

EliA™



CCP

EliA™
Excellence in Autoimmunity



The EliA™ System

Time for the Essentials

- completely automated (true walk-away, overnight runs)
- easy instrument management by custom-made software
- barcode-reader (optional for ImmunoCAP™ 100€)
- protocols, QC and raw data easily accessible
- optional host link
- detailed QC management
- integrated stock management system on the ImmunoCAP™ 250

Cost efficient and flexible

- autoimmunity and allergy on the same instrument
- different autoimmune tests in the same run
- no batching of samples necessary – small runs can be handled cost-effectively
- once-monthly calibration – curve control each run
- several ImmunoCAP™ instruments can be linked

A boost in service for your laboratory and your clinicians

- sample – result turnaround the same day
- STAT function on ImmunoCAP™ 250 for immediate testing of emergency samples
- overnight runs possible
- detailed documentation of results (patient or requester specific)
- ImmunoCAP™ 100€ – up to 46 determinations in less than 2.5 hours
- ImmunoCAP™ 250 – fully automated random access – up to 350 determinations per shift
- multiple methods in one run
- positive identification and traceability of samples and reagents on ImmunoCAP™ 250



EliA™



EliA™ CCP – Fully Automated Anti-CCP Detection

The CCP Test

- for determination of anti-CCP antibodies to aid in the diagnosis of Rheumatoid Arthritis using second generation CCP
- valuable in early arthritis (esp. in cases of Rheumatoid Factor negativity) and as a predictor of severe joint damage (according to recent literature)

High Clinical Relevance

- excellent diagnostic performance in routine use
- high clinical sensitivity and specificity proven in studies with over 2500 samples

High Technical Performance

- low variances and high reproducibility for consistent results
- high lot-to-lot consistency due to validated production procedures

Efficiency Also in Calibration

- one curve for all EliA™ IgG tests
- parameter-independent calibration
- stored curve, valid for one month
- combination of different tests in the same run

Easy Handling

- serum as well as plasma can be used
- automated sample dilution
- efficient small run handling



Picture 1: RA-early stage, hands



Picture 2a: RA-late stage, hands



Picture 2b: RA-late stage, x-ray of hands

Rheumatoid Arthritis

RA is the most common form of inflammatory joint disease and affects 1-2% of the general population, but its diagnosis remains principally a clinical one. The major challenge lies in differentiating RA from the many other forms of arthritis that share several presenting symptoms but vary widely both in outcomes and therapeutic options. The serological marker Rheumatoid Factor (RF) is a well-established analyte but is of limited clinical value due to its poor specificity for RA.

With a growing body of evidence indicating that joint destruction and functional decline in RA are improved by early, aggressive therapeutic intervention, the need for an unequivocal early diagnosis has become critical.

The Antigen

In the late 1990s it was recognised that antibodies to perinuclear factor (APF), keratin (AKA) and filaggrin were specific for Rheumatoid Arthritis and in 2000, Schelleken's group showed that these antibodies all recognised the same antigen: Cyclic Citrullinated Peptides (CCP). Other groups were able to demonstrate that anti-CCP antibodies are not only highly specific for RA, they also appear early in the disease process when diagnosis is most difficult and intervention most effective. The ELISA based on this work was made commercially available. Two years later a second generation CCP assay with improved performance characteristics was introduced. EliA™ CCP is based on this second generation assay and combines the advantages of a fully-automated system with the well-accepted clinical benefits of this diagnostic and predictive marker.

