

Multi-center evaluation of autoantibodies to the major ribosomal P epitope C22

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Background: Anti-ribosomal P autoantibodies (aabs) represent a specific serological marker in the diagnosis of systemic lupus erythematosus (SLE). The major autoreactivity of anti-Rib-P aabs has been localized to the C-terminal region, which shows high degree of identity on all three Rib-P antigens (P0, P1 and P2).

Objective: To evaluate the prevalence of aabs to the major ribosomal P antigen C22 in SLE patients and various controls by a multi-center approach and to shed more light on the reported association between anti-C22 aabs and clinical features in SLE patients.

Methods: Sera collected from SLE patients and various controls were tested for anti-C22 aabs by ELISA (Dr. Fooke). SLE activity index (SLEDAI) was calculated for each patient in two centers (Israel and Berlin). Aab profiles were generated for the SLE samples from Canada using two profile assays (recomLine ANA/ENA, Mikrogen, Neuried, Germany; QuantaPlex INOVA; CA, US). Results were statistically evaluated.

Results: Using the recommended cut-off value (1.5 RU), sensitivities and specificities ranged between 10.7% and 29.0% and between 98.1% and 100.0%, respectively.

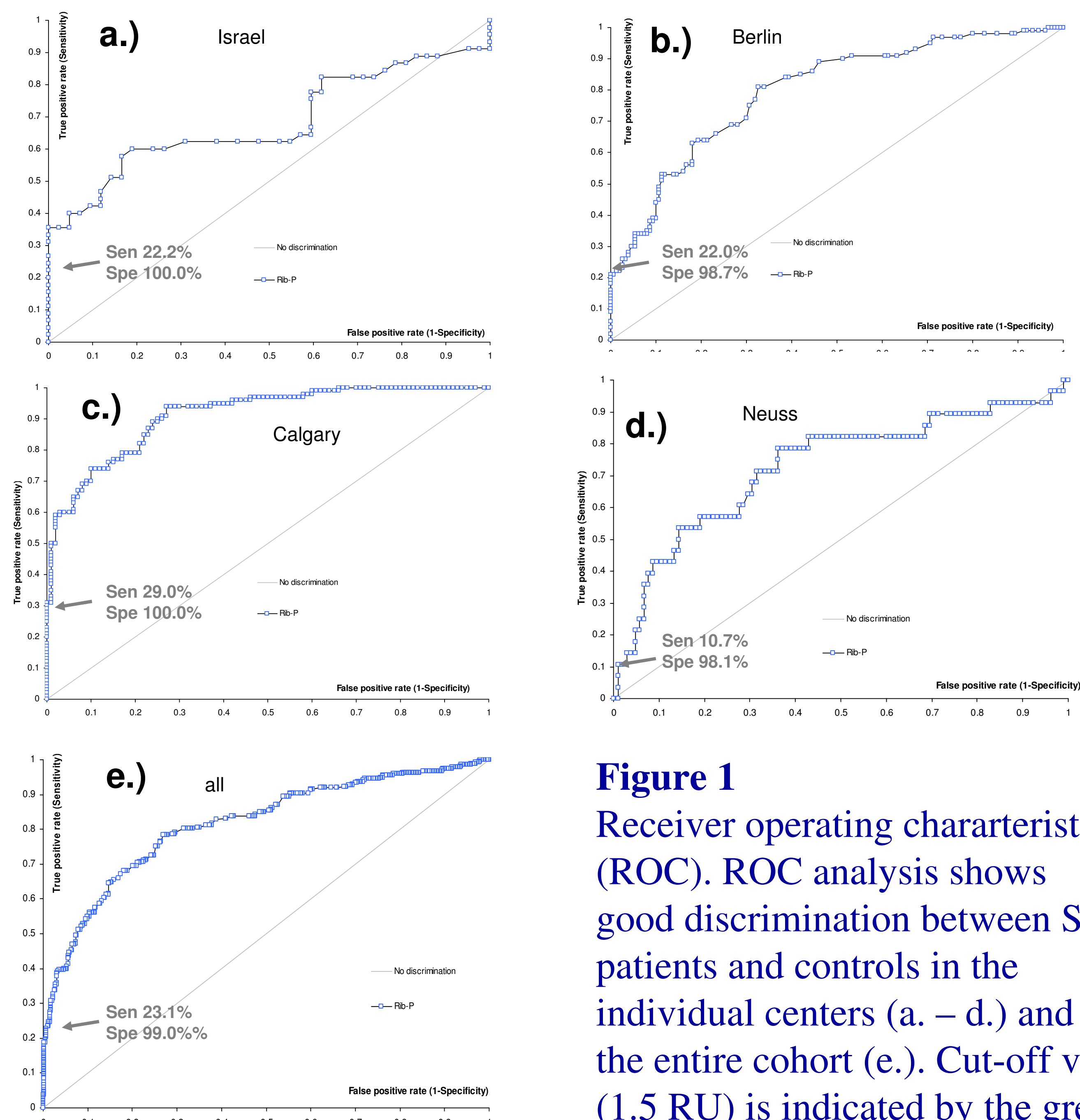


Figure 1 Receiver operating characteristics (ROC). ROC analysis shows good discrimination between SLE patients and controls in the individual centers (a. – d.) and for the entire cohort (e.). Cut-off value (1.5 RU) is indicated by the grey arrows and corresponding sensitivities and specificities are provided.

In the controls, anti-C22 aabs were rarely detectable and the titre in the individual groups statistically relevant variations (see Fig 2). Overall sensitivity and specificity was 23.1% and 99.0%, respectively. Prevalence of other aabs was higher in the group of anti-C22 positive samples such as anti-Chromatin or anti-Sm, but the differences were not significant. Anti-C22 aabs were associated with decreased C3/C4 levels, but not with other serological or clinical features. Moderate association between anti-C22 aabs and SLEDAI score was observed in Israel ($p=0.02$).

