

Newly launched EliA TSH-R assay.

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Phadia User Group Meeting 2017

Autoimmune thyroid diseases

- **Up to 5%** of people in western countries are affected by autoimmune thyroid diseases (AITDs)
- AITDs are up to **6 times more common** in women than men
- **About 80%** of the susceptibility to develop AITDs is attributable to genetic factors
- **Graves' disease** and **Hashimoto's thyroiditis** are the most clinically significant forms of AITDs

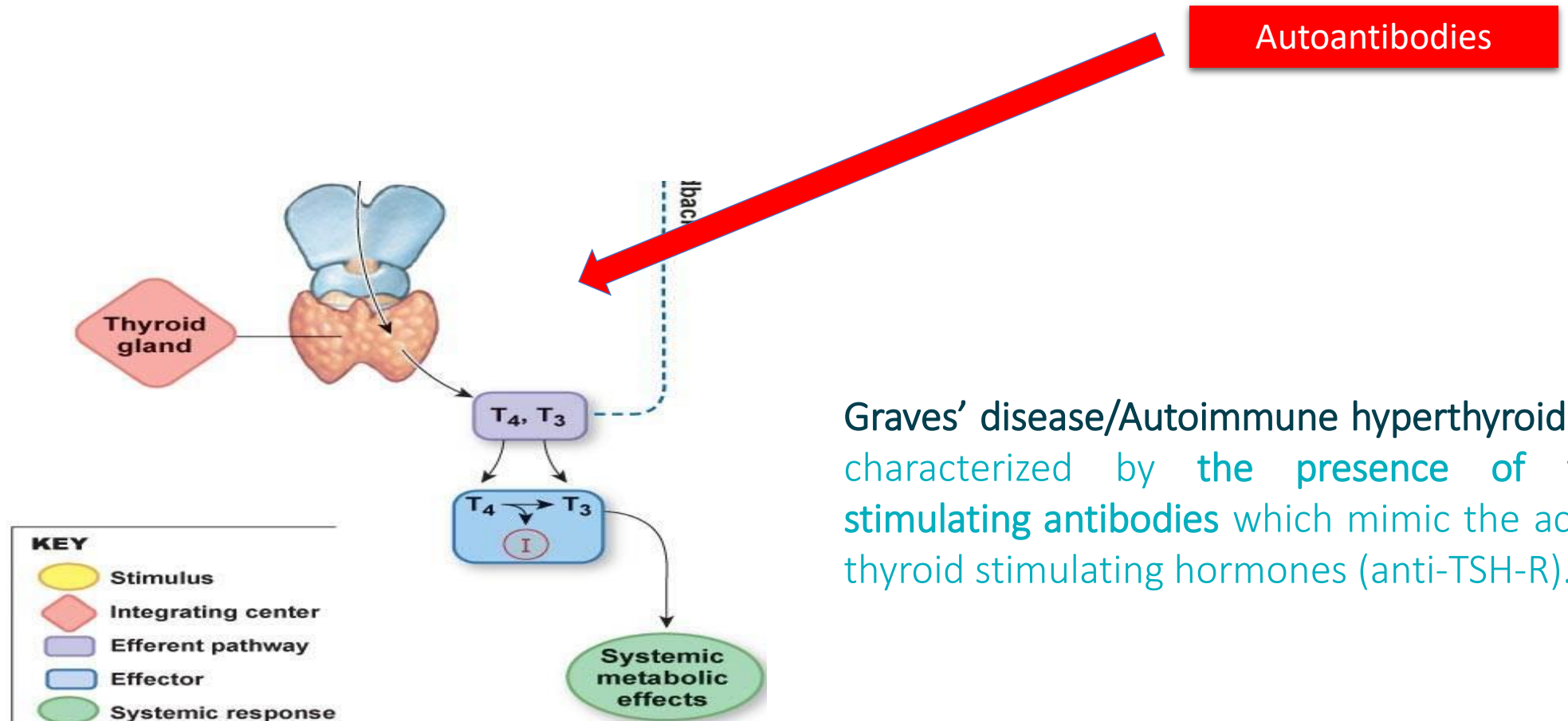
Pathogenesis of AITDs

AITDs are characterised by:

- Significant infiltration of the thyroid gland by T or B cells
- The production of thyroid-reactive autoantibodies such as anti-TPO, anti-TG, and anti-TSH-R


Testing for thyroid autoantibodies provides assistance in reaching a clinical diagnosis





Graves' disease/Autoimmune hyperthyroidism: is characterized by the presence of thyroid stimulating antibodies which mimic the action of thyroid stimulating hormones (anti-TSH-R).

