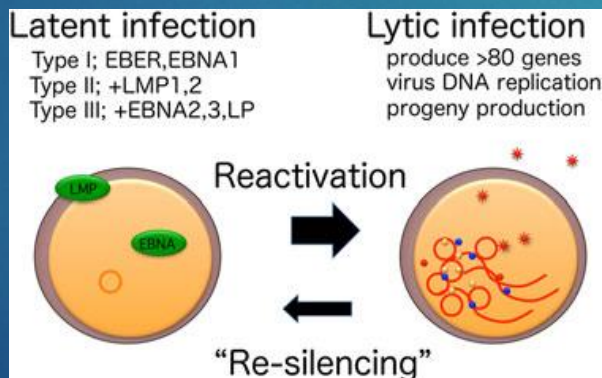
DISCLOSURES & FUNDINGS

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OPPORTUNISTIC VIRAL INFECTIONS IN IBD

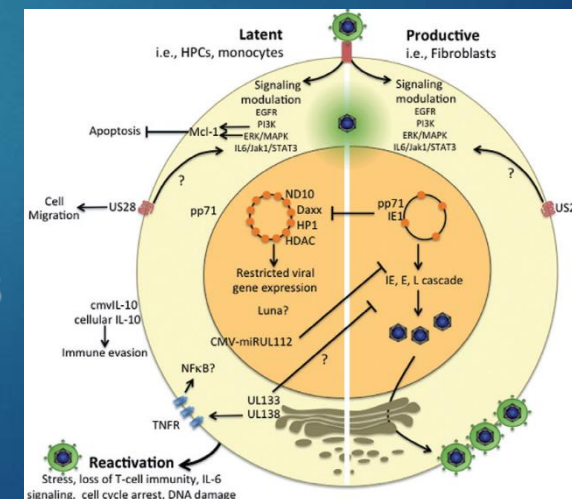
- ✓ The treatment of **inflammatory bowel diseases (IBD)**, namely ulcerative colitis (UC) and Crohn's disease (CD), relies on the use of steroids, immunosuppressants and biological agents.
- ✓ The growing use of **aggressive therapies** has led to an increased risk of opportunistic infections, including that caused by Epstein-Barr virus (EBV) and human Cytomegalovirus (HCMV).
- ✓ **EBV** and **HCMV** are Herpesviridae able to establish latency in target cells and reactivating in cases of reduced host immunity giving rise to both systemic and end-organ diseases.