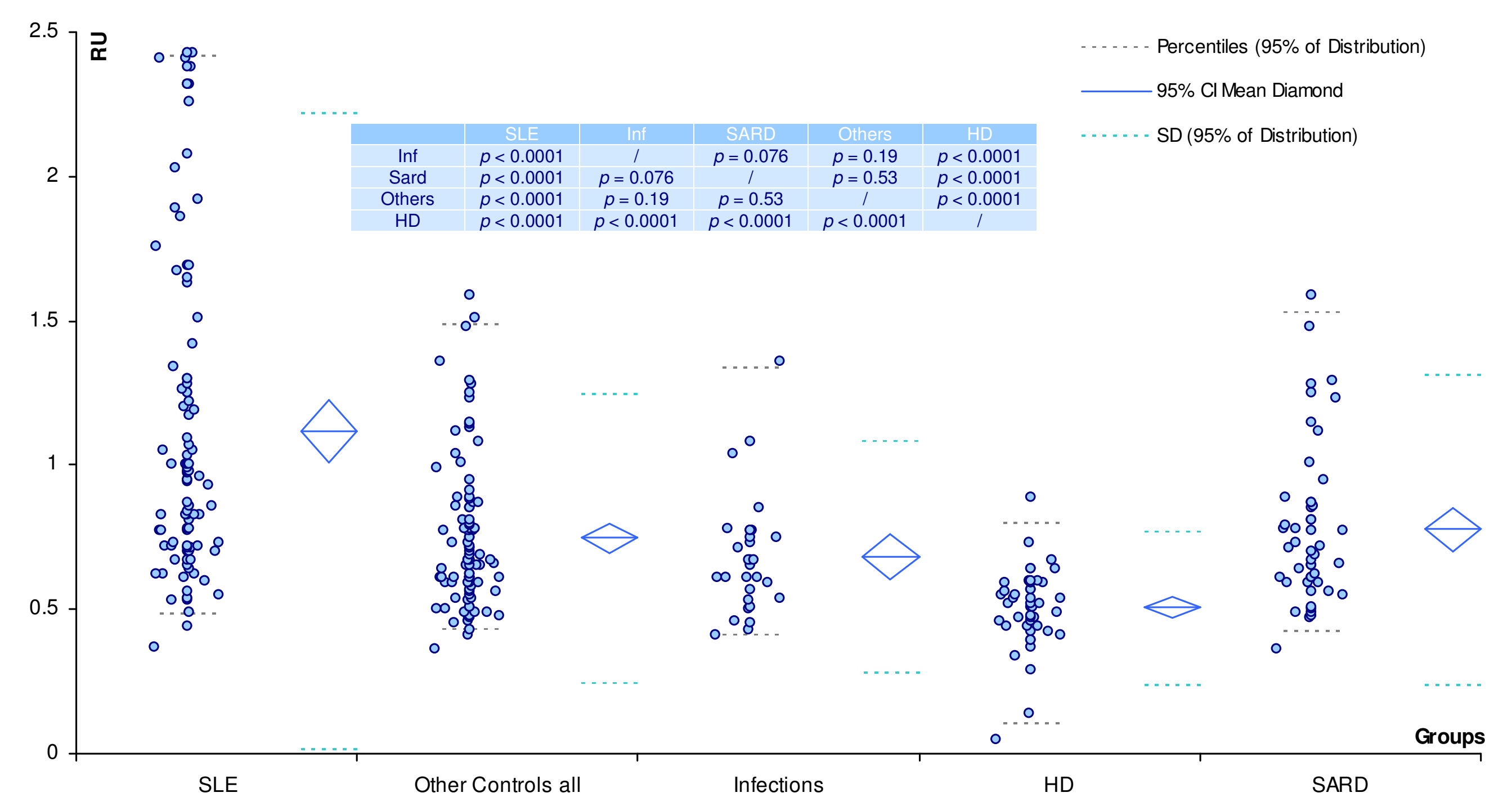


Figure 2 Comparative descriptive analysis of the Berlin cohort. Differences between groups were analysed by Student's t-test (see Table in Figure). Control groups: Other controls all (n=100, all controls except healthy donors), infections (n=39, HCV, HBV, HIV), systemic autoimmune rheumatic diseases (n=48, SARD), healthy donors (n=50, HD).

Table 1 Prevalence of anti-C22 antibodies in various diseases

Group	Berlin	Israel	Canada	Neuss	All
SLE	22/100 (22%)	10/45 (22.2%)	29/100 (29%)	3/28 (10.7%)	64/273 (23.1%)
HD	0/50 (0%)	0/42 (0%)	0/43 (0%)	n.d.	0/135 (0%)
SSc	0/14 (0%)	n.d.	0/15 (0%)	0/4 (0%)	0/33 (0%)
RA	0/23 (0%)	n.d.	0/23 (0%)	0/14 (0%)	0/60 (0%)
SjS	0/6 (0%)	n.d.	0/13 (0%)	0/7 (0%)	0/26 (0%)
MCTD	1/4 (25%)	n.d.	n.d.	0/4 (0%)	0/8 (0%)
Overlaps	n.d.	n.d.	0/6 (0%)	0/5 (0%)	0/11 (0%)
HIV	0/10 (0%)	n.d.	n.d.	n.d.	0/10 (0%)
HBV	0/10 (0%)	n.d.	n.d.	n.d.	0/10 (0%)
HCV	0/10 (0%)	n.d.	n.d.	n.d.	0/10 (0%)
