



## Anti-TSH Receptor (TRAb) *Fast* ELISA (IgG)



**Indication:** Test system for the in vitro determination of autoantibodies against TSH receptor in human serum for the diagnosis of the following disease: Graves' disease.

**Clinical significance:** The functions of the thyroid are controlled by the hypothalamus in the brain stem via the pituitary gland. Hormones formed in the hypothalamus regulate the emission of TSH (thyroidea stimulating hormone) that is produced in the pituitary gland inducing the thyroid gland to release the thyroid hormones T3 (triiodothyronine) and T4 (tetraiodothyronine = thyroxine). An increase of T3 and T4 levels in the serum are in general an indication of a hyperthyroid functional disorder (hyperthyrosis), whereas low levels of T3 and T4 hormones are allocated to a hypothyroid functional disorder (hypothyrosis). Aside from a disorder of the thyroid hormone regulation, thyroiditis can be the cause of the symptoms of either hyper- or hypothyrosis. A differentiation is made between an acute (bacterial infection), a subacute (non-infectious), and a chronic thyroiditis (autoimmune disease). During the autoimmune process antibodies against one or several of the three autoantigens, thyroid peroxidase (TPO), thyroglobulin (TG) and TSH receptor (TR), of the thyroid are formed. TSH receptor autoantibodies (TRAb) are heterogeneous regarding their biological effect and either stimulate or block thyroid function. The determination of TRAb is mainly performed if Graves' disease is suspected. This autoimmune disease is characterised by symptoms of the Merseburg triad (struma, exophthalmus and tachycardia). Approximately 2% of the female and 0.2% of the male population are affected by a manifest Graves' disease. 60% of all cases of hyperthyroidism can be ascribed to Graves' disease.

The prevalence of TRAb in patients with Graves' disease is 90 to 100%. Thus TRAb are considered to be diagnostic markers and are utilized for differential diagnostics from an autonomy of the thyroid gland. High TRAb titers in patients with Graves' disease following a long thyrostatic therapy show an increased risk for reoccurrence of the disease. Moreover, increased TRAb concentrations in the third trimester of pregnant women with Graves' disease indicate a hyperthyrosis in the fetus. Where normal values are found, the diagnosis can be supported by the determination of antibodies against TPO with a prevalence of 60 – 70%. Additionally antibodies against TG are found in 20 – 50% of the cases.

**Application of the Anti-TSH Receptor *Fast* ELISA (3<sup>rd</sup> generation):** Immunoassays for the determination of TRAb detect autoantibodies that are directed against the binding site of TSH and inhibit the binding of TSH to the TSH receptors. The term 1<sup>st</sup> generation test refers to radioimmunoassays (RIA; synonym RRA, radio-receptor assays) that are based on displacement of radioactively labelled TSH molecules from solubilized thyrocyte membranes by TRAb from the patient serum. In 2<sup>nd</sup> generation test systems such as ELISA, RIA (RRA) and LIA (synonym LRA, luminescence receptor assays) TRAb from positive samples bind to porcine or human TSH receptors immobilised on the walls of a reaction vessel. The bound TRAb inhibit the binding of labelled TSH. The amount of labelled TSH detected in the solid phase, as determined by photometry or measurement of radioactivity or luminescence, is inversely proportional to the TRAb concentration in the sample. Studies have shown that the TRAb concentration measured in a test system is not influenced by the origin of the immobilised TSH receptor (human or porcine). In the new 3<sup>rd</sup> generation Anti-TSH Receptor (TRAb) *Fast* ELISA (IgG) bound TRAb from positive samples inhibit the binding of labelled thyroidea stimulating, monoclonal antibodies (M22, in the form of M22-peroxidase). The extinction value measured for the 2<sup>nd</sup> generation is inversely proportional to the TRAb concentration in the sample. 3<sup>rd</sup> generation ELISA have a higher sensitivity with a constant specificity and a shorter processing time compared to former ELISA. Moreover, the test has improved automatability.

