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Study of antigen-specific humoral immune responses against HCMV in patients with Psoriasis

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HCMV and Psoriasis

B. KIRBY et al (2000). Investigation of Cytomegalovirus and Human Herpes Viruses 6 and 7 as Possible Causative Antigens in Psoriasis. *Acta Derm Venereol 80*, 404-406.

•Twenty-one of 29 (72%) patients had IgG antibodies to CMV, compared with 50% in our general control population
•There was no correlation between infection with CMV, clinical severity of psoriasis and previous treatment with systemic therapy.

➢Infection with CMV is unlikely to play an important role in psoriasis pathogenesis

K. Asadullah et al (1999). A high prevalence of cytomegalovirus antigenaemia in patients with moderate to severe chronic plaque psoriasis: an association with systemic tumour necrosis factor alpha overexpression. *British Journal of Dermatology 141* , 94-102.

•CMV antigenaemia in psoriasis (43%) compared with healthy laboratory staff (12%, $P < 0.01$) and blood donors (6%, $P < 0.001$).
•Clearance of CMV antigenaemia was observed with antipsoriatic treatment.
•CMV antigenaemia was symptomless, and was associated with seropositivity for anti-CMV IgG but not IgM antibodies, indicating subclinical activation of latent infection.

➢Active, subclinical CMV infection may be of pathophysiological importance in psoriasis

HCMV and Psoriasis

Weitz Mario et al, (2011), Persistent CMV infection correlates with disease activity and dominates the phenotype of peripheral CD8+ T cells in psoriasis, Experimental dermatology. Jul;20(7):561-7

•Psoriasis severity was higher in CMV-seropositive patients and positively correlated to the severity of CMV-antigenaemia.
• In comparison to CMV-seropositive healthy controls, CMV-seropositive psoriasis patients showed a reduced frequency of circulating CMV-specific T cells that increased under effective antipsoriatic therapy.

➢Data support the concept of an interactive relationship between psoriasis and CMV infection which may be mediated by peripheral CD8+ T cells.

Aim of the study

Our aim was to systematically investigate antibody reactivity against individual HCMV antigens and to assess their clinical relevance.

Materials-Methods

➢Sera from 51 Ps and 51 matched healthy controls (HC) were tested. IgG anti-HCMV antibodies were tested by Western immunoblotting (Euroimmune AG, Germany)

Table 1. Major demographic characteristics of 51 patients with Psoriasis (Ps) and 51 healthy controls (HC).

	Ps (n=51)	**HC (n=51)**	**P** $_{\text{Ps vs HC}}$
Age	50.1 ± 14.7	47.3 ± 16.1	0.364 NS*
Sex Males Females	 27 (52.9%) 24 (47.1%)	 17 (33.3%) 34 (66.7%)	0.072 NS**
HCMV positivity	33 (64.7%)	34 (66.7%)	1.000 NS**

Age data represent mean ± standard deviation. All other data represent number of cases and corresponding percentages in brackets. *p-values were calculated using 2-tailed t-test for Equality of Means, equal variances were not assumed. **p-values were calculated using Pearson Chi-square or Fisher's Exact Test (2-sided) after correcting for continuity. Abbreviations: NS, not significant.