Epstein-Barr virus



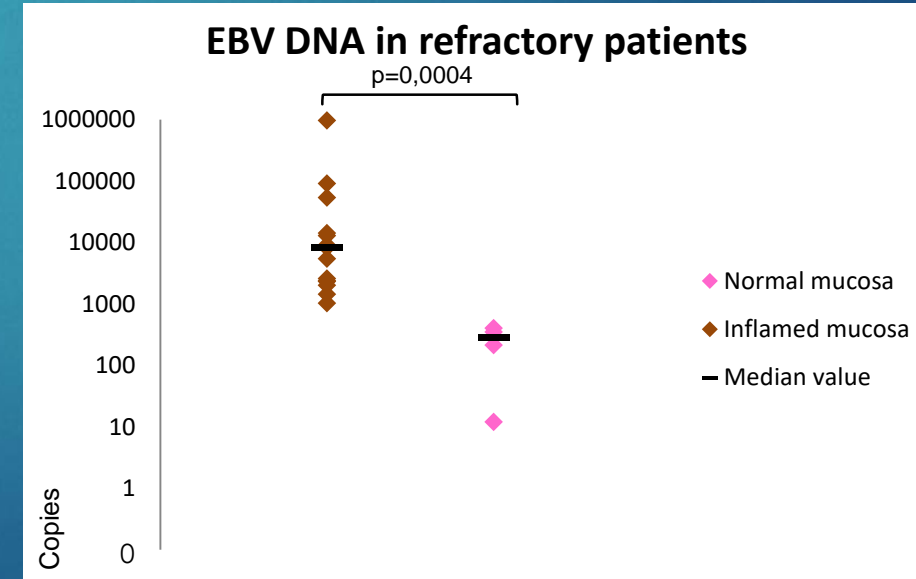
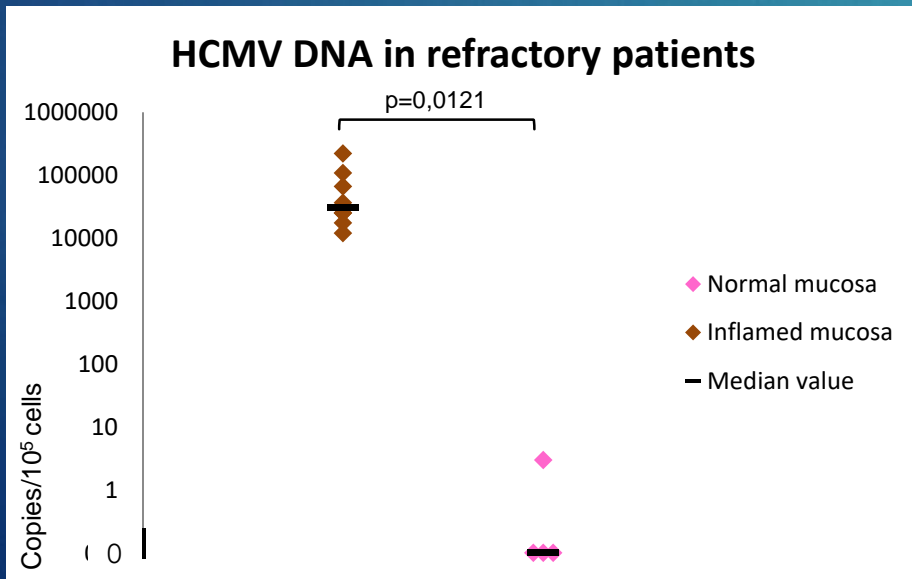
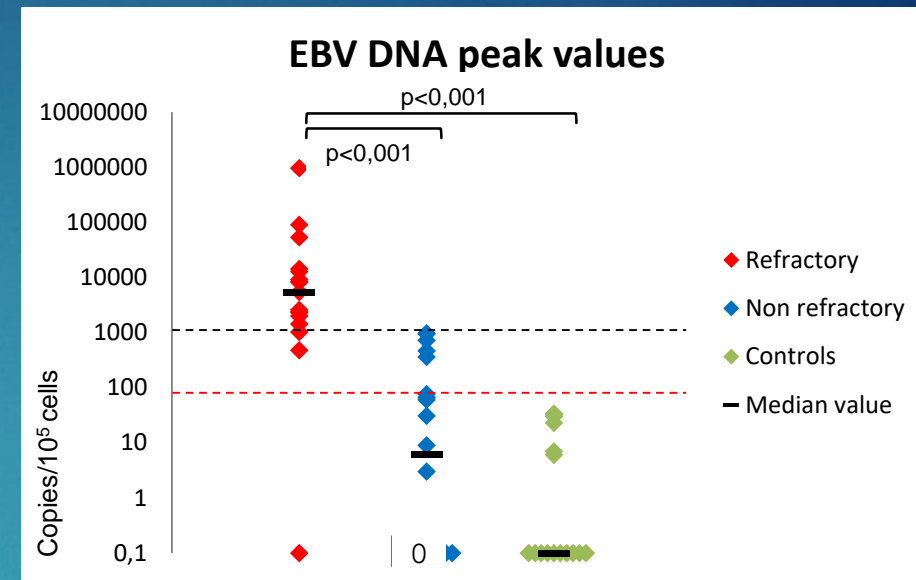
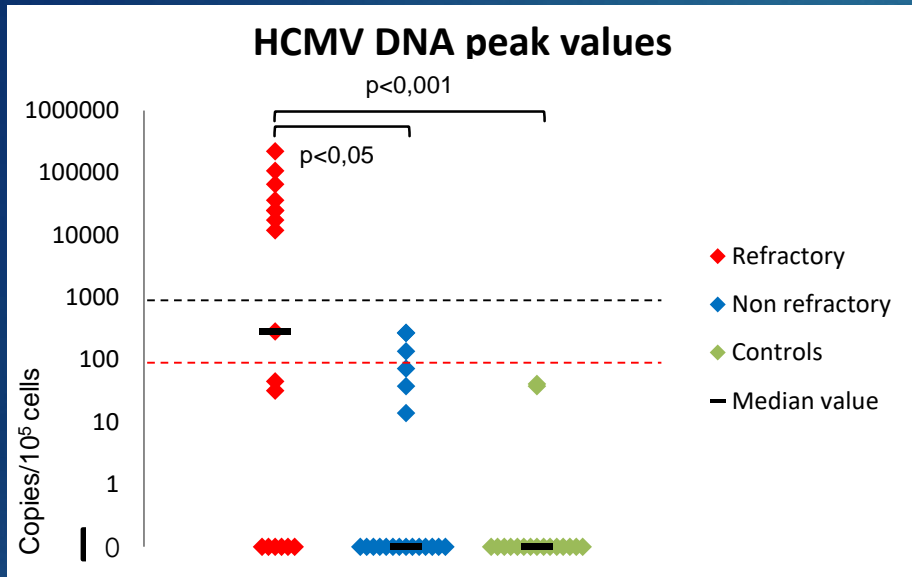
Murata T, et al. Rev Med Virol 2014

