Anti-Sa ELISA (IgG)

Indication: Test system for the in vitro determination of antibodies of the immunoglobulin class IgG against Sa in human serum or plasma for the diagnosis of the following disease: rheumatoid arthritis.

Clinical significance: Serological antibody diagnosis is critically important for the early detection and confirmation, as well as assessing the progression, therapeutic success and prognosis of rheumatoid arthritis (RA). In addition to the traditional identification of the rheumatoid factor as a possible indication of RA, autoantibodies against citrullinated antigens (CCP, cyclic citrullinated peptide) as a highly specific marker contribute substantially to diagnosing RA. Both the qualitative and quantitative detection of anti-Sa (Sa = patient with the name of Savoie, in whom the antibodies against citrullinated vimentin were first discovered) can also be used to evaluate the activity (progression, therapeutic success) of RA.

Anti-Sa antibodies are autoantibodies with a high specificity of almost 100% for patients with RA in Europe, Asia and America. Citrullinated vimentin expressed in synovial membrane is the target antigen of these autoantibodies. Although anti-Sa antibodies exhibit a lower sensitivity (anti-Sa Westernblot 40%, anti-Sa ELISA up to 60%), their prognostic value for a severe form of RA progression is unsurpassed. Their high predictive value of as much as 99% for RA is closely associated with severe joint involvement as well as extraarticular manifestations. Autoantibodies against CCP and against Sa can be detected in approximately 75% or roughly 60% of RA patients, respectively, very early in the progression of the disease. As a result, the diagnosis can be made early and an adequate therapy can ensue quickly. With regard to the prognosis of the illness, radiological examinations indicate that among patients with anti-CCP antibodies or even more so with anti-Sa antibodies severe joint damage occurs significantly more frequently than with anti-CCP negative or anti-SA negative patients. This increases the significance of detecting both anti-CCP and anti-Sa as a prognostic marker for the development and progression of RA.

Panel	n	Anti-Sa positive	Anti-CCP positive
Rheumatoid arthritis	237	114 (48.1%)	157 (66.4%)
Early rheumatoid arthritis (ERA)	74	28 (37.8%)	44 (59.9%)
Juvenile idiopathic arthritis	55	1 (1.8%)	2 (3.6%)
Sensitivity for rheumatoid arthritis	237	48.1%	66.4%
Psoriasis arthritis	181	0	3 (1.6%)
SLE	190	2 (1.1%)	8 (4.2%)
Asymptomatic blood donnors*	408	3 (0.7%)	n.d.
Asymptomatic blood donnors*	400	n.d.	2 (0.5%)
Specificity for rheumatoid arthritis	779/771	99.5%	98%

*Different groups of asymptomatic blood donors were used.

A significant correlation has been demonstrated between the level of the anti-Sa antibody titre and the degree of severity of RA, as well as its disease activity (disease activity score: DAS28 = internationally accepted composite score for the evaluation of RA disease activity). Consequently, the anti-Sa ELISA is quite suitable for the stratification of RA.

Because anti-CCP ELISA and anti-Sa ELISA overlap and confirm one another in part in terms of their validity, and in particular complement one another (with regard to early detection, confirmation, progression, therapeutic success and prognosis of RA), the parallel implementation of these two serological tests currently offers the greatest possible diagnostic security.

Application of the Anti-Sa ELISA: The marker anti-Sa offers an even higher specificity than anti-CCP and is strongly associated with active rheumatoid arthritis, whereas anti-CCP may occur years before the onset of the disease. The determination of anti-Sa antibodies thus enables rheumatologists to diagnose an active disease. Moreover, anti-Sa also serves as a prognostic marker to predict the progression and the severity of the disease. Furthermore, anti-Sa seems to be better suited for the evaluation of the therapy success in RA patients than all other available parameters.

However, anti-Sa should not be considered as a substitute for anti-CCP. Due to its high sensitivity and specificity, as well as predictive value, anti-CCP remains the recommended marker for diagnosing RA.