Colitis ulcerosa	1/11 (9.1%)	n.d.	n.d.	n.d.	1/11 (9.1%)
Borreliosis	0/9 (0%)	n.d.	n.d.	n.d.	0/9 (0%)
Spondylitis ankylosans	n.d.	n.d.	n.d.	0/13 (0%)	0/13 (0%)
Psoriatic arthropathy	n.d.	n.d.	n.d.	0/21 (0%)	0/21 (0%)
Polymyalgia rheumatica	n.d.	n.d.	n.d.	0/15 (0%)	0/15 (0%)
PBC	0/2 (0%)	n.d.	n.d.	0/3 (0%)	0/5 (0%)
WG	n.d.	n.d.	n.d.	0/3 (0%)	0/3 (0%)
Others	0/1 (0%)	n.d.	n.d.	1/16 (6.3%)	1/17 (xxx)
Controls all	2/150 (1.3%)	0/42 (0%)	0/100 (0%)	2/105 (1.9%)	4/397 (1.0%)
Sensitivity	22%	22.2%	29%	10.7%	23.1%
Specificity	98.7%	100%	100%	98.1%	99.0%
AUC	0.80	0.68	0.91	0.73	0.81

Conclusion: Anti-C22 aabs are frequently found in SLE with high disease specificity. Although association between anti-C22 reactivity and SLEDAI score was observed in one center, anti-C22 are not appropriate for measuring global disease activity. The lack of association between anti-C22 aabs and reported clinical manifestations remains a matter of further research.