Materials-Methods

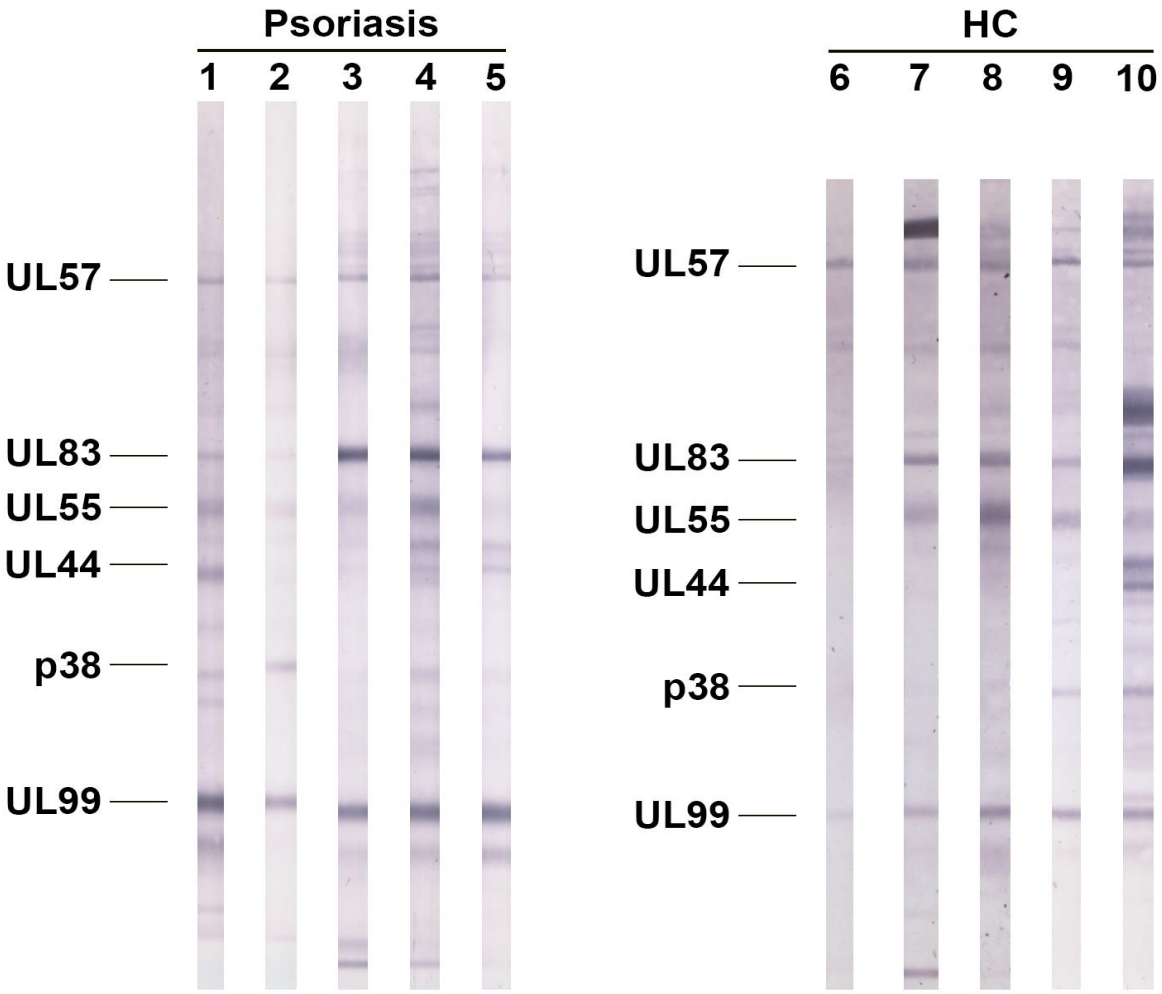


Figure 1. Antibody reactivity against HCMV antigens by Western immunoblotting in representative psoriasis (Ps, 1-5) patients and healthy controls (HC, 6-10).

Results: Frequencies

- Positivity against HCMV was found in 33 (64.7%) patients with Ps and in 34 (66.7%) HCs.
- Amongst positive individuals, antibodies against UL57 (p=<0.001) and against UL83 (p=0.006) were significantly less frequent in patients with Ps than in HCs (Figure 2).

Table 4. Frequencies of immunoreactive HCMV-specific antigens as detected by Western immunoblotting in sera of 33 anti-HCMV positive patients with Psoriasis (Ps) and 34 anti-HCMV positive healthy controls (HC).

	Ps (n=33)	HC (n=34)	$p_{\text{Ps vs HC}}$
UL57 positive	17 (51.5%)	32 (94.1%)	**<0.001**
UL83 positive	19 (57.6%)	30 (88.2%)	**0.006**
UL55 positive	16 (48.5%)	17 (50.0%)	1.000 NS
UL44 positive	6 (18.2%)	10 (29.4%)	0.429 NS
p38 positive	11 (33.3%)	10 (29.4%)	0.934 NS
UL99 positive	30 (90.9%)	31 (91.2%)	1.000 NS

Data represent number of cases and corresponding percentages in brackets. *p*-values were calculated using Pearson Chi-square or Fisher's Exact Test (2-sided) after correcting for continuity. Underlined *p*-values correspond to higher frequency in the control group. *p-values* <0.05 are shown in bold; *p*-values with a statistical tendency (<0.100) are also shown. Abbreviations: NS, not significant.