Human Cytomegalovirus



Goodrum F, et al. Cell Microbiol 2012

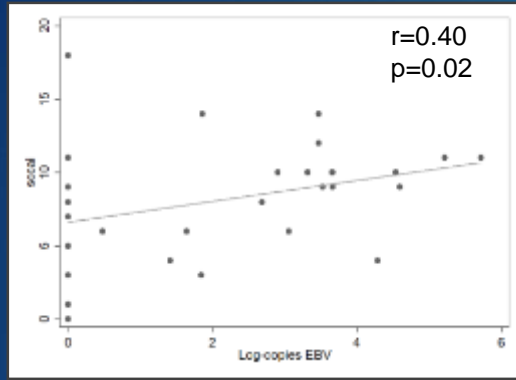
MUCOSAL VIRAL DNA LOAD IN IBD PATIENTS



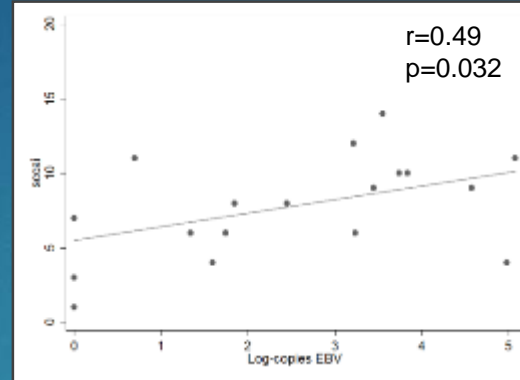
EBV LOAD CORRELATES WITH DISEASE ACTIVITY INDEXES

SCCAI

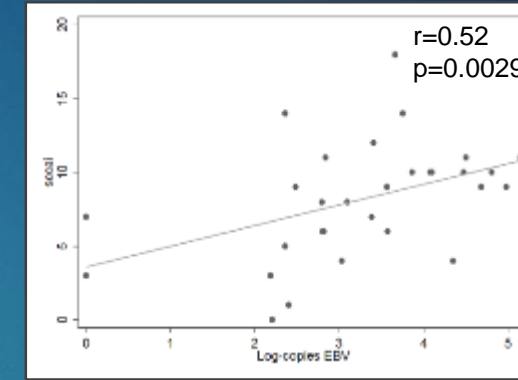
ENTEROCYTES



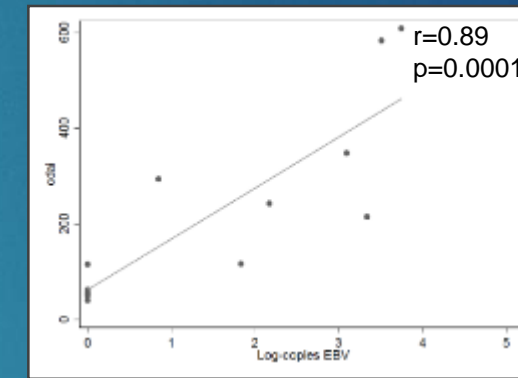
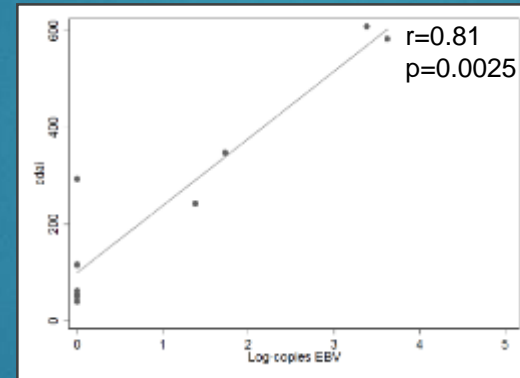
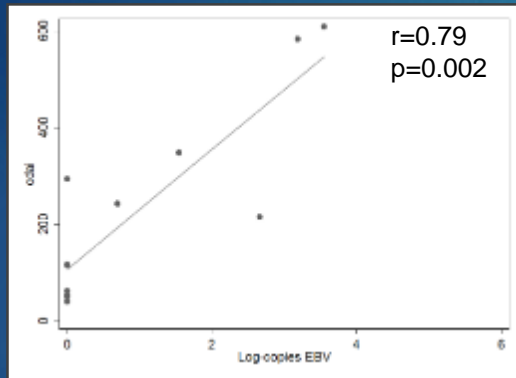
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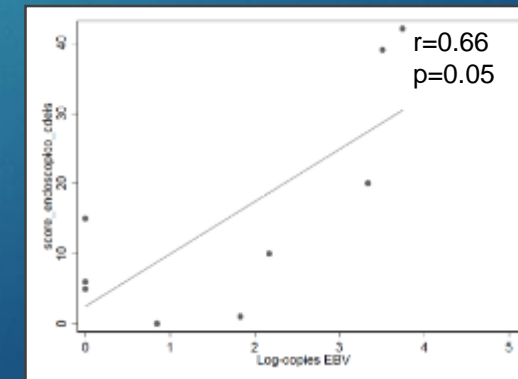
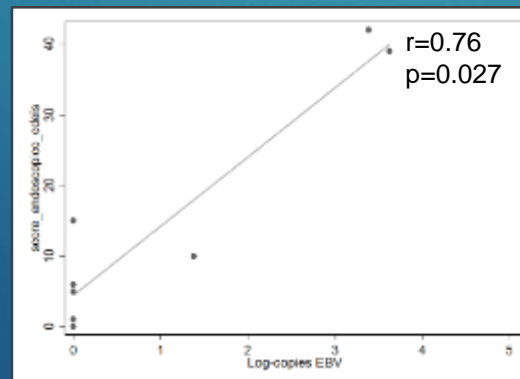
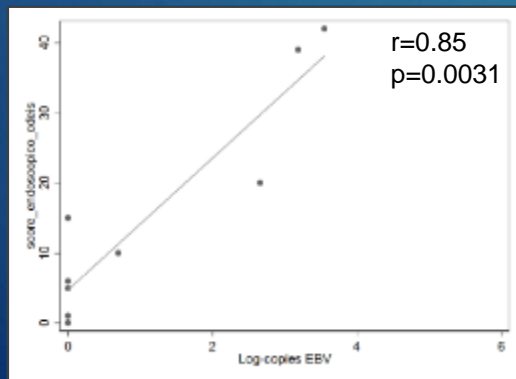
LPMCs