### EUROIMMUN Microplate ELISA

#### Autoantibody determination:

AMA M2-3E (IgG)  
ANCA Profile (IgG)  
ANA Screen (IgG)  
ANA Screen 9 or 11 (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)  
GA  
GAD/IA-2 Pool  
glomerular basement membrane (GBM; IgG)  
β<sub>2</sub>-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)  
ovary (IgAGM, IgG typing)  
pancreatic cells (PCA; IgG)  
PM-Scl (PM-1; IgG)  
phosphatidylserine (IgA, IgG, IgM, IgAGM)  
PR3 hn-hr (IgG)  
PR3 capture (IgG)  
rheumatoid factor (IgA, IgG, IgM)  
ribosomal P-proteins (IgG)  
Ss (IgG)  
Scl-70 (IgG)  
single-stranded DNA (ssDNA; IgG)  
SLA/LP (IgG)  
Sm (IgG)  
spermatozoa (IgAGM, IgG typing)  
SS-A (Ro; IgG)  
SS-B (La; IgG)  
thyroglobulin (TG; IgG)  
thyroid peroxidase (TPO; IgG)  
tiss. transglutaminase (endomg.; IgA, IgG, IgAGM)  
TSH receptor (TBI; IgG)  
TRAK Fast (IgG)  
zona pellucida (IgAGM, IgG typing)

#### Latex agglutination tests:

spermatozoa  
ovary  
zona pellucida

#### Further autoimmune diagnostics:

gliadin (GAF-3X; IgA, IgG)  
Saccharomyces cerevisiae (IgA, IgG)

#### Infectious serology:

Adenovirus (IgA, IgG, IgM)  
Bordetella pertussis (IgA, IgG, IgM)  
Bordetella FHA (IgA, IgG)  
Borrelia (IgG, IgM)  
Borrelia VisE (IgG)  
Brucella abortus (IgA, IgG, IgM)  
Campylobacter jejuni (IgA, IgG)  
Chlamydia pneumoniae (IgA, IgG, IgM)  
Chlamydia trachomatis (IgA, IgG, IgM)  
Cytomegalovirus (IgG, IgM)  
Dengue virus (IgG, IgM)  
Diphtheria toxoid (IgG)  
Echinococcus granulosus (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)  
Hanta virus "Eurasia" + "America" (IgG, IgM)  
Helicobacter pylori (IgA, IgG)  
Helicobacter pylori CagA (IgA, IgG)  
HSV-1 (glycoprotein C2; 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)  
Influenza Pool (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)  
Tetanoxoid (IgG)  
Toxoplasma gondii (IgG, IgM)  
Treponema pallidum (IgG, IgM)  
Varicella zoster virus (IgG, IgM)  
West Nile virus (IgG, IgM)  
Yersinia enterocol. virulence fact. (IgA, IgG)

#### Allergology:

total IgE  
Allercoat™ 6-ELISA (650 different allergens and allergen mixtures)  
Software EUROIMMUN Allercoat™

#### Serum proteins and tumour markers:

anti-p53

#### Bone metabolism marker:

25-OH-Vitamin-D

#### Saliva diagnostics:

alpha-amylase  
cortisol  
slgA

#### Software/Automation:

EUROLabOffice  
EUROIMMUN Analyzer I + I-2P

\* Currently not available as IVD in the EU.

Made in Germany



## 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 6: nRNP/Sm, Sm, RNP70, RNPA, RNPC, SS-A, Ro-52, SS-B, Scl-70, PM-Scl, Jo-1, CENP B, PCNA, dsDNA, 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, RP15, 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, PL7, PL12, 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\*\* PNM2 (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, VisE Bg, VisE Bb, VisE 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)

#### Westemblot:

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. VisE)  
Anti-HSV (HSV-1 + HSV-2 gG2)  
Helicobacter pylori (VacA, Cag A; IgA, IgG)  
Treponema pallidum + cardiolipin

### Allergology:

#### EUROASSAY:

Food Profile (IgE)  
Inhalation Profile (IgE)  
Pediatric/Atopy Profile (IgE)  
Insect Venom Profile (IgE)

#### EUROLINE:

Atopy Profile (IgE; also region-specific profiles)  
Food Profile (IgE; also region-specific profiles)  
Inhalation Profile (IgE; also region-specific profiles)  
Paediatric Profile (IgE)  
Pollen-Food Cross Reaction Profile (IgE)  
Insect Venom 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