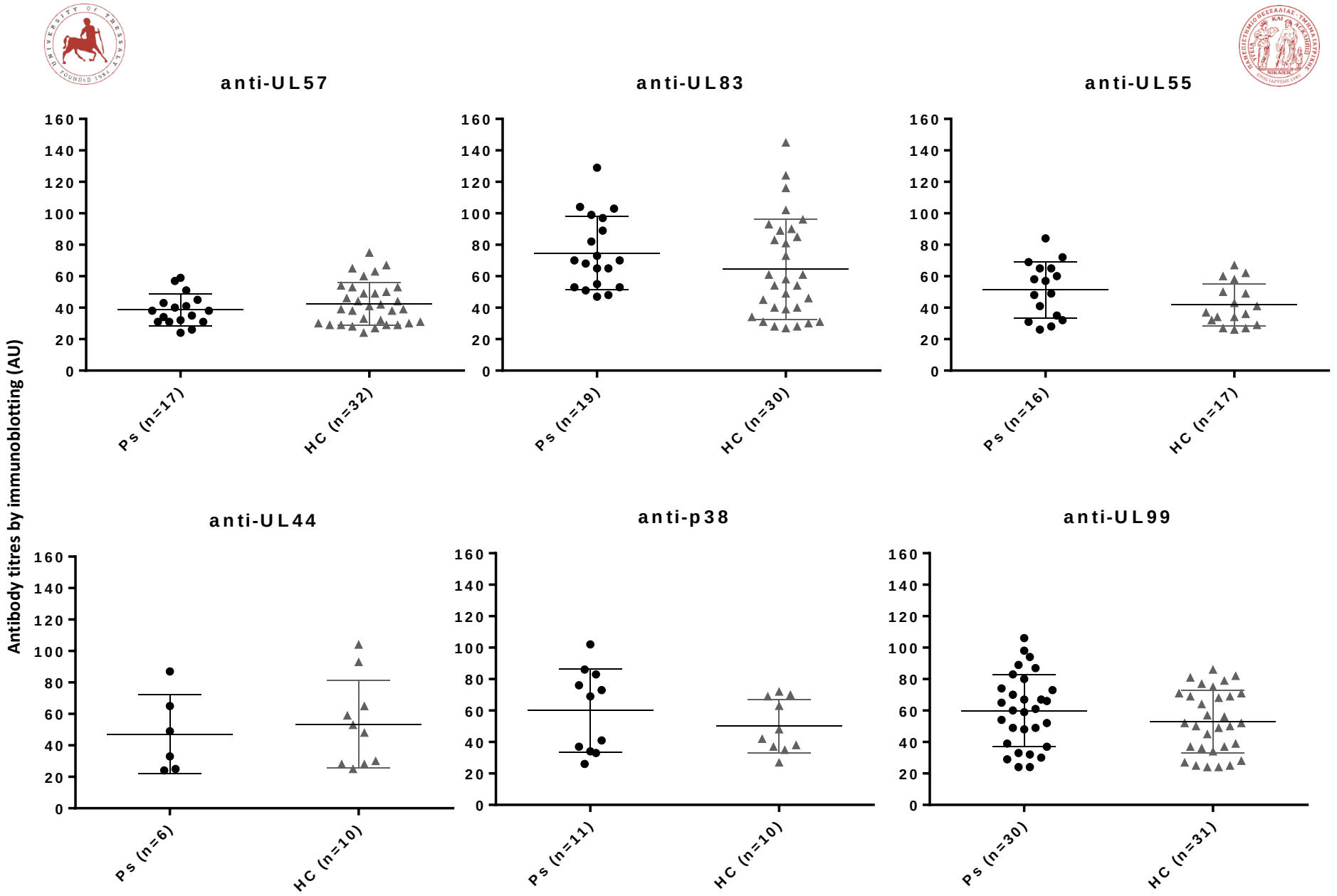
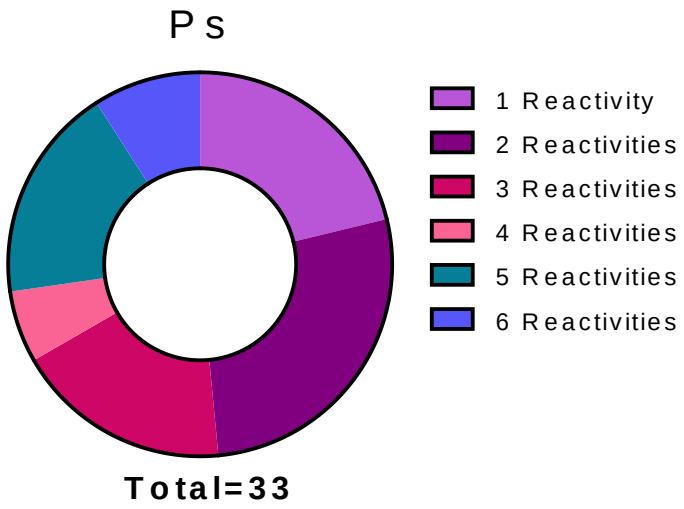
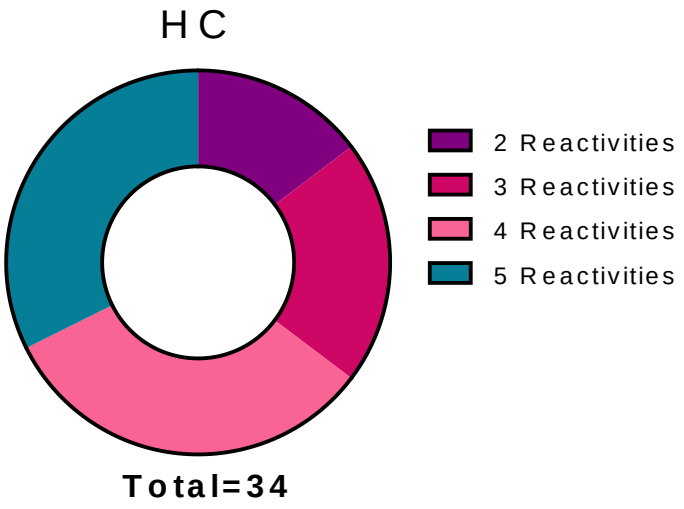