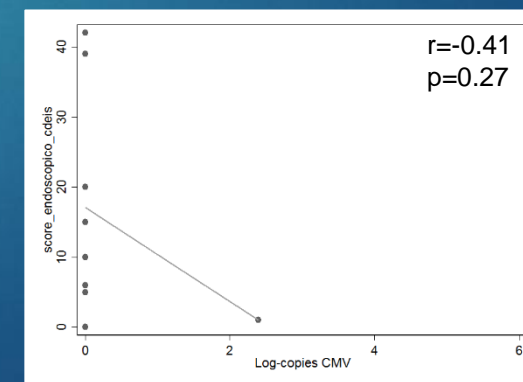
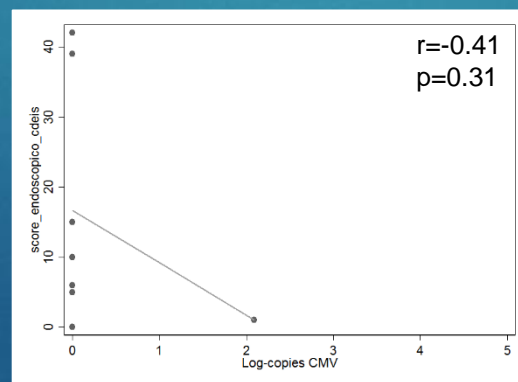
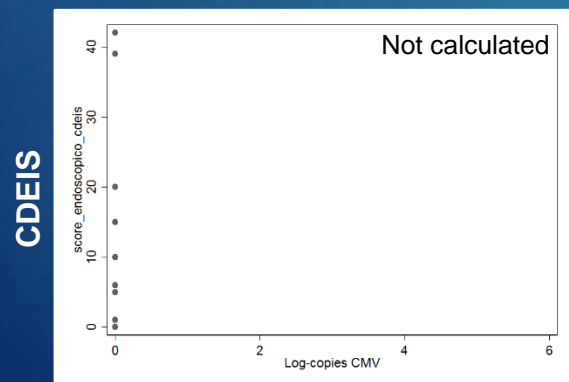
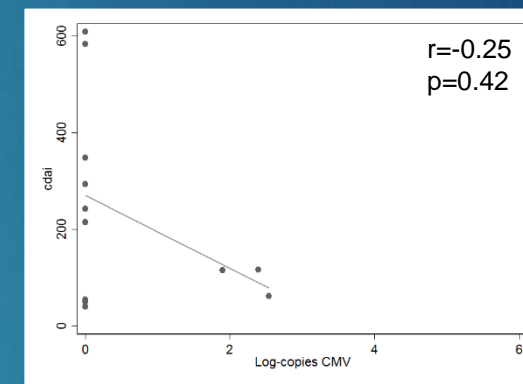
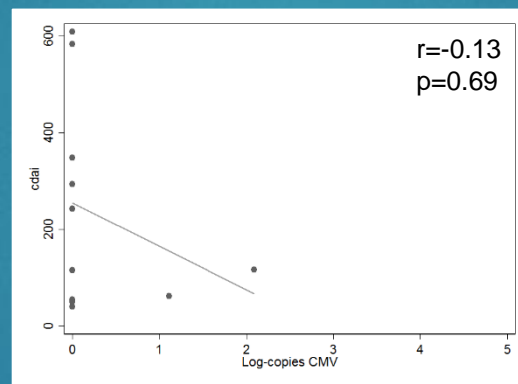
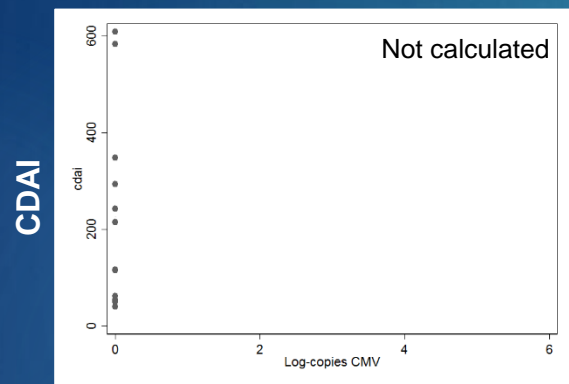
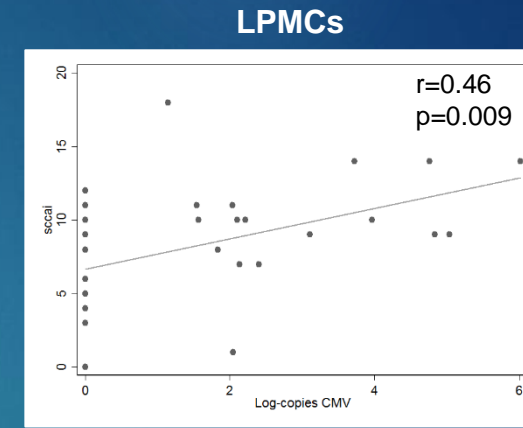
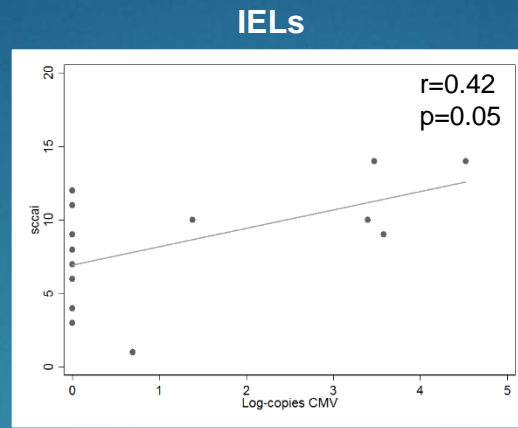
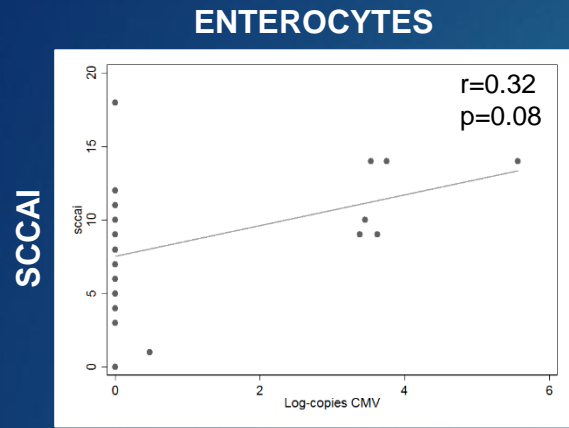
CDAI