EUROIMMUN Microplate ELISA

Autoantibody determination:
AMA M2-3E (IgG)
ANCA Profile (IgG)
ANA Screen (IgG)
ANA Screen 9 or 11 (IgG)
ANA VarioProfile (IgG)
BP180-NC16A-4X (IgG)
BP230-CF (IgG)
C1q (IgG)
cardiolipin (IgA, IgG, IgM, IgAGM)
circulating immune complexes (CIC)
cyclic citrullinated peptide (CCP; IgG)
centromere protein B (IgG)
desmoglein 1 (IgG)
desmoglein 3 (IgG)
double-stranded DNA (dsDNA, nDNA; IgG)
dsDNA-NcX (IgG)
ENA Pool (IgG)
ENA PoolPlus (IgG)
ENA ProfilePlus 1 or 2 (IgG)
ENA SLE Profile 1 or 2 (IgG)
GAD
GAD/IA-2 Pool
glomerular basement membrane (GBM; IgG)
ß2-glycoprotein 1 (IgA, IgG, IgM, IgAGM)
histones (IgG)
IA-2
intrinsic factor (IgG)
Jo-1 (IgG)
liver cytosolic antigen type 1 (LC-1; IgG)
liver-kidney microsomes (LKM-1; IgG)
myeloperoxidase (MPO; IgG)
nRNP/Sm (IgG)
nucleosomes (IgG)
p53 (IgG)
parietal cells (PCA; IgG)
PM-Scl (PM-1; IgG)
phosphatidylserine (IgA, IgG, IgM, IgAGM)
proteinase 3 (IgG)
PR3 hn-hr (IgG)
PR3 capture (IgG)
rheumatoid factor (IgA, IgG, IgM)
ribosomal P-proteins (IgG)
Sa (IgG)
Scl-70 (IgG)
single-stranded DNA (ssDNA; IgG)
SLA/LP (IgG)
Sm (IgG)
SS-A (Ro; IgG)
SS-B (La; IgG)
thyroglobulin (TG; IgG)
thyroid peroxidase (TPO; IgG)
tissue transglutaminase (endomy.; IgA, IgG)
TSH receptor (TBII; IgG)
TRAk Fast (IgG)

Further autoimmune diagnostics:
gliadin (GAF-3X; IgA, IgG)
Saccharomyces cerevisiae (IgA, IgG)

Infectious serology:
Adenovirus (IgA, IgG, IgM)
Borrelia (IgG, IgM)
Borrelia VlsE (IgG)
Chlamydia pneumoniae (IgA, IgG, IgM)
Chlamydia trachomatis (IgA, IgG, IgM)
Cytomegalovirus (IgG, IgM)
Diphtheria toxoid (IgG)
Epstein-Barr virus capsid ag (IgA, IgG, IgM)
Epstein-Barr virus early ag (IgA, IgG, IgM)
Epstein-Barr virus nuclear ag, EBNA-1 (IgG)
Helicobacter pylori (IgA, IgG)
Helicobacter pylori CagA (IgA, IgG)
HSV-1 (glycoprotein C1; IgA, IgG, IgM)
HSV-2 (glycoprotein G2; IgA, IgG, IgM)
HSV-1/2 Pool (IgA, IgG, IgM)
Influenza virus type A (IgA, IgG, IgM)
Influenza virus type B (IgA, IgG, IgM)
Legionella pneumophila (IgA, IgG, IgM)
Measles virus (IgG, IgM)
Mumps virus (IgG, IgM)
Mycoplasma pneumoniae (IgA, IgG, IgM)
Parainfluenza virus Pool (IgA, IgG, IgM)
Parvovirus B19 (IgG, IgM)
RSV (IgA, IgG, IgM)
Rubella virus (IgG, IgM)
SARS-CoV (IgG)
TBE virus (IgG, IgM)
Tetanus toxoid (IgG)
Toxoplasma gondii (IgG, IgM)
Treponema pallidum (IgG, IgM)
Varicella zoster virus (IgG, IgM)
Yersinia enterocol. virulence fact. (IgA, IgG)

Allergology:
total IgE
Allercoat™ 6-ELISA (600 different allergens and allergen mixtures)

Serum proteins and tumour markers:
anti-p53

* Currently not available as IVD in the EU.