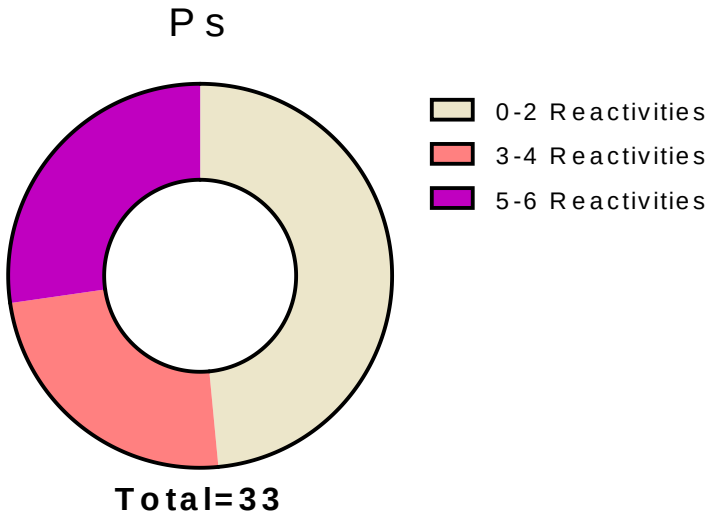
Figure 2. Scatter plots illustrating antibody titres by Western immunoblotting against individual HCMV antigens in sera of psoriasis (Ps) patients and healthy controls (HC).