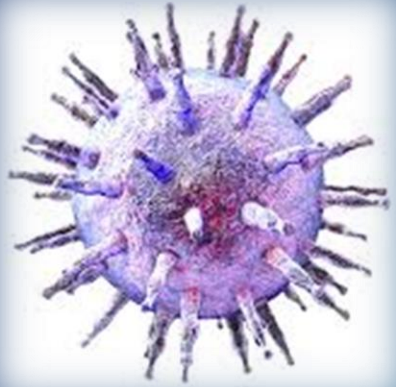


CDEIS



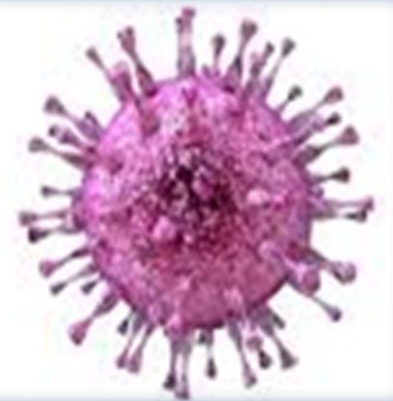
HCMV LOAD DOES NOT CORRELATE WITH DISEASE ACTIVITY INDEXES





AIM

TO EVALUATE EBV- AND HCMV-SPECIFIC T-CELL IMMUNITY IN IBD PATIENTS



METHODS: STUDY POPULATION

23 IBD PATIENTS

Age		54 ± 16	
Sex		♀ : ♂ = 6 : 17	
IBD		4 CD 19 RCU	
Response to therapy		13 responders	10 refractory
Clinical score	CDAI	120±61	p<0.05 350±60
	SCCAI	4±1	p<0.05 9±3
Endoscopic score	CDEIS	9±7	p<0.05 40±2
	UCEIS	3±1	p<0.05 8±1
Therapy	PREDN	2	2
	AZA	2	2
	Anti TNFa	2	3
	AZA+PREDN	1	-
	AZA+anti TNFa	1	2
	PREDN+anti TNFa	2	1

20 IBS PATIENTS

Age	45 ± 8
Sex	♀ : ♂ = 8 : 12

METHODS

VIRAL LOAD ASSESSMENT

✓ Immunoistochemistry



✓ PCR for HCMV- and EBV-DNA



VIRAL-SPECIFIC IMMUNITY EVALUATION



✓ Interferon- γ enzyme-linked immunospot (ELISPOT)

(Results normalized to T-cell subsets counts)

Correlation with clinical parameters

METHODS: ELISPOT ASSAY

Evaluation of EBV- and HCMV-specific T cell response



Estimation of CD4+ and CD8+ T cells capable of immediate secretion of IFN γ upon antigen stimulation

Antigens

EBV

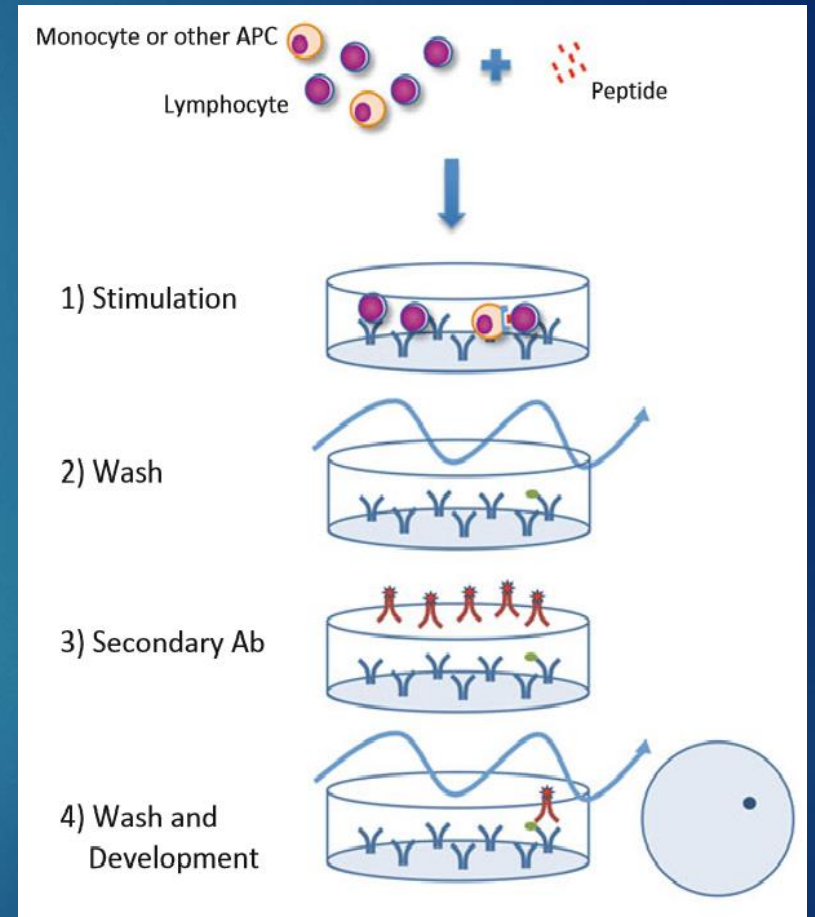
Lytic pool (BZLF1, BMRF-1)

Nuclear antigen pool (EBNA1, EBNA 3a, EBNA 3b, EBNA 3c)

