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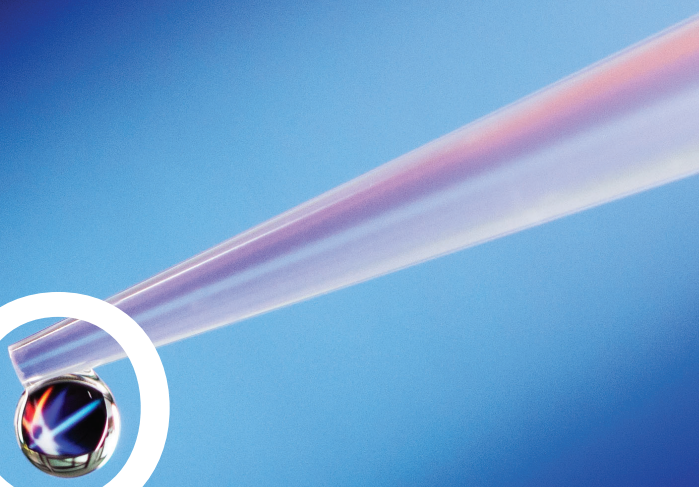

Hormones | Thyroid

Technical Note

Medix Biochemica

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Introduction

The thyroid gland is one of the most important components of the endocrine system. The hormones produced by the thyroid gland play key roles in regulating our metabolism, body temperature, blood pressure, and heart rate.

The main hormone produced by the thyroid gland is thyroxine (T4), which is converted into triiodothyronine (T3) in the tissues. T4 production by the thyroid gland is regulated by the pituitary gland, through the secretion of thyroid stimulating hormone (TSH). Thyroid disorders are common, and can cause a range of different symptoms with wide reaching health impacts. Hyperthyroidism, for example, is a condition with elevated circulating free thyroid hormones, whereas hypothyroidism is characterized by a lack of thyroid hormones. Both conditions can be caused by autoimmune disorders, such as Graves' disease that leads to an overactivity of the thyroid gland, or Hashimoto's thyroiditis, in which the thyroid gland is inactivated by antithyroid autoantibodies. The prevalence of thyroid diseases is about ten times higher in women than in men. Early detection of thyroid disorders and consistent treatment monitoring by accurate and specific diagnostic tests are essential for patients' wellbeing in all thyroid-related diseases.

Medix Biochemica has over 35 years of experience in producing premium-quality monoclonal antibodies for detection of thyroid hormones. Our optimized, industrial-scale in vitro production methods, certified batch-to-batch consistency, as well as expert customer service have made Medix Biochemica one of the most important antibody suppliers for the IVD community. Medix Biochemica also offers a large variety of antigens and biospecimens that can be used for assay validations and as control materials.

In this technical note, we present Medix Biochemica hormone products related to thyroid health with a focus on items for which we have produced technical data. The results shown are from prototype assays (unoptimized), indicating proof of concept with clinical samples. Further assay optimization may be required to obtain the best performance. The full item lists can be found on www.medixbiochemica.com under each analyte.

Thyroglobulin (Tg)

Thyroglobulin is the predominant protein produced by the thyroid gland. This homodimeric 660 kDa glycoprotein acts as a substrate for the synthesis of the thyroid hormones triiodothyronine (T3) and thyroxine (T4). In addition, this T3 and T4 precursor serves as a storage protein for iodide that ensures sufficiency of this essential element.[1]

Thyroglobulin is also produced by thyroid cancer cells, and is thus commonly used to monitor the treatment of cancer patients who have undergone thyroidectomy.

However, as thyroglobulin is also produced by normal thyroid cells, it is not suitable as a diagnostic cancer biomarker. Blood thyroglobulin levels can also be elevated in some cases of Grave's disease. Thyroglobulin has recently been suggested a potential biomarker for iodine deficiency.[1–4]

Medix Biochemica's product selection contains several anti-thyroglobulin mouse monoclonal antibodies and a native antigen.

