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EliA Symphony^S – the first fully automated random access assay using only recombinant human antigens and a synthetic SmD peptide to screen for autoantibodies against extractable nuclear antigens (ENA)

Gerben Zuiderveld[1], Jérémie Gautier[2], Christian Konrad[1] and Stephan Giesler[1]
[1]Thermo Fisher Scientific, Freiburg, Germany; [2]Cerba Xpert, Saint-Ouen l'Aumône, France

BACKGROUND

Connective tissue diseases (CTDs) are a group of closely related multisystem conditions with many similar clinical features. The diverse and overlapping symptoms, particularly early in the course of the disease, make diagnosis challenging [1, 2]. The screening of patients for autoantibodies against the so-called extractable nuclear antigens (ENA), a subset of antinuclear autoantibodies (ANA), are an important aid in the diagnosis of CTDs, e.g. Sjögren's Syndrome (SjS), Systemic Lupus Erythematosus (SLE), Systemic Sclerosis/Scleroderma (SSc), Poly-/Dermatomyositis (PM/DM) and Mixed Connective Tissue Disease (MCTD) [1].

Solid phase assays are available to screen patients for autoantibodies against ENAs. These assays have a high specificity to minimize false positive test results but also include antigens, e.g. Ro52 and Jo-1, to detect antibodies that have been reported to be frequently missed by immunofluorescence assays (IFA) [2]. Current ENA screening assays differ in antigen composition and the sources of the antigens used. The recently developed EliA™ Symphony^S† is a screening assay for autoantibodies against ENA (U1RNP, SS-A/Ro52, SS-A/Ro60, SS-B/La, Scl-70, Sm, Jo-1 and CENP-B). EliA Symphony^S is the second generation of EliA Symphony and, in contrast to existing screening assays, uses only recombinant human proteins and a synthetic SmD3 peptide [3, 4].

OBJECTIVE

Using a defined serum panel of patients clinically diagnosed with CTD as well as various disease controls, we aimed to analyze the clinical performance of EliA Symphony^S and to compare it with the QUANTA Flash® ENA7 assay (INOVA Diagnostics), which is comprised of recombinant and native antigens, but excludes CENP-B in its analyte composition.[5]

METHODS

A serum panel comprising 404 samples from patients diagnosed with SLE, SjS, SSc, PM/DM and MCTD and 229 disease controls was analyzed with both EliA Symphony^S and the screening assay from the other manufacturer to analyze and compare clinical performance.

Antigen	EliA Symphony^S	INOVA QUANTA Flash ENA7
SS-A/Ro52	Human recombinant	Recombinant*
SS-A/Ro60	Human recombinant	Recombinant*
SS-B/La	Human recombinant	Recombinant*
Scl-70	Human recombinant	Recombinant*
Jo-1	Human recombinant	Recombinant*
CENP-B	Human recombinant	- not applicable -
RNP	Human recombinant (RNP70,A,C)	Calf thymus
Sm	SmD_3 peptide	Calf thymus

Table 1: Overview of antigens used in the tests analyzed in this study [4 - 6].
*Species not stated in references.

	Number (n=404)	Disease controls	Number (n=229)
Systemic Lupus Erythematosus	97	Rheumatoid Arthritis	85
Sjögren's Syndrome	96	Viral Infection	99
Systemic Sclerosis	87	Bacterial Infection	20
Poly -/ Dermatomyositis	78	Tumor	25
Mixed Connective Tissue Disease	46		

Table 2: Overview of serum panel analyzed in this study.

RESULTS – CLINICAL PERFORMANCE

	Sensitivity	Specificity	PPV	NPV	LR +	LR -
EliA Symphony^S (equiv = neg)	66.6%	93.0%	0.94	0.61	9.5	0.36
EliA Symphony^S (equiv = pos)	68.3%	92.6%	0.94	0.62	9.2	0.34
INOVA QUANTA Flash ENA7	67.8%	91.3%	0.93	0.62	7.8	0.35

Positive Predictive Value (PPV); Negative Predictive Value (NPV); Likelihood Ratio (LR)

Table 3: Clinical performance of EliA Symphony^S and INOVA Quanta Flash ENA7 analyzing the sample cohort from table 2.

Since INOVA Quanta Flash ENA7 does not have an equivocal range, samples reported as equivocal (equiv) with EliA Symphony^S were reported as negative (neg) or positive (pos) for result comparison purposes

	EliA Symphony^S	QUANTA Flash ENA7
Total agreement	95.1%	
Positive agreement	93.1%	
Negative agreement	96.8%	
Samples above measuring range	25.7%	43.1%

Table 4: EliA Symphony^S and QUANTA Flash ENA7 are anti-ENA antibody screening assays, however an international standard for antigen composition and titer does not exist. Therefore, only the agreement and not the correlation between the two tests was determined. The upper limit of the measuring range from the respective test manuals were applied [4, 6].

RESULTS II – CLINICAL PERFORMANCE IN SYSTEMIC SCLEROSIS PATIENTS

	Sensitivity	Specificity	PPV	NPV	LR +	LR -
EliA Symphony^S (equiv = neg)	67.8%	93.0%	0.79	0.88	9.7	0.35
EliA Symphony^S (equiv = pos)	72.4%	92.6%	0.79	0.90	9.8	0.30
INOVA QUANTA Flash ENA7	66.7%	91.3%	0.74	0.88	7.6	0.37

CONCLUSIONS

- An excellent clinical performance of the EiA Symphony^S assay supports the diagnosis of CTDs.
- The EliA Symphony^S test produces fewer false positive results due to its performance characteristics, thereby supporting an evidence-based diagnosis, and likely a lower cost of care".
- Employing only recombinant antigens and synthetic peptides offers the benefits of recombinant protein technology, e.g. high lot-to-lot consistency without the negatives of native antigen sources, e.g. quality variances of native material and inadvertent co-purification of other (unknown) proteins.
- The inclusion of CENP-B in the EliA Symphony^S antigen composition, provides the laboratory with the capability to screen patient samples, e.g. from SSc patients, where the predominant autoantibodies is CENP.

REFERENCES

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† EliA Symphony^S is CE-marked only and not for sale in the US at the time of this printing

TRADEMARKS

CONTACT: Gerben.Zuiderveld@thermofisher.com

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