*mean with SD

Results: Reactivities







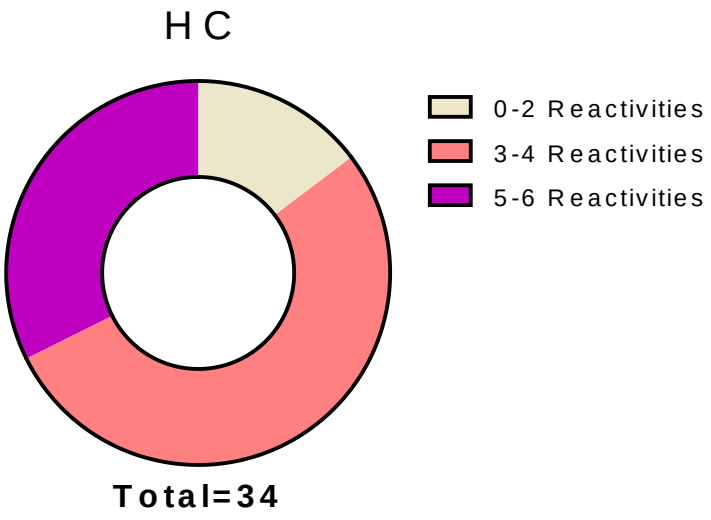


Figure 3 . Pie charts illustrating the proportion of serum samples of anti-HCMV 33 positive patients with psoriasis and 34 anti-HCMV positive healthy controls (HC) that were reactive with multiple HCMV antigens UL57, UL83, UL 55, UL44, p38 and UL99.

