Anti-CENP-A and CENP-B antibodies in SLE

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Background: Anti-centromere antibodies (ACA) are a serological marker for the diagnosis of systemic sclerosis (SSc). Recently it has been shown that a CENP-A peptide (patent pending) used in ELISA represents a reliable analyte in the detection of ACA. In SSc, the sensitivity of the CENP-A peptide ELISA was comparable to CENP-B recombinant protein ELISA. Testing the control groups surprisingly showed that the specificity of the CENP-A ELISA in SLE control groups was much higher compared to CENP-B ELISA. Therefore the CENP-A peptide seems to be a more specific marker for the discrimination of SLE and SSc. This is of special interest considering the overall prevalence of SLE and SSc in the population: SLE is 100 fold more prevalent as SSc, i.e. the number of ACA pos SLE sera is higher than the number of ACA pos SSc sera. The aim of this study was to analyse the prevalence of anti-CENP-A peptide antibodies and anti-CENP-B antibodies in SLE.

Methods: Sera from SLE patients (n=455) were tested for anti-nuclear antibodies (ANA) by indirect immunofluorescence on HEp-2 cells (ImmunoConcepts). Sera with a centromere staining pattern were further analysed by CENP-A and CENP-B ELISA as well as by a line immunoassay (LIA) with recombinant CENP-B (recomLine Scleroderma IgG, Mikrogen, Neuried, Germany).