Anti-human Tg monoclonal antibodies and antigens

Tg Antibody	Catalog #	Concentration (mg/mL)	Shelf Life (Months at +2–8°C)	Subclass	Applications Tested
2802	100331	5	24	IgG_1	ELISA
2803	100332	5	36	IgG_{2b}	ELISA
2804	100333	5	36	IgG_1	ELISA
2805	100334	5	36	IgG_1	ELISA

Tg Antigen	Purity	Catalog #
Native Tg, human thyroid, lyophilized	≥ 95%	528-11

Pair recommendations

		Detection			
		2802	**2803**	**2804**	**2805**
Capture	**2802**	–	–	+	+
	2803	–	–	+	+
	2804	–	–	–	–
	2805	+	+	+	–

FIA: 2802 (capture) - 2805 (detection)

Kinetic parameters

Tg Antibody	Association Rate Constant, k_{on} (1/Ms)	Dissociation Rate Constant, k_{off} (1/s)	Dissociation Constant, K_D (M)
2802	8.6×10^{3}	1.2×10^{-5}	1.4×10^{-9} = 1.4 nM
2803	1.7×10^{5}	3.7×10^{-5}	2.2×10^{-10} = 0.22 nM
2804	7.2×10^{4}	7.9×10^{-4}	1.1×10^{-8} = 11 nM
2805	6.2×10^{5}	1.3×10^{-5}	2.1×10^{-11} = 0.02 nM

Thyroid Stimulating Hormone (TSH)

Thyroid stimulating hormone (TSH, also known as thyrotropin) is a glycoprotein hormone secreted by the anterior pituitary gland. In response to TSH, the thyroid gland secretes the hormone thyroxine (T4) that is converted into triiodothyronine (T3) in the liver and other organs. As T3 affects several cellular metabolic pathways, TSH is considered a key regulator of the normal development and metabolism of the body.

TSH is an approximately 30 kDa heterodimeric protein formed by two noncovalently linked subunits, alpha and beta. The alpha subunit is shared with human FSH, hCG, and LH. The structure is stabilized by a unique segment of the beta subunit, called the seatbelt, which is wrapped around the alpha subunit.[1,2]

In clinical diagnostics, measurements of serum TSH are most often used to diagnose and manage thyroid disorders, including both hyperthyroidism (overactive thyroid) and hypothyroidism (underactive thyroid). TSH levels often change before other thyroid hormone levels in the body become too low or high, making it a good early indicator for issues in thyroid function.[3] Reported TSH levels have varied historically depending on the test method or platform used, and different organizations have recommended different reference intervals for normal TSH levels. In general, levels between 0.4 to 4 mIU/L are now considered normal in adults, excluding pregnant women. The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) initiated standardization and harmonization efforts for free T4 and TSH levels, and is currently working with national partners on implementing these reference systems. Their aim is in making results obtained with different diagnostic systems and at different time points more comparable to each other. [4, 5]

Medix Biochemica has been a leading provider of monoclonal antibodies recognizing human TSH for more than 35 years. We offer a wide selection of mouse monoclonal antibodies against both the alpha subunit and the full human TSH as well as antigens.

Scientific publications: page 11

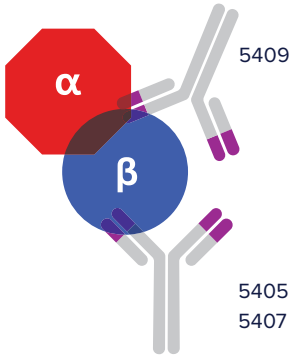
Anti-human TSH monoclonal antibodies and antigens

TSH Antibody	Catalog #	Concentration (mg/mL)	Shelf Life (Months at +2–8°C)	Subclass	Applications Tested
5401	100023	1	12	IgG_1	ELISA ,CLIA, LF
5404	100026	5	36	IgG_1	ELISA, CLIA, LF
5405	100819	5	36	IgG_{2a}	ELISA, CLIA, LF
5407	100254	5	24	IgG_1	ELISA, CLIA, LF
5408	100033	1	36	IgG_1	ELISA, CLIA, LF
5409	100034	5	36	IgG_1	ELISA, CLIA, LF

TSH Antigen	Purity	Catalog #
Native TSH, human pituitary, lyophilized	≥ 95%	996-51
Recombinant TSH	N/D	610175

Pair recommendations

		Detection					
		5401	5404	5405	5407	5408	5409*
Capture	5401	–	–	+	+	–	+
	5404	–	–	+	+	–	+
	5405	–	–	–	–	+	+[A]
	5407	–	–	–	–	+	+[A]
	5408	–	–	+	+	–	+
	5409*	–	–	+	+	–	–



* Recognizes an epitope at the junction of alpha and beta subunits in hTSH
A) Recommendation for detection of TSH with highest sensitivity