Thyroiditis




HYPERTHYROIDISM
such as Graves' disease

Overactive thyroid gland

Production of T₃ and T₄ hormones is usually increased²

Production of thyroid-stimulating hormone (TSH) decreased²



HYPOTHYROIDISM
such as Hashimoto's thyroiditis

Underactive thyroid gland


Production of T₃ and T₄ hormones is usually decreased²

Production of thyroid-stimulating hormone (TSH) increased²

1: American Thyroid Association, 2015. Thyroiditis. Available from <http://www.thyroid.org/> [accessed August 2016].

2: Schott M, et al. *J Lab Med* 2006; 34(4): 254–257.

Signs and symptoms

HYPERTHYROIDISM – Graves' disease	
Anxiety	<p>LONG-TERM UNTREATED HYPERTHYROIDISM:²</p> <ul style="list-style-type: none"> • Psychiatric illness • Cardiac disease • Arrhythmia • Sudden cardiac death 
Irritability	
Sleeping difficulty	
Fatigue	
Rapid or irregular heartbeat	
Heat sensitivity	
Weight loss, despite normal food intake	
Goiter	
Brittle hair	
Diarrhoea	

Tables adapted from Rema J, et al. 2012¹

1: American Thyroid Association, 2015. Thyroiditis. Available from <http://www.thyroid.org/> [accessed August 2016].

2: Schott M, et al. *J Lab Med* 2006; 34(4): 254–257.

Other AITDs known to affect thyroid hormone levels/synthesis:

- Atrophic thyroiditis
- Postpartum thyroiditis
- Drug-induced thyroiditis (e.g. interferon- or amiodarone-induced)
- Polyglandular autoimmune syndromes
- Subclinical thyroiditis

Anti-TSH-R antibodies are absent in most of these AITDs^{2,3}

but are prevalent in **almost 100% of Graves' disease patients***

The specificity of anti-TSH-R antibodies for Graves' disease provides assistance in the clinical diagnosis of AITDs

NEW EliA TSH-R!

High sensitivity and excellent specificity

Helps identify patients with high accuracy

Equivocal range

Improve diagnostic guidance

Recombinant human TSH-R with the correct conformation (folding) produced in eukaryotic cells

High sensitivity can be achieved by ensuring the presentation of the relevant epitopes

EliA anti-TSH-R conforms to the latest international calibration standard NIBSC 08/204

Traceable and reproducible calibration

The first competitive EliA assay

Easily integrated into existing laboratory workflows

Fully automated Phadia Laboratory Systems

Increasing operational efficiency leading to an optimized workflow

Automated vs Manual

Manual anti-TSH-R ELISA



Automated ELiA anti-TSH-R

The information below is derived from the Directions for Use of several manual anti-TSH-R ELISA tests¹

- Shorter time to first result
- Smaller sample volume
- Single-well testing
- No duplicate required
- Optimized workflow – less hands-on time, increased cost-efficiency
- High accuracy through automation – reliable and reproducible results