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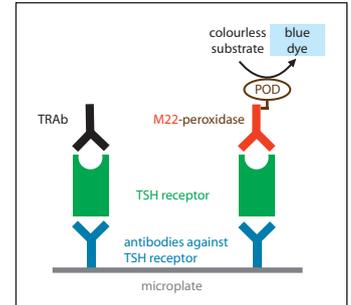
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# Test characteristics

## Anti-TSH Receptor (TRAb) Fast ELISA (IgG)

**Principles of the test:** The Anti-TSH receptor (TRAb) Fast ELISA (IgG) provides a quantitative in-vitro assay for the determination of human autoantibodies against TSH receptor (TRAb). The test kit contains microtiter strips each with 8 break-off reagent wells coated with TSH receptor. In the first reaction step, the patient sera are incubated in the wells. If the sample is positive, specific antibodies bind to the TSH receptors. The bound antibodies inhibit the binding of a thyroidea stimulating, human, monoclonal antibody (M22, in the form of M22-peroxidase), which is pipetted into the reagent wells during the second incubation step. In the third incubation step bound antibodies are made visible by a colour reaction using a chromogen/substrate solution. The intensity of the colour formed is inversely proportional to the concentration of antibodies against TSH receptor.



**Reproducibility:** The reproducibility of the test was investigated by determining the intra- and inter-assay coefficients of variation (CV) using 2 sera with values at different points on the calibration curve. The intra-assay CVs are each based on 20 determinations and the inter-assay CVs are each based on 15 determinations.

Serum	Intra-assay variation, n = 20		Inter-assay variation, n = 15	
	Mean value (IU/l)	CV (%)	Mean value (IU/l)	CV (%)
1	1.96	7.2	2.17	9.7
2	7.14	3.9	4.58	7.0

**Comparison of the EUROIMMUN Anti-TSH Receptor Fast ELISA (3<sup>rd</sup> generation) with the Anti-TSH Receptor ELISA (2<sup>nd</sup> generation):** In a study 82 sera from Graves' disease patients and 101 sera from a control panel<sup>1</sup> were investigated. The sensitivity of the Anti-TSH Receptor Fast ELISA (3<sup>rd</sup> generation) is 85% and is higher than the sensitivity of the 2<sup>nd</sup> generation Anti-TSH Receptor ELISA (77%). The specificity of both test systems is 100%.

Panel	n	Anti-TRAb ELISA	
		3 <sup>rd</sup> gen. pos.	2 <sup>nd</sup> gen. pos.
Graves' disease	82	70 (85%)	63 (77%)
Control panel <sup>1</sup>	101	0 (0%)	0 (0%)

<sup>1</sup> Blood donors (n = 44), other thyroid diseases (n = 57)

**Comparison of the EUROIMMUN Anti-TSH Receptor Fast ELISA (3<sup>rd</sup> generation) with the Anti-TSH Receptor RIA (2<sup>nd</sup> generation):** 74 sera from Graves' disease patients and 30 sera from a control panel<sup>2</sup> were investigated. The sensitivity of the Anti-TSH Receptor Fast ELISA (3<sup>rd</sup> generation) is 85% and is higher than the sensitivity of the 2<sup>nd</sup> generation Anti-TSH Receptor RIA (72%). The specificity of both test systems is 100%.

Panel	n	Anti-TRAb ELISA	Anti-TRAb RIA
		3 <sup>rd</sup> gen. pos.	2 <sup>nd</sup> gen. pos.
Graves' disease	74	63 (85%)	53 (72%)
Control panel <sup>2</sup>	30	0 (0%)	0 (0%)

<sup>2</sup> Blood donors (n = 23), other thyroid diseases (n = 7)

### Technical data:

Antigen	Porcine TSH receptor
Calibration	Quantitative, in international units per liter (IU/l). Calibration serum 1: 40 IU/l Calibration serum 2: 8 IU/l Calibration serum 3: 2 IU/l Calibration serum 4: 1 IU/l; cut off Calibration serum 5: 0,1 IU/l
Sample dilution	Serum; 75 µl undiluted.
Reagents	Ready for use. Exception: wash buffer (10x) and M22-peroxidase (lyophilisate).
Test procedure	60 min / 25 min / 25 min. Room temperature. Fully automatable.
Measurement	450 nm. Reference wavelength between 620 nm and 650 nm.
Kit format	96 single break-off wells, incl. all necessary reagents.
Order no.	EA 1015-9601-1 G