Latent membrane protein (LMP) pool

HCMV

whole HCMV proteins IE-1, IE-2, pp65

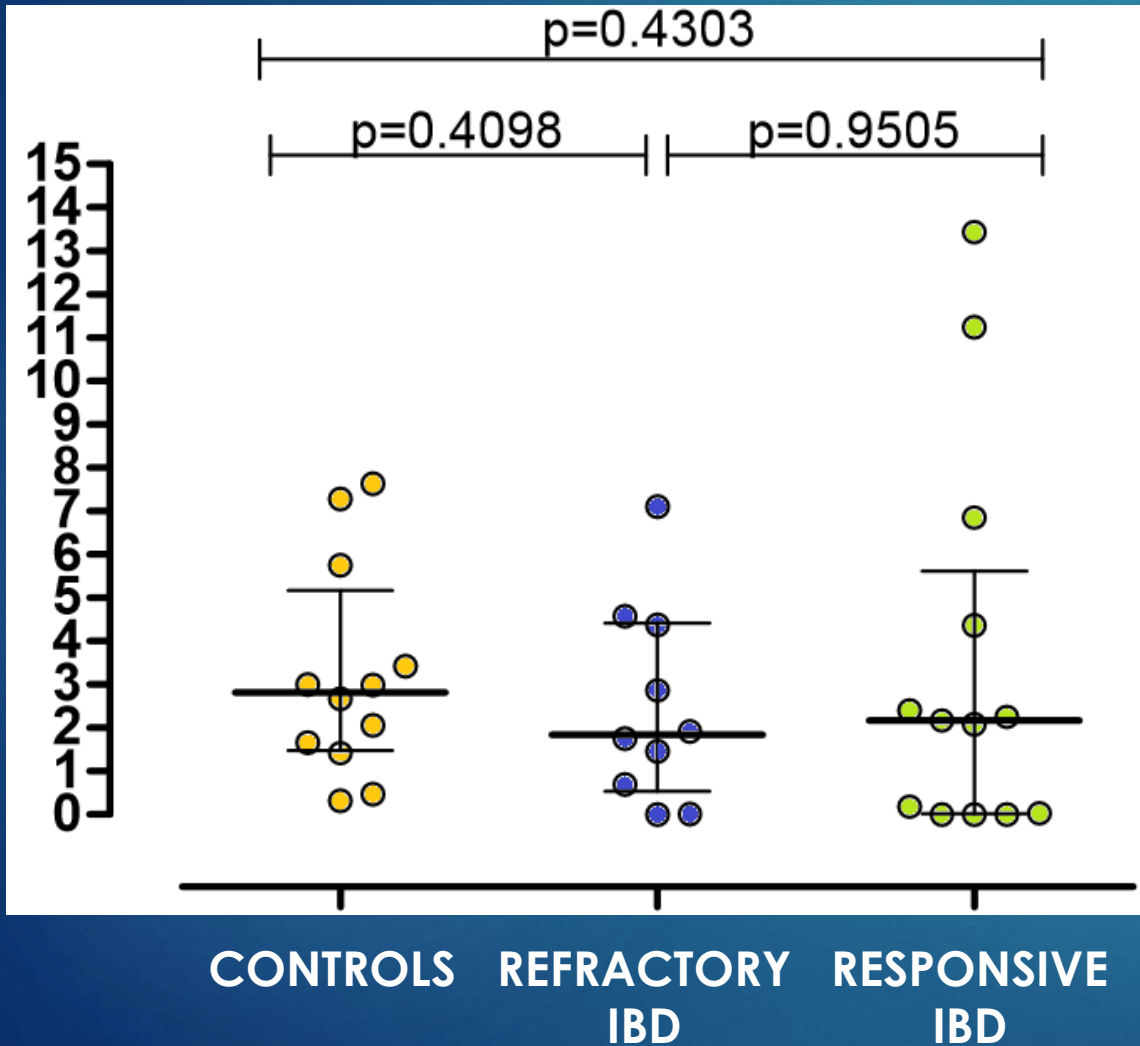


Navarrete, in *ELISA: Methods and Protocols, Methods in Molecular Biology* 2015

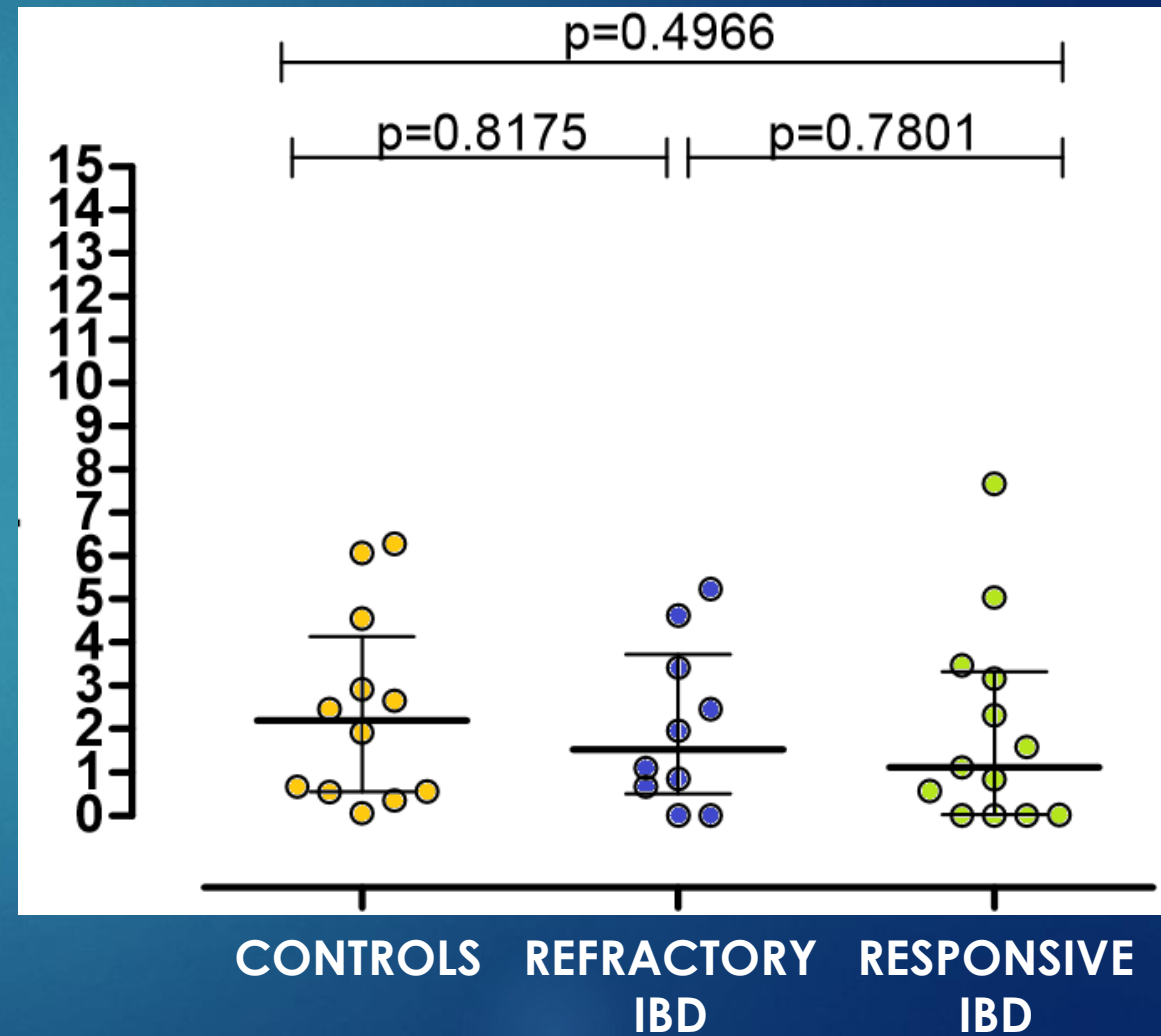
RESULTS

HCMV – SPECIFIC T-CELL RESPONSE

Normalized CMV CD4 response



Normalized CMV CD8 response