■ Excellent differentiation from other diseases

High Clinical Relevance

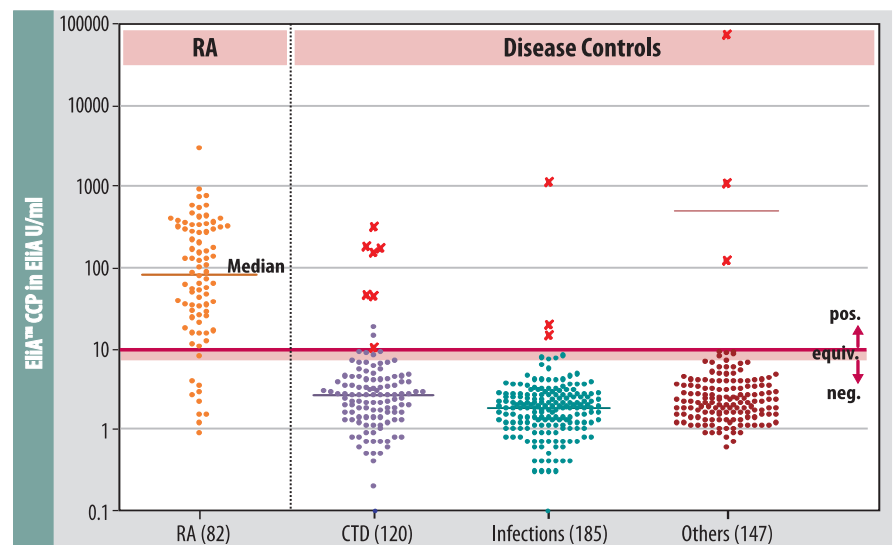


Figure 1: Clinical performance of EliA™ CCP. Disease Controls found positive by EliA™ CCP and confirmed as positive by a reference CCP ELISA are presented with crosses.

The data demonstrate the excellent ability of EliA™ CCP to differentiate RA from CTD like SLE, Sjögren's Syndrome and Mixed Connective Tissue Disease, infections and various other diseases like osteoarthritis.

■ **Excellent clinical sensitivity and specificity**

n = 534 (82 RA, 452 Dis. Contr.)	EliA™ CCP positive > 10 EliA U/ml
Clinical Sensitivity	87.8 %
Clinical Specificity	96.7 %
Positive Predictive Value	82.8 %
Negative Predictive Value	97.8 %
Efficiency	95.3 %

Table 1: Clinical performance of EliA™ CCP (in house data)

The results detailed in figure 1 and table 1 demonstrate that EliA™ CCP has an exceptionally good clinical performance as shown in several evaluations. The high sensitivity and specificity result in excellent efficiency and underline the diagnostic relevance of the test.

■ **Outstanding specificity compared to RF**

Study Site	No. of Patients / Controls	Sensitivity of EliA CCP / RF (in %)	Specificity of EliA CCP / RF (in %)
M. Gaubitz, Münster, Germany	185 / 315	68 / 62	96 / 80

Table 2: Sensitivity and specificity obtained in routine (shown at the 4th International Congress on Autoimmunity 2004 in Budapest)

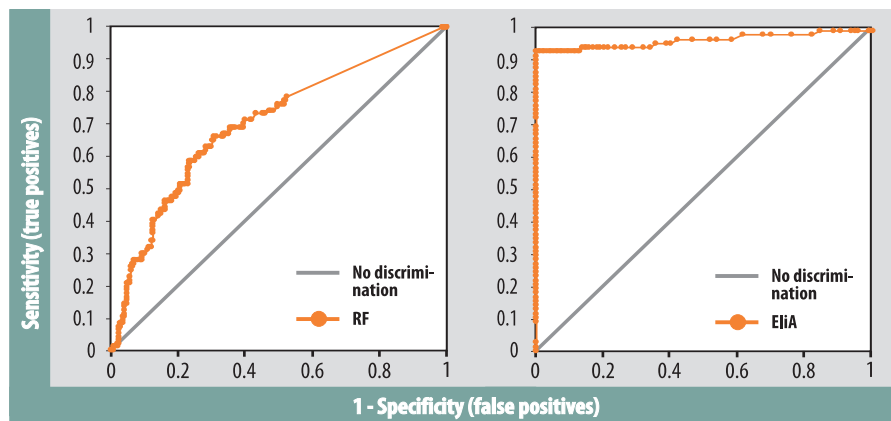


Figure 2: ROC plot for RF as calculated for RA vs Controls

Figure 3: ROC plot for EliA™ CCP as calculated for RA vs Controls

Based on clinically well-defined sample panels Mengozzi et al compared ROC (Receiver Operator Characteristics) curves (G. Mengozzi et al, shown at the 4th International Congress on Autoimmunity 2004 in Budapest).