Sensitivity and specificity

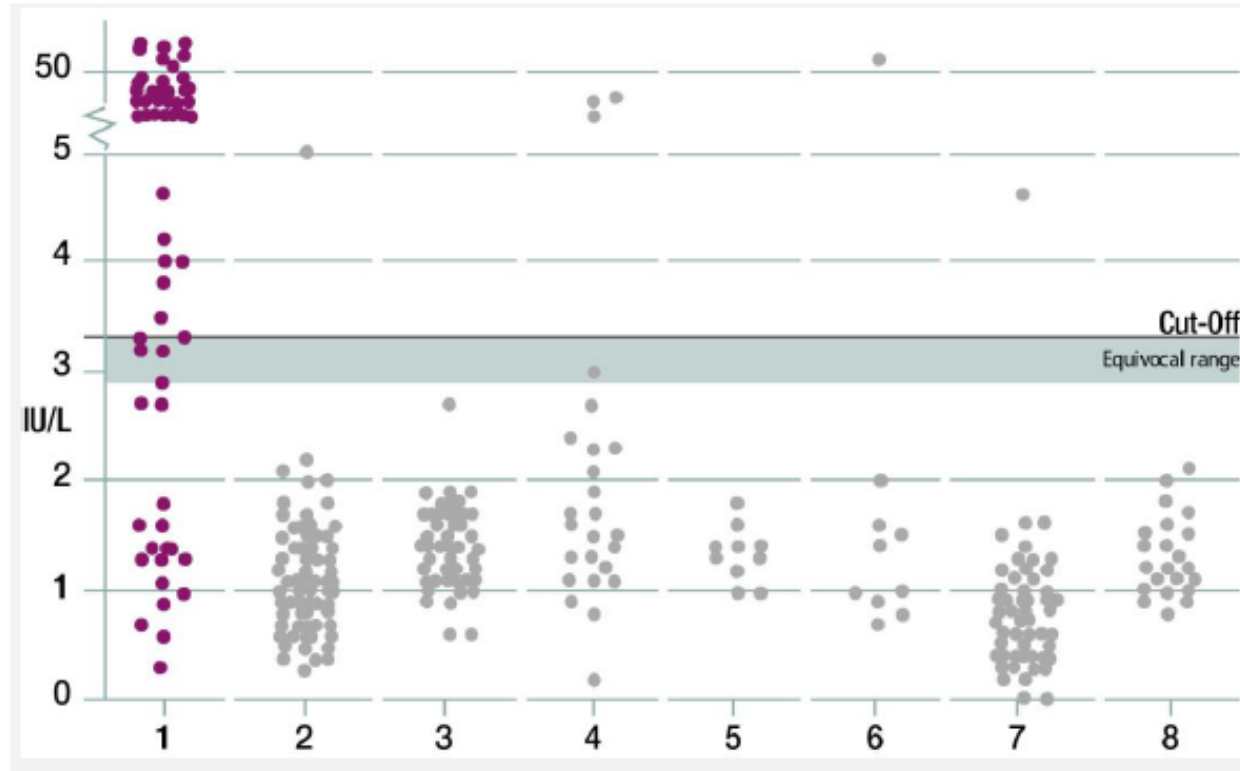
	EliA anti-TSH-R (equivocal = neg)	Supplier 1	Supplier 2
Sensitivity (%)	79.0	85.0	84.0
Specificity (%)	97.7	92.0	94.0
LR+	33.9	10.6	14.0
LR -	0.22	0.16	0.17

Internal study of 400 clinically defined serum samples: 100 Graves' disease patients (treated + untreated) and 300 disease controls (100 Hashimoto's thyroiditis, 50 non-autoimmune thyroid diseases, 25 CTD/SLE, 10 IBD, 10 PBC, 80 infectious diseases including: HIV, HBV, HCV and other infections), and 25 cancer¹

- EliA anti-TSH-R is designed to have the highest clinical relevance with an optimized combination of sensitivity and specificity

A high specificity and good sensitivity helps in the clinical diagnosis of Graves' disease

Differentiate Graves' disease from other diseases with EliA anti-TSH-R



Anti-TSH-R is mostly prevalent in Graves' disease^{1,2,3}

Total clinically defined samples (n=400)

Patients

1: Graves' disease - treated and untreated (n=100)

Disease controls

2: Hashimoto's thyroiditis (n=100)

3: Non autoimmune thyroid diseases (n=50)

4: Connective tissue disease (CTD n=25)

5: Inflammatory bowel disease (IBD; n=10)

6: Primary biliary cirrhosis (PBC; n=10)

7: Infectious diseases (e.g. HBV, HCV, HIV; n=80)

8: Cancer (n=25)

Equivocal range for better diagnostic guidance

	Cut-Off (IU/L)		
	Negative	Equivocal	Positive
EliA anti-TSH-R	<2.9	2.9–3.3	>3.3

Antibody titers of patients:

- Usually decline under treatment and might be found in the equivocal range^{1,2}
- Are influenced by lifestyle (e.g. smoking, pregnancy)²
- Vary up to 10-fold among different Graves' disease patients^{3,4}

EliA anti-TSH-R uses human recombinant TSH-R

Human antigen for human antibody detection without contaminating proteins¹ – NOT purified from animal thyroid glands

No contamination with other proteins potentially causing lower specificity

Production with high purity and reproducibility in eukaryotic expression system¹

High lot-to-lot consistency – maximum accuracy and precision within and between lots²

State of the art recombinant antigen leading to clinically relevant results on a fully automated standardized laboratory system