Made in Germany

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EUROIMMUN Immunoblots

Autoantibody determination:

EUROASSAY:

flexible profiles of up to 7 antigens from:

ENA and related antigens: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, dsDNA, histones, nucleosomes, CENP B, PM-Scl, ribosomal P-proteins, AMA M2

liver antigens: LKM-1, LC-1, SLA/LP, AMA M2, M4, M9

ANCA antigens: MPO, PR3

thyroid antigens: TG, TPO

EUROLINE:

ANA Profile 1: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1, CENP B, dsDNA, nucleosomes, histones, ribosomal P-proteins

ANA Profile 3: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, PM-Scl, Jo-1, CENP B, PCNA, dsDNA, nucleosomes, histones, ribosomal P-proteins, AMA M2

ANA Profile 5: nRNP/Sm, Sm, RNP70, RNPA, RNPC, SS-A, Ro-52, SS-B, Scl-70, PM-Scl, Jo-1, CENP B, PCNA, dsDNS, nucleosomes, histones, ribosomal P-proteins, AMA M2

Anti-ENA Profile 1: nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, Jo-1

Systemic Sclerosis Profile: Scl-70, CENP A, CENP B, RP11, RP155, Fibrillarin, NOR90, Th/To, PM-Scl100, PM-Scl75, Ku, PDGFR, Ro-52

Myositis Profile 3: Mi-2, Ku, PM-Scl100, PM-Scl75, SRP, Jo-1, PL-7, PL-12, OJ, EJ, Ro-52

Liver Profiles: AMA M2, 3E (BPO), Sp100, PML, gp210, LKM-1, LC-1, SLA/LP, Ro-52

Neuronal Antigens Profile 2: amphiphysin, CV2.1** PNMA2 (Ma-2/Ta), Ri, Yo, Hu

Anti-Ganglioside Profile 1: GM1, GD1b, GQ1b

Anti-Ganglioside Profile 2: GM1, GM2, GM3, GD1a, GD1b, GT1b, GQ1b

ANCA Profiles: MPO, PR3, GBM

EUROLINE-WB:

neuronal antigens (+ recomb. Hu, Yo, Ri)
HEp-2 cell antigens (+ SS-A and Ro-52, CENP B)

Infectious serology:

EUROLINE:

Bordetella pertussis (IgA, IgG)
Borrelia-RN-AT (p18, p19, p20, p21, p58, OspC, p39, p83, LBb, LBa, VlsE Bg, VlsE Bb, VlsE Ba)
EBV Profile (IgG, IgM, VCA gp125, VCA p19 and EBNA-1, p22, EA-D)
Hanta virus (IgG, IgM)
TORCH Profile* (T. gond., rubella, CMV, HSV-1, -2)

Westernblot:

Borrelia burgdorferi (IgG, IgM)
Borrelia afzelii (IgG, IgM)
Borrelia garinii (IgG, IgM)
Epstein-Barr virus (IgG, IgM)
Rubella virus (IgG)
Treponema pallidum (IgG, IgM)
Yersinia enterocol. virulence fact. (IgA, IgG)

EUROLINE-WB:

Anti-Borrelia (B. afzelii + rec. VlsE)
Anti-HSV (HSV-1 + HSV-2 gG2)
Helicobacter pylori (IgA, IgG)
Treponema pallidum + cardiolipin

Allergology:

EUROASSAY:

Domestic Animal Profile (IgE)
Food Profile (IgE)
Inhalation Profile (IgE)
Insect Venom Profile (IgE)
Latex Profile (IgE)
Latex plus Profile (with ficus and fruit; IgE)

EUROLINE:

Atopy Profile (IgE)
Food Profile (IgE)
Inhalation Profile (IgE)
Paediatric Inhalation Profile
Pollen–Food Cross Reaction Profile (IgE)

Software/Automation:

EUROLineScan
camera system EUROBlotCamera
scanner system EUROBlotScanner
incubation processor EUROBlotMaster

EUROIMMUN Radioimmunoassays

Autoantibody determination:

thyroid peroxidase (TPO; IgG)
thyroglobulin (TG; IgG)
TSH receptor (IgG)
acetylcholine receptor (ACHR; IgG)
glutamic acid decarboxylase (GAD; IgG)
insulin (IAA; IgG)
P/Q calcium channel* (VGCC; IgG)
tyrosine phosphatase (IA2; IgG)
dsDNA (IgA/IgG/IgM)

Antigen determination:

thyroglobulin (TG)

Hormone determination:

free triiodothyronine (FT3)
free thyroxine (FT4)
thyrotropin (TSH)
calcitonin

* Currently not available as IVD in the EU.
** CV2 partial protein, which only contains the N-terminally localised epitopes of the antigen.