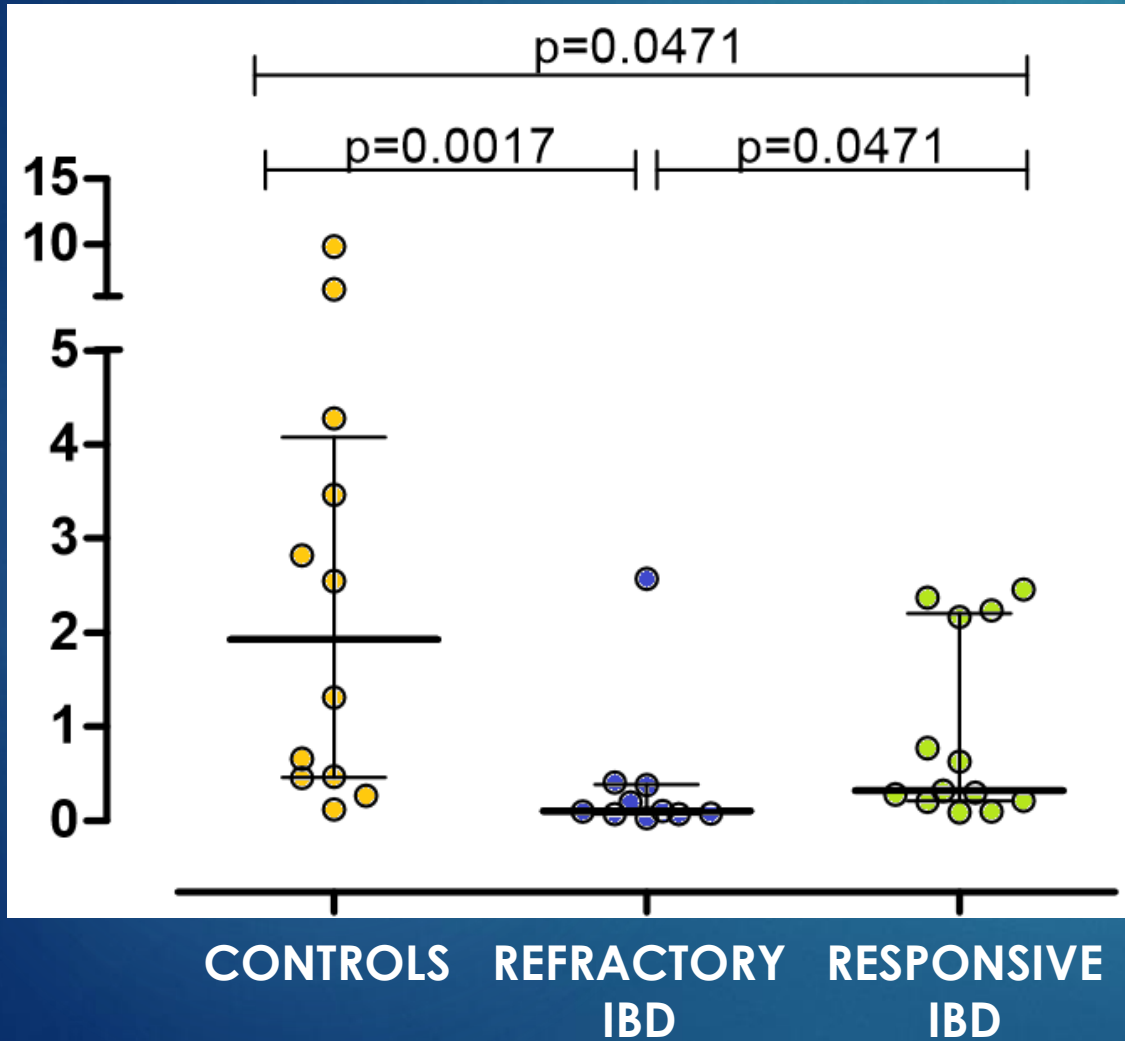


RESULTS

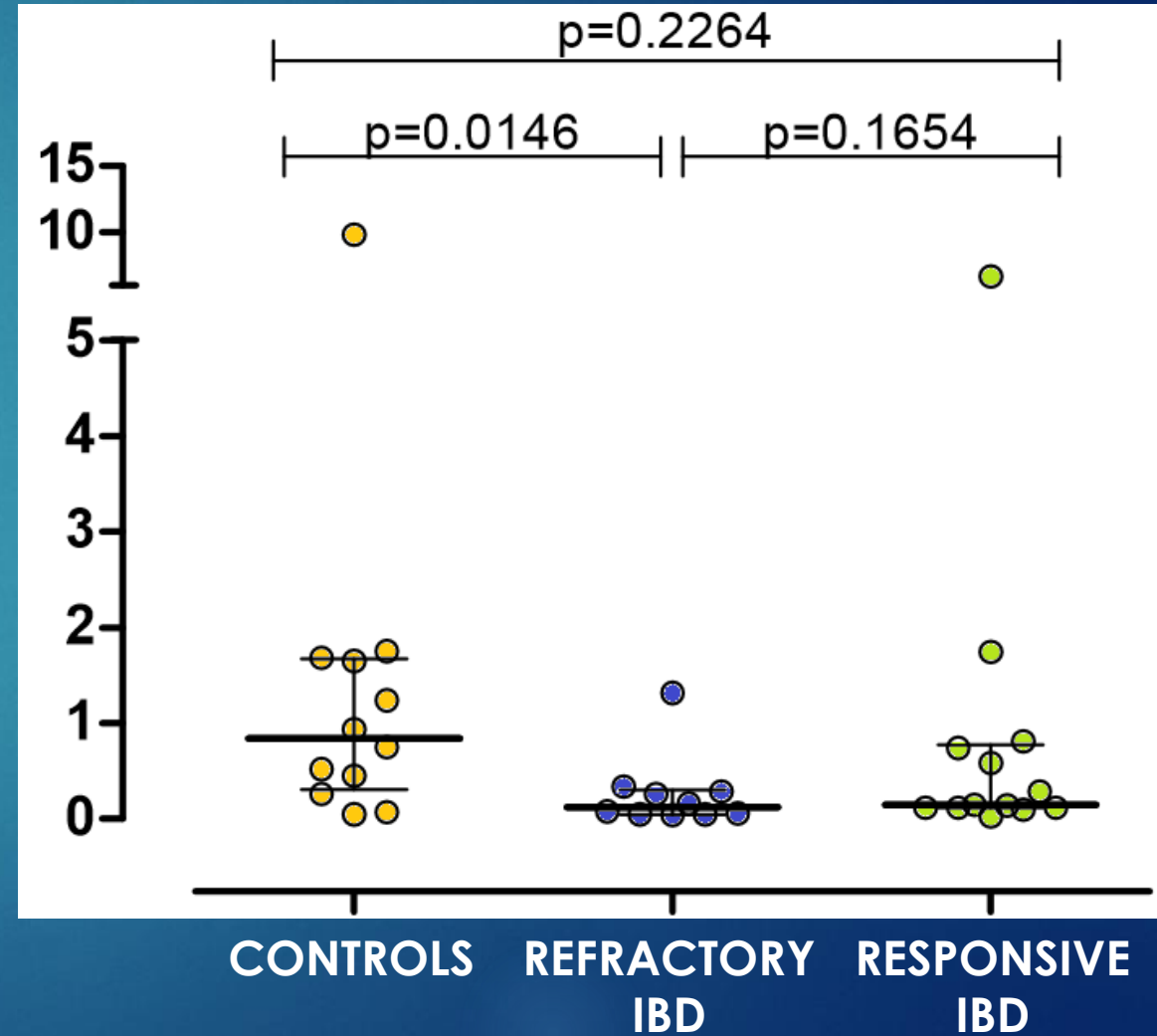
EBV – SPECIFIC T-CELL RESPONSE



Normalized EBV CD4 response



Normalized EBV CD8 response



RESULTS

- ✓ No correlation was found between CMV- and EBV-specific T cell response and clinical nor endoscopic activity scores
- ✓ No difference in CMV- and EBV-specific T cell response according to IBD therapy

CONCLUSIONS

- ✓ EBV-specific immunity is reduced in refractory IBD patients compared to responders and IBS subjects
- ✓ The ELISPOT assay represents a novel approach for quantifying and monitoring virus-specific T-cell immunity in IBD



*thank you for
your attention*