EliA anti-TSH-R is calibrated using the most recent standard

- EliA anti-TSH-R is calibrated against the World Health Organisation 2nd International Standard for Thyroid Stimulating Antibody: NIBSC 08/204
- EliA anti-TSH-R result is displayed in IU/L

GOOD TO KNOW

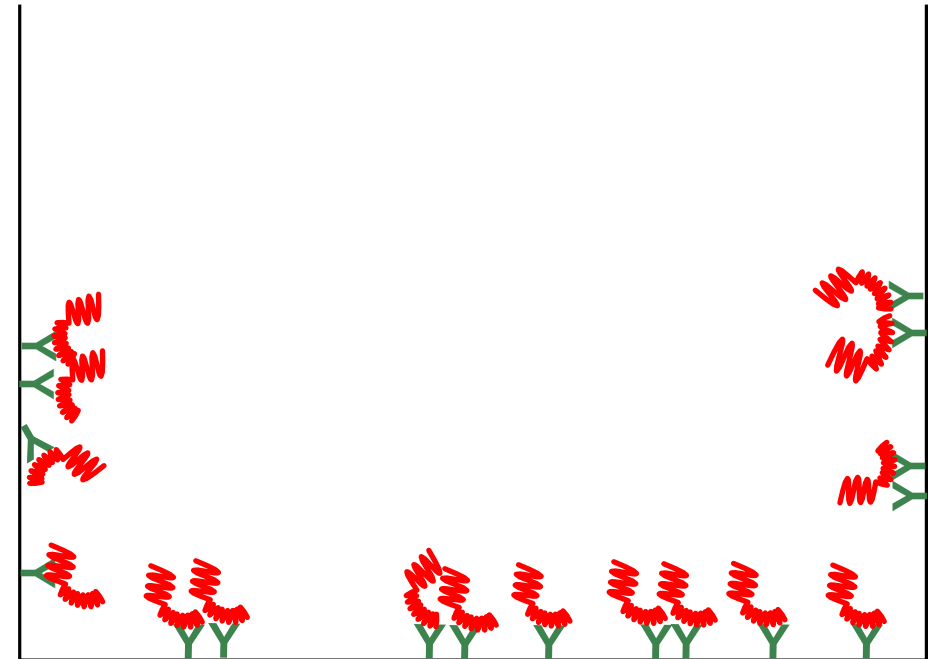
Results from assays which use different standards should not be compared quantitatively¹

Results from assays using the same standard but apply a different assay design should not be compared quantitatively¹

Coating Concept competitive EliA

Desing of the well:

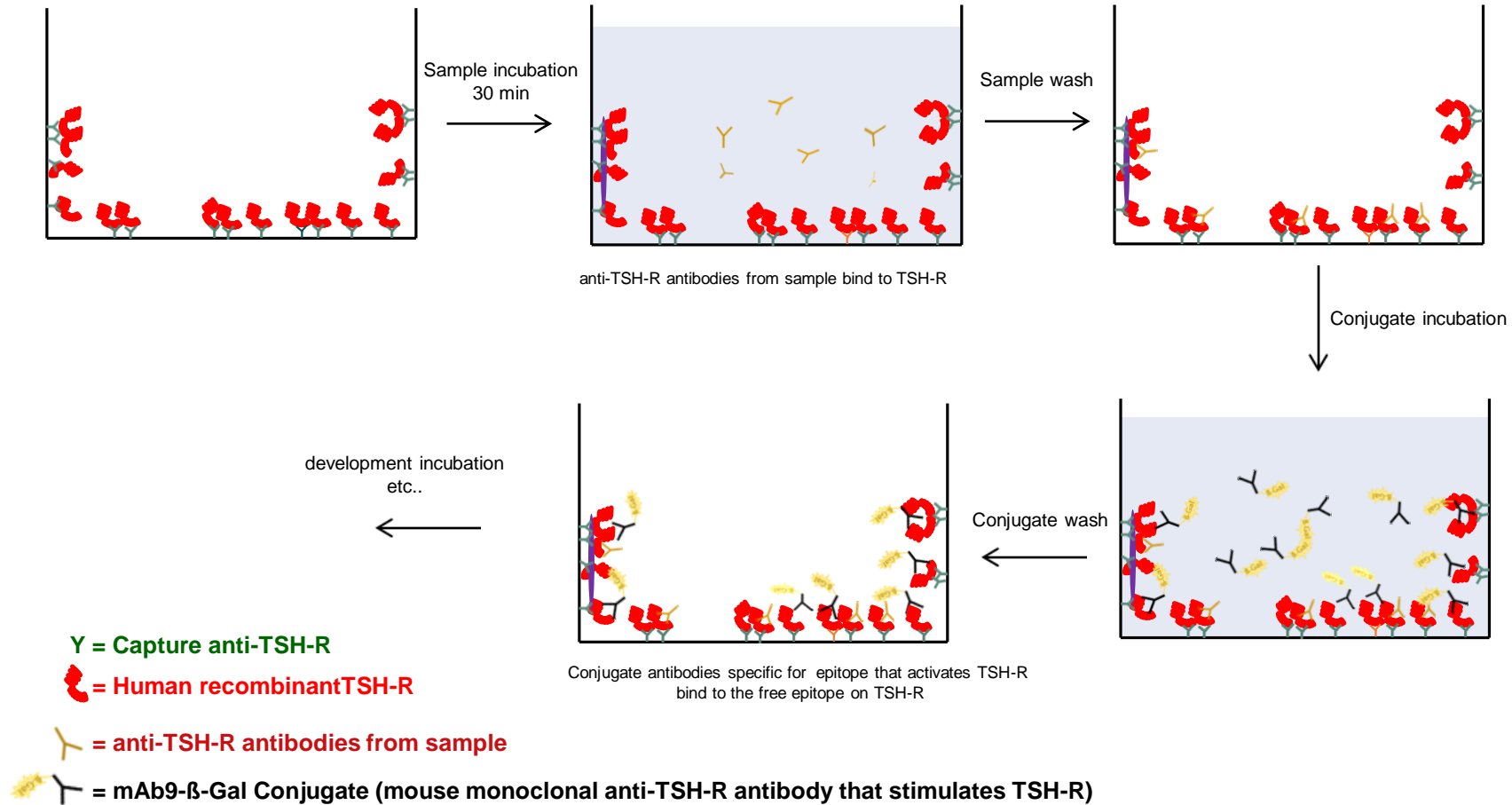
Recombinant human TSH-R immobilized via capture antibody to well



Y= capture anti TSH-R

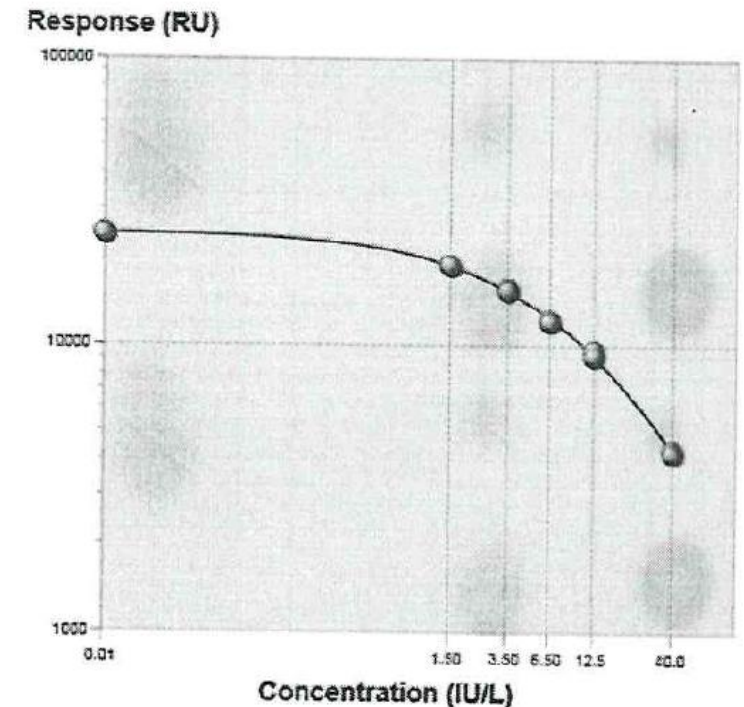
☞ = human recombinant TSH-R

Coating Concept competitive EliA



What it's different compared to other EliA tests? abacus dx

- First competitive assay
- Only serum and not plasma specimen
- The curve will be the other way round
- First EliA test with a 1:2 dilution
- Unique and less sample diluent
- One common thyroid positive control
- Same negative IgG, IgM, IgA QC
- Prime - mandatory



EliA anti-TSH-R on fully automated Phadia Laboratory Systems

abacus dx

Easily integrates into existing workflows

EliA anti-TSH-R can be performed at the same time as EliA and ImmunoCAP tests – eliminating the need to batch