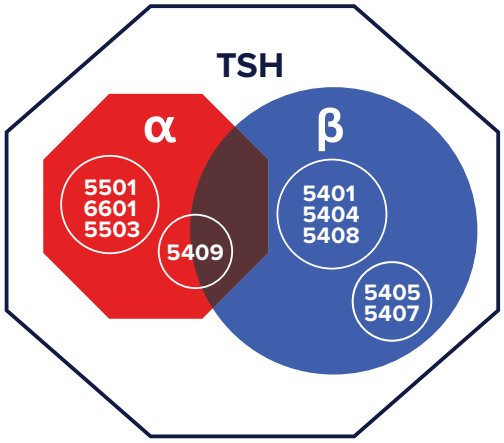
CLIA: 5405 (capture) – 5409 (detection), 5407 – 5409 and 5409 – 5407
LF: 5405 (membrane) – 5409 (particles), 5407 – 5409, 5408 – 5405, 5408 – 5407, 5408 – 5409, 5409 – 5407

Kinetic parameters

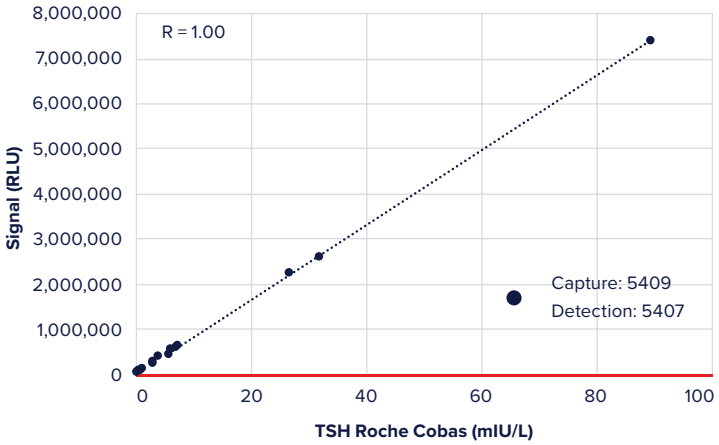
TSH Antibody	Association Rate Constant, k_{on} (1/Ms)	Dissociation Rate Constant, k_{off} (1/s)	Dissociation Constant, K_D (M)
5401	3.6×10^{5}	7.0×10^{-5}	2.0×10^{-10} = 0.20 nM
5404	8.5×10^{5}	3.9×10^{-5}	4.6×10^{-11} = 0.05 nM
5405	1.2×10^{6}	1.9×10^{-4}	1.5×10^{-10} = 0.15 nM
5407	1.1×10^{6}	2.0×10^{-4}	1.8×10^{-10} = 0.18 nM
5408	9.6×10^{5}	3.8×10^{-5}	4.0×10^{-11} = 0.04 nM
5409	2.1×10^{6}	1.0×10^{-4}	4.8×10^{-11} = 0.05 nM

Epitope regions

TSH antibodies can be divided into different epitope groups. Antibodies in the same group detect the same or overlapping epitopes.



Correlation of TSH CLIA assay



TSH detection from clinical samples with Medix Biochemica antibody pair showed excellent correlation to results obtained with CLIA reference method (Roche Cobas assay).

Thyroxine (T4)

Thyroxine, or 3,5,3',5'-tetraiodothyronine (T4) is a small hapten prohormone synthesized and secreted by the thyroid gland. T4 is secreted in the bloodstream, where almost all of it is bound to three major serum transport proteins: mostly thyroxine-binding globulin (TBG), but also transthyretin and human serum albumin. Only 0.02 to 0.03% of total serum T4 circulates in the unbound form. The thyroid-hormone-binding plasma proteins are evenly distributed to maintain a stable T4 concentration in the body. The thyroid gland secretes an estimated 110 nmol of T4 daily. T4 synthesis is controlled by thyroid stimulating hormone (TSH). Secreted T4 binds to the nuclear thyroid hormone receptor (TR), which is involved in the regulation of all intermediary metabolic processes of carbohydrates, lipids, and proteins. T4 also serves as a reservoir for the more metabolically active thyroid hormone, T3, which can be produced from T4 by deiodination. In the fetus and during childhood, thyroid hormones are critical for functions such as brain development, neuronal differentiation, and formation of neural processes.[1-4]

Medix Biochemica offers anti-T4 mouse monoclonal antibodies and a conjugated antigen, which can be used for a competitive immunoassay for T4 detection.