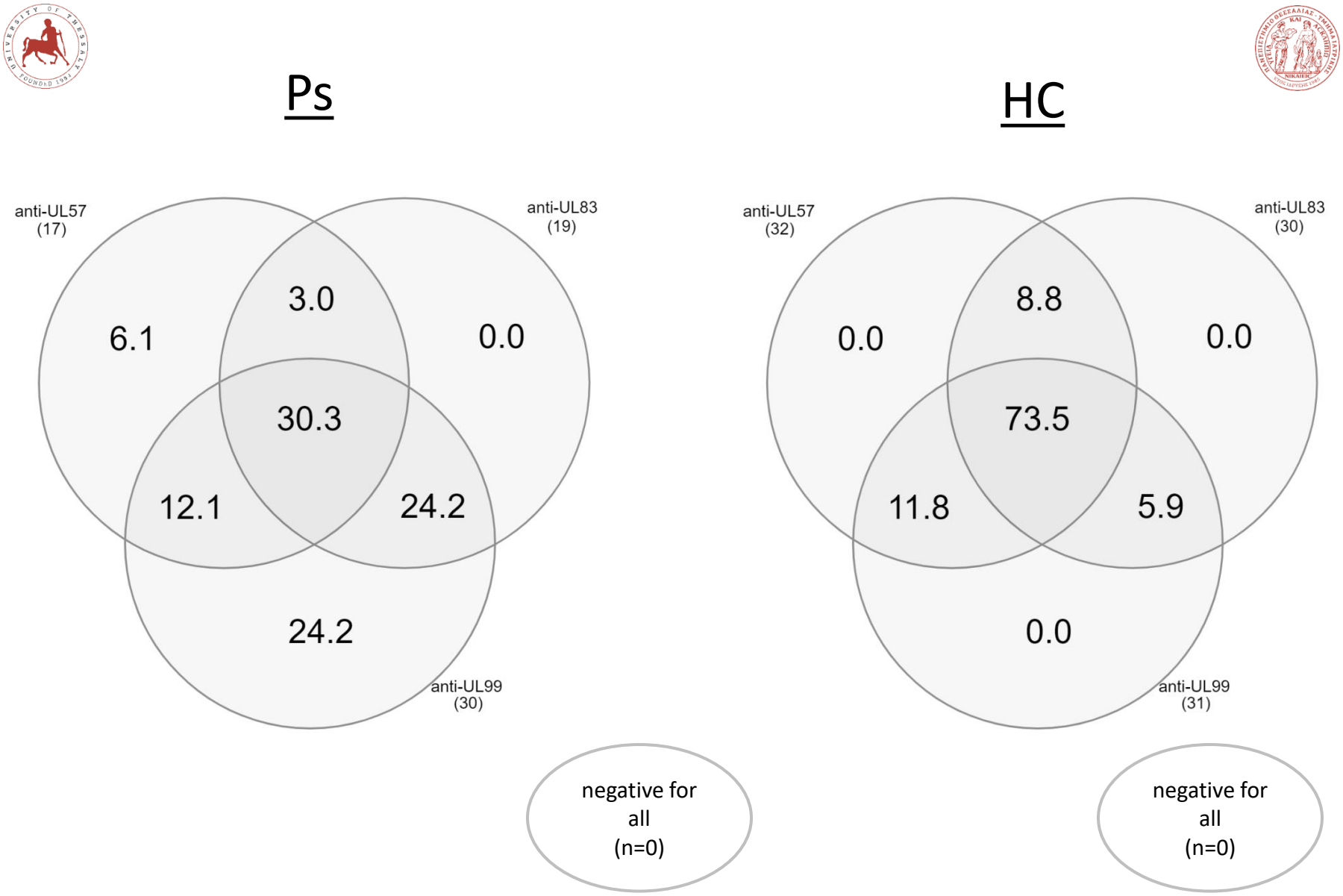


Figure 4. Venn diagrams illustrating the patterns of anti-UL57, anti-UL83 and anti-UL99 overlapping reactivities in anti-HCMV positive patients with psoriasis and healthy controls

Results: Correlations

Table 6. Correlations of anti-Human cytomegalovirus (HCMV) antigen reactivities and clinical features of the disease with other anti-HCMV antigen reactivities and clinical features of the disease in sera of 33 HCMV(+) patients with psoriasis (Ps).

		Ηλικία	Ηλικία έναρξης νόσου	Διάρκεια νόσου	PASI	UL57	UL83	UL55	UL44	p38	UL99
Ηλικία	R	1	0.615	0.435	-0.053	0.321	0.315	0.151	0.347	0.154	0.228
	p		**<0.001**	**0.013**	0.779 ns	0.069	0.074	0.402 ns	**0.048**	0.393	0.202
	N	33	32	32	31	33	33	33	33	33	33
Ηλικία έναρξης νόσου	R		1	-0.442	-0.074	0.414	0.421	0.167	0.289	0.373	0.495
	p			**0.011**	0.691 ns	**0.019**	**0.016**	0.361 ns	0.109 ns	**0.035**	**0.004**
	N		32	32	31	32	32	32	32	32	32
Διάρκεια νόσου	R			1	0.027	-0.094	-0.091	-0.009	0.088	-0.228	-0.285
	p				0.886 ns	0.608 ns	0.621 ns	0.962 ns	0.633 ns	0.209 ns	0.115 ns
	N			32	31	32	32	32	32	32	32
PASI	R				1	0.268	0.003	0.351	0.046	0.003	0.023
	p					0.145 ns	0.989 ns	0.053	0.808 ns	0.989 ns	0.904 ns
	N				31	31	31	31	31	31	31
UL57	R					1	0.333	0.426	0.509	0.471	0.185
	p						0.058	**0.014**	**0.002**	**0.006**	0.302 ns
	N					33	33	33	33	33	33
UL83	R						1	0.229	0.688	0.284	0.501
	p							0.199 ns	**<0.001**	0.109 ns	**0.003**
	N						33	33	33	33	33
UL55	R							1	0.253	0.376	0.340
	p								0.156 ns	**0.031**	0.053
	N							33	33	33	33
UL44	R								1	.451	0.285
	p									**0.008**	0.108 ns
	N								33	33	33
p38	R									1	0.513
	p										**0.002**
	N									33	33
UL99	R										1
	p										
	N										33

R represents Pearson's correlation coefficient. p represent *p* value (2 tailed) associated with the correlation. *p*-values <0.05 are shown in bold; *p*-values with a statistical tendency (<0.100) are also shown.
Abbreviations:

Conclusion

- Significant differences in the prevalence of responses against HCMV is evident between Ps and healthy individuals as antibodies against UL57 and UL83 were more frequent in healthy controls suggesting a protective role.

- Responses to UL57 ($p=0.019$), UL83($p=0.016$), p38 ($p=0.035$) and UL99 ($p=0.004$) correlated with age at onset. No correlation was found between the presence of anti-HCMV antibodies and other clinical features of the disease.