The two studies demonstrate the outstanding better specificity of EliA™ CCP compared to Rheumatoid Factor (RF).

■ **Better sensitivity than RF in early RA**

Disease duration	No	RF positive	Anti-CCP positive
< 2 years, early	46	34 (73.9 %)	42 (91.3 %)
> 2 years, late	44	35 (79.5 %)	40 (90.9 %)

Table 3: EliA™ CCP and RF in early RA (B. Gilburd et al, shown at the 4th International Congress on Autoimmunity 2004 in Budapest)

The earlier the diagnosis – the better!

EliA™ CCP supports making the diagnosis at an early stage.

■ **Confirmed value in routine setting**

Study Site	No. of Patients / Controls	Sensitivity (in %)	Specificity (in %)
M. Herold, Innsbruck, Austria	66 / 328	80,3	97

Table 4: Sensitivity and specificity obtained in routine

The design of the evaluation was chosen in order to evaluate the performance of EliA™ CCP in a routine situation. The high specificity was confirmed. Differences in sensitivity may be due to differences in the patient characteristics in terms of severity and stage of disease.

Technical Data

■ Product	EliA™ CCP
■ Antigen	2 nd generation CCP
■ Standardisation	6 point standard curve
■ Cut-off	neg. <7 U/ml; equiv. 7–10 U/ml; pos. >10 U/ml
■ Measuring Range	0.4 U/ml – at least 340 U/ml
■ Dilution	1:100 (automated)
■ Sample Material	Serum, Plasma (EDTA, citrate, heparin)
■ Normal Distribution	Mean 2.6 U/ml, 95 th percentile 4.3 / 6.2 U/ml
■ Reproducibility	Intra-run CV* 5.1–10.5 % Inter-run CV* 2.6–7.7 %

*for details see Directions For Use

Ordering Information

	<i>Package size</i>	<i>Article No.</i>
■ EliA™ CCP Well	4 x 12	14-5515-01
■ EliA™ CCP Control (neg + pos)	3 x 2	83-1009-01
■ EliA™ IgG Calibrator Well	4 x 12	14-5509-01
■ EliA™ Reagents – ImmunoCAP™ 100€		
EliA™ IgG Conjugate	6 x 48	83-1002-01
EliA™ IgG Conjugate	2 x 48	83-1005-01
EliA™ IgG Calibrators	1 curve	83-1000-01
EliA™ IgG Curve Control	6 runs	83-1001-01
EliA™ Sample Diluent	6 x 30	83-1003-01
■ EliA™ Reagents – ImmunoCAP™ 250		
EliA™ IgG Conjugate 50	6 x 50	83-1017-01
EliA™ IgG Conjugate 200	6 x 200	83-1018-01
EliA™ IgG Calibrator Strips	6 x 1 curve	83-1015-01
EliA™ IgG Curve Control Strips	5 x 6 runs	83-1016-01
EliA™ Sample Diluent	6 x 188	83-1023-01
■ General Reagents – ImmunoCAP™ 100€		
ImmunoCAP™ Development Solution	6 x 48	10-9478-01
ImmunoCAP™ Stop Solution	6 x 240	10-9479-01
ImmunoCAP™ Washing Solution	6 x 1 l	10-9422-01
ImmunoCAP™ Washing Solution	2 x 5 l	10-9202-01
■ General Reagents ImmunoCAP™ 250		
ImmunoCAP™ Development Solution	6 x >170	10-9440-01
ImmunoCAP™ Development Solution	6 x 110	10-9441-01
ImmunoCAP™ Stop Solution	6 x 590	10-9442-01
ImmunoCAP™ Washing Solution	6 x 1 l	10-9422-01
ImmunoCAP™ Washing Solution	2 x 5 l	10-9202-01
Dilution Plates	60 plates x 96 wells	12-3907-08

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