Anti-T4 monoclonal antibodies and antigens

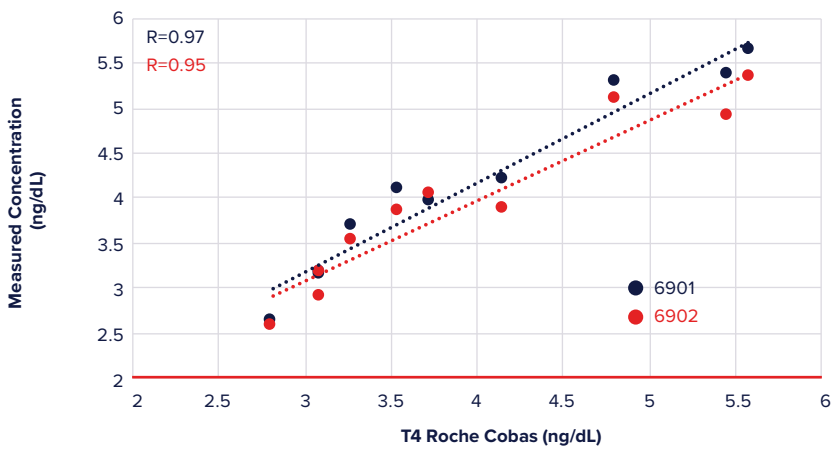
T4 Antibody	Catalog #	Concentration (mg/mL)	Shelf Life (Months at +2–8°C)	Subclass	Applications Tested
6901	100348	5	36	IgG_1	ELISA
6902	100801	5	18	IgG_1	ELISA

T4 Antigen	Catalog #
T4 BSA conjugate	581-10

Kinetic parameters

T4 Antibody	Association Rate Constant, k_{on} (1/Ms)	Dissociation Rate Constant, k_{off} (1/s)	Dissociation Constant, K_D (M)
6901	1.2×10^6	9.3×10^{-5}	8.2×10^{-11} = 0.08 nM
6902	1.7×10^6	Does not dissociate under tested conditions	

Correlation of T4 CLIA assay



T4 detection from clinical samples with Medix Biochemica antibodies as part of competitive assay showed good correlation with reference chemiluminescence immunoassay (CLIA) method (Roche Cobas assay).

Triiodothyronine (T3)

Triiodothyronine (T3) is a 651 Da thyroid hormone secreted by the thyroid gland into our bloodstream. A majority, approximately 80%, of the T3 in the blood originates from conversion of T4 (thyroxine) into T3 by deiodination in organs like kidneys and liver. Nearly all of T3 and T4 in the bloodstream is bound to plasma proteins and free hormone levels are in the picomolar range.

T3 is the metabolically active form of thyroid hormones. It plays a vital role in many bodily functions such as metabolic rate, heart function, muscle control and brain development and function. T3 can be measured with TSH and T4 levels to diagnose thyroid disorders, especially overactive thyroid (hyperthyroidism).[1-2]

Medix Biochemica offers an antibody and antigen pair which can be used for competitive immunoassay development for detecting T3.

Anti-human T3 monoclonal antibodies and antigens

T3 Antibody	Catalog #	Concentration (mg/mL)	Shelf Life (Months at +2–8°C)	Subclass	Applications Tested
10550	700015	> 1.0	60	IgG_1	ELISA

T3 Antigen	Catalog #
T3 BSA conjugate	581-05

Kinetic parameters

T3 Antibody	Association Rate Constant, k_{on} (1/Ms)	Dissociation Rate Constant, k_{off} (1/s)	Dissociation Constant, K_D (M)
10550	1.3×10^{6}	8.4×10^{-5}	6.9×10^{-11} = 0.07 nM

Biospecimens

Medix Biochemica offers a wide range of biospecimens related to thyroid dysfunction and testing which can be used as control and test materials for immunoassay development as well as confirmatory/exploratory research purposes. Additionally, Medix Biochemica offers custom biological collections to tailor to your needs including, but not limited to, custom collection containers, protocols, donor inclusion/exclusion criteria, and donor questionnaires.

Product: Urine
Use: Urine has been used for monitoring and detection of thyroid issues. Women that are either pregnant or over 30 as well as individuals over 60 are more likely to develop thyroid issues as compared to the general population. Furthermore, those diagnosed with either type 1 or type 2 diabetes are at increased risk of developing thyroid disorders.