Made in Germany

Version: 05/10
EA_151a_D_UK_A02

Test characteristics Anti-Sa ELISA (IgG)

Clinical sensitivity and specificity: Sera from 237 patients with rheumatoid arthritis, 55 patients with juvenile idiopathic arthritis (JIA), 181 patients with psoriasis arthritis (PSA) and 408 healthy blood donors were investigated using the EUROIMMUN Anti-Sa ELISA. The sensitivity of the ELISA for rheumatoid arthritis was 48.1%, with a specificity of 99.5%. In the juvenile idiopathic arthritis panel 1.8% of patients were positive.

Reference range: Levels of anti-Sa antibodies were analysed in 408 sera from healthy blood donors of between 17 and 67 years of age (148 women, 260 men) using the EUROIMMUN Anti-Sa ELISA. With a cut-off of 20 RU/ml, 0.7% of the blood donors were anti-Sa positive.

Blood donors, n=408		
Percentile	98th	99th
Cut-off	3.7 RU/ml	16.3 RU/ml

ROC analysis: In the analysis of 237 samples from patients with rheumatoid arthritis and 589 control samples from 181 patients with psoriasis arthritis and 408 asymptomatic blood donors the following data were yielded:

Cut-off	Specificity	Sensitivity
5.9 RU/ml	98 %	57 %
16.7 RU/ml	99 %	53 %

Reproducibility: The reproducibility of the test was investigated by determining the intra- and inter-assay coefficients of variation using 3 sera. The intra-assay CVs are based on 20 determinations and the inter-assay CVs on 4 determinations performed in 6 different test runs.

	Intra-assay variation, n = 20		*Inter-assay variation, n = 4 x 6*	
Serum	Mean value (RU/ml)	CV (%)	Mean value (RU/ml)	CV (%)
1	31	8.9	28	9.1
2	119	3.5	112	8.0
3	160	2.4	165	4.3

Correlation of the Anti-Sa ELISA with the Anti-CCP ELISA: The sensitivity of the Anti-Sa ELISA and the Anti-CCP ELISA determined using 237 sera from RA patients was 48% and 66%, respectively. The sensitivity of the Anti-Sa ELISA was 38% in the panel of 74 ERA sera and 2% in the panel of JIA sera. The specificity of the Anti-Sa ELISA and the Anti-CCP ELISA amounted to 99.5% and 98%, respectively.

RA patients, n=237		Anti-Sa ELISA	
		positive	negative
Anti-CCP ELISA	positive	106	51
	negative	8	72

PSA patients, n=181		Anti-Sa ELISA	
		positive	negative
Anti-CCP ELISA	positive	0	3
	negative	0	178

JIA patients, n=55		Anti-Sa ELISA	
		positive	negative
Anti-CCP ELISA	positive	1	1
	negative	0	53

ERA patients, n=74		Anti-Sa ELISA	
		positive	negative
Anti-CCP ELISA	positive	27	17
	negative	1	29

Technical data:

Antigen	The ELISA was developed in cooperation with Prof. Menard (McGill University Montreal, Canada). The reagent wells are coated with citrullinated or non-citrullinated Sa antigen (blank).
Calibration	Quantitative, in relative units per milliliter (RU/ml). Calibration serum 1: 200 RU/ml Calibration serum 2: 20 RU/ml; cut-off Calibration serum 3: 2 RU/ml
Sample dilution	Serum or plasma; 1:101 in sample buffer.
Reagents	Ready for use, with the exception of the wash buffer (10x). Colour-coded solutions, in most cases exchangeable with those in other EUROIMMUN ELISA kits.
Test procedure	60 min / 30 min / 30 min. Room temperature.
Measurement	450 nm. Reference wavelength between 620 nm and 650 nm.
Test kit format	96 reagent wells. Kit includes all necessary reagents for 48 determinations (double determination required).
Order number	EA 151a-4802 G

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