Provides flexibility to the laboratory

EliA anti-TSH-R, EliA anti-TPO, EliA anti-TG from one sample in one run

Increases operational efficiency

Full automation decreases hands-on time, increases accuracy and reproducibility of test results

***EliA anti-TSH-R is currently available on the P250, in development on Phadia2500/5000**

EliA TSH-R

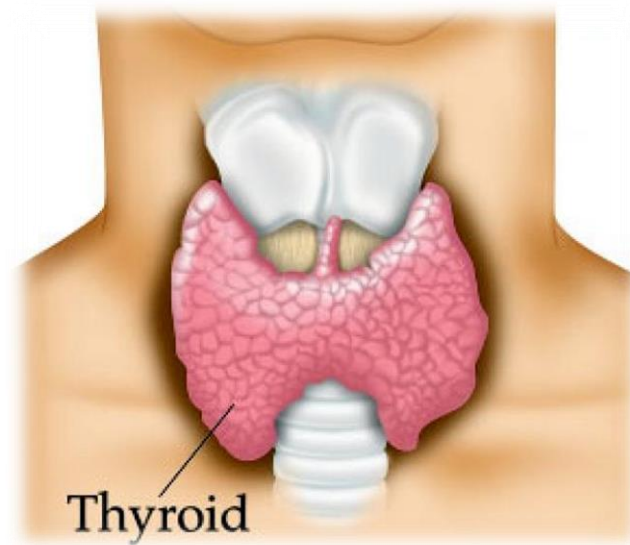
Anti = antibodies against

T = thyroid

S = stimulating

H = hormone

R = receptor



The TSH receptor in the **EliA anti-TSH-R** is a human recombinant protein which is **also used** in the well established **BRAHMS TRAK human tests** from **Thermo Fisher Scientific**.

B·R·A·H·M·S TRAK human **it's considered the gold standard** for differential diagnosis and follow-up in Graves' disease.

Clinical performance of EliA™ anti-TSH-R

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Abstract

Background

The thyroid-stimulating hormone receptor (TSH-R) is, together with the thyroid-stimulating hormone (TSH), a key protein in the regulation of thyroid function. The TSH-R is a primary antigen in Graves' disease (GD) hyperthyroidism, and the presence of TSH-R specific antibodies is a diagnostic criterion for this condition. Lately, automated assays measuring TSH-R specific antibodies have been found useful in the diagnosis of particularly GD.

Aim

The objective of this study was to analyze the performance of the automated quantitative EliA anti-TSH-R test (Phadia AB, Uppsala, Sweden) designed to measure serum antibodies specific for epitopes in the TSH-binding domain of the TSH-R using a competitive assay design. EliA anti-TSH-R test performance was analyzed using 100 clinically defined serum samples from untreated and treated GD patients. Serum samples from 100 individuals diagnosed with Hashimoto's thyroiditis and 200 patients diagnosed with other diseases served as disease controls. For comparison, two automated tests for the measurement of anti-TSH-R antibodies from different manufacturers were included in this analysis. These tests differ from EliA anti-TSH-R in not having an equivocal range.

Results

In this study, EliA anti-TSH-R showed a high sensitivity of 79% and an excellent specificity of 97.7%. Considering samples found within the equivocal range as positive, the sensitivity was 83% and the specificity 97.3%. Compared to the assays of manufacturer 1 and 2, EliA anti-TSH-R showed a similar sensitivity but a higher specificity. The overall agreement with manufacturer 1 and 2 was 93.2% and 95.3%, respectively.

Conclusion

Good clinical performance was demonstrated for the EliA anti-TSH-R test, with high sensitivity and outstanding specificity. EliA anti-TSH-R was found to support the diagnosis and assessment of patients with GD.

thermoscientific

Assay	Agreement with BRAHMS TRAK human RIA	Correlation with BRAHMS TRAK human RIA
EliA anti-TSH-R	95%	0.91 [#]
Manufacturer 2	95%	Not determined [*]

Table 2: Agreement and Pearson correlation coefficient of EliA anti-TSH-R and a different automated anti-TSH-R test (manufacturer 2) with BRAHMS TRAK human RIA (# 4 GD samples were found above the measuring range of EliA anti-TSH-R and not included for the calculation of the correlation coefficient; ^{*}20 Graves' disease samples and 6 disease controls were found above the measuring range of the manufacturer 2 test. Therefore, the correlation was not determined).

Thank you

For your attention