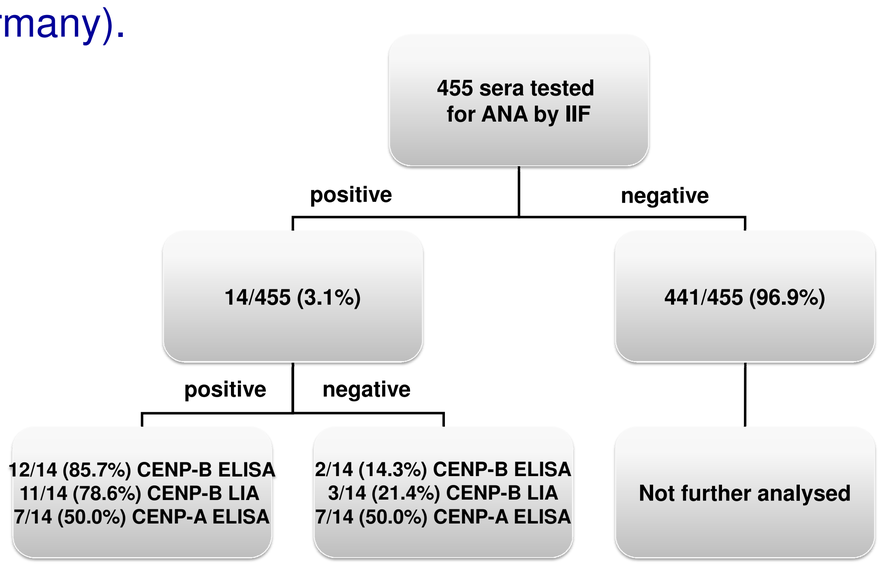

Figure 1 Test scheme of SLE sera analyzed for anti-centromere antibodies

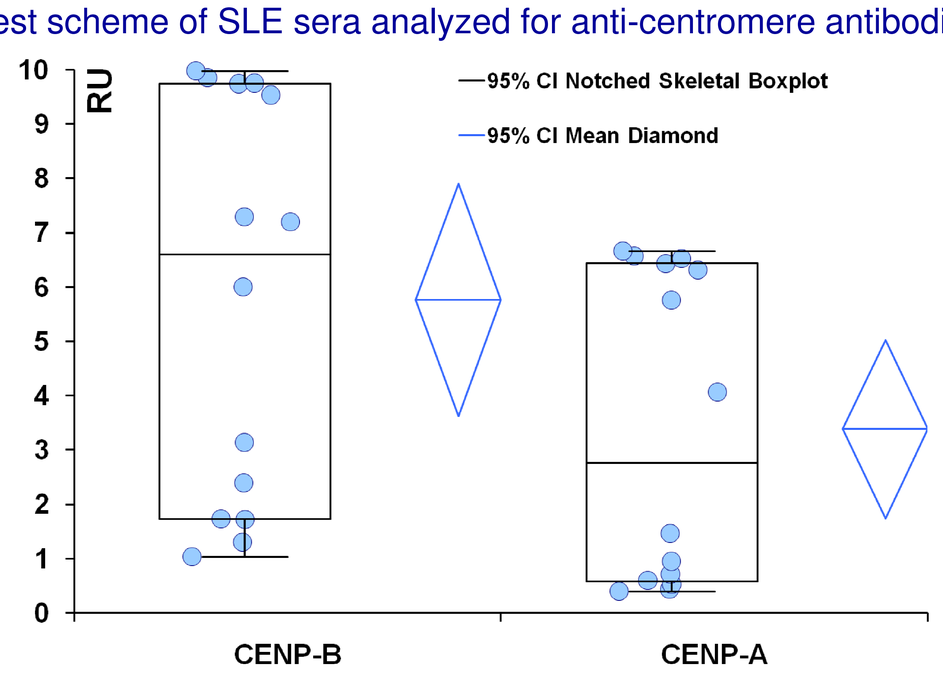

Figure 1 Descriptive-Comparative Analysis of CENP-A and CENP-B ELISA results. Only 50% of the ACA pos samples tested positive in CENP-A ELISA; CENP-A allows for far better discrimination of SLE vs. SSc

Results: 14/455 (3.1%) sera displayed a CENP staining pattern in IIF. Of those 12/14 (85.7%) were positive by CENP-B ELISA, 11/14 (78.6%) by CENP-B LIA and 7/14 (50.0%) by CENP-A ELISA. All (7/7) anti-CENP-A positive sera were also positive for anti-CENP-B by ELISA and LIA. The titre of anti-CENP-B antibodies measured by ELISA was significantly higher in the CENP-A positive group than in the CENP-A negative group (p=0.0030). Quantitative comparison showed a significant correlation between the CENP-A and CENP-B ELISA results according to the Spearman test (p=0.0027; r=0.74).

Table 1 Results of IIF cenp pos. SLE Sera in different Test systems (CENP A+B ELISA CENP-B LIA and IIF)

Samples ID	CENP-B ELISA [RU]	CENP-A ELISA [RU]	CENP-B LIA	IIF
17-0736	9.7	6.7	3+	3-4+
17-0876	1.7	0.4	negative	3+
17-1085	2.4	6.4	2+	2-3+
17-0600	1.0	0.6	negative	1-2+
17-0783	7.3	6.3	3+	3+
17-1135	1.7	0.4	1+	1-2+
17-0532	3.1	0.5	1+	2-3+
17-1147	10.0	6.5	4+	4+
17-1183	6.0	1.5	3+	2+
19-0127	9.5	4.1	3+	1-2+
260	7.2	0.7	3+	3-4+
311	9.9	5.8	3+	2-3+
619	1.3	0.9	negative	1-2+
869	9.7	6.6	3+	3+

Conclusion: This study confirms that CENP-B is more frequently targeted by autoantibodies in ACA positive SLE than the CENP-A peptide. Therefore, anti-CENP-A peptide antibodies are the more specific marker for the serological discrimination between SSc and SLE than anti-CENP-B antibodies.The two ACA positive sera that were negative for anti-CENP-A and anti-CENP-B antibodies may contain antibodies to other CENP antigens (e.g. CENP-C). Additional investigations are needed to address that question. After further confirmatory studies, CENP-A peptides should be considered as the antigen of choice for the detection of ACA in SSc. Considering the fact that SLE is approximately 100 times more prevalent than SSc, the number of anti-CENP-B positive anti-CENP-A negative SLE patients is 2-3 orders of magnitude higher than the prevalence of ACA in SSc. The anti-CENP-A Peptide ELISA offers highly increased specificity at a sensitivity comparable to CENP-B Protein ELISA kits.

presented at: **7th International Congress on Autoimmunity Ljubljana 2010**

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