Product	Catalog #
Urine, normal, pooled	991-03-P
Urine, normal, single	991-03-S
Urine, normal, female	991-03-F
Urine, pregnancy samples, 1st trimester	991-03-PT1
Urine, pregnancy samples, 2nd trimester	991-03-PT2
Urine, pregnancy samples, 3rd trimester	991-03-PT3
Urine, normal, ages 31–40 years old	991-03-AS2
Urine, normal, ages 41–50 years old	991-03-AS3
Urine, normal, ages 51–64 years old	991-03-AS4
Urine, geriatric, ages 65–74 years old	991-03-GER1
Urine, geriatric, ages 75–84 years old	991-03-GER2
Urine, geriatric, ages 85+ years old	991-03-GER3
Urine, type 1 diabetes	991-03-D1
Urine, type 2 diabetes	991-03-D2

Product: Saliva
Use: Saliva is a non-invasive sampling method used to measure levels of free thyroid hormones and monitor thyroid health. Women that are either pregnant or over 30 as well as individuals over 60 are more likely to develop thyroid issues as compared to the general population.

Product	Catalog #
Saliva, normal, pooled	991-05-P
Saliva, normal, single	991-05-S
Saliva, pregnancy samples, 1st trimester	991-05-PT1
Saliva, pregnancy samples, 2nd trimester	991-05-PT2
Saliva, pregnancy samples, 3rd trimester	991-05-PT3
Saliva, normal, ages 31–40 years old	991-05-AS2
Saliva, normal, ages 41–50 years old	991-05-AS3
Saliva, normal, ages 51–64 years old	991-05-AS4
Saliva, geriatric, ages 65–74 years old	991-05-GER1
Saliva, geriatric, ages 75–84 years old	991-05-GER2
Saliva, geriatric, ages 85+ years old	991-05-GER3

Product: Whole blood, plasma & serum
Use: Whole blood is used as a direct method for measuring many thyroid hormones and antibodies and assess thyroid health.

Product	Catalog #
Whole blood, normal, pooled	991-50-P
Whole blood, normal, single	991-50-S
Anti-thyroid peroxidase (anti-TPO) positive human plasma	991-58-S-ATPO

The standard single and pooled catalog numbers are above; however, Medix Biochemica is capable of sourcing high quality human donor samples through customized collections to meet the needs of the diagnostic market.

Please inquire about customization of the biological fluids listed here or for details about other biospecimens that are relevant to your needs.

Discover Complete List of Biospecimens

Analyte List

Full range of antibodies and antigens primarily used for assessing thyroid health offered by Medix Biochemica.

	Antibody	Antigen
Calcitonin	✓	
Thyroglobulin (Tg)	✓	✓
Thyroid stimulating hormone (TSH)	✓	✓
Thyroxine (T4)	✓	✓
Thyroxine binding globulin (TBG)		✓
Triiodothyronine (T3)	✓	✓

Discover Our Hormones Portfolio

Page 4

Scientific articles describing the use of Medix Biochemica's monoclonal anti-TSH antibodies include:

- von Lode P, Hagren V, Palenius T & Lövgren T (2003). One-step quantitative thyrotropin assay for the detection of thyrotropin assay for the detection of hypothyroidism in point-of-care conditions. Clin Biochem 36:121–128.
- Wu FB, Han SQ & He YF (2002). Time-resolved immunofluorometry of serum hTSH with enhanced sensitivity. J Immunoassay Immunochem 23:191–210.
- Helenius T & Tikanoja S (1986). A sensitive and practical immunoradiometric assay of thyrotropin. Clin Chem 32:514–518.

References:

Thyroglobulin:

1. Di Jeso B & Arvan P (2016). Thyroglobulin from molecular and cellular biology to clinical endocrinology. Endocr Rev 37:2–36
2. American Thyroid Association (2014). Thyroid Function Tests. Available in: https://www.thyroid.org/wp-content/uploads/patients/brochures/FunctionTests_brochure.pdf (Accessed 06/2023).
3. Ma ZF & Skeaff SA (2014). Thyroglobulin as a biomarker of iodine deficiency: a review. Thyroid 24:1195–1209.
4. van de Graaf SA, Ris-Stalpers C, Pauws E et al. (2001). Up to date with human thyroglobulin. J Endocrinol 170:307–321.

TSH:

1. Grossmann M, Szkudlinski MW, Wong R et al. (1997). Substitution of the seat-belt region of the thyroid-stimulating hormone (TSH) beta-subunit with the corresponding regions of choriogonadotropin or follitropin confers luteotropic but not follitropic activity to chimeric TSH. J Biol Chem 272:15532–15540.
2. Szkudlinski MW, Fremont V, Ronin C & Weintraub BD (2002). Thyroid-stimulating hormone and thyroid-stimulating hormone receptor structure-function relationships. Physiol Rev 82:473–502
3. American Thyroid Association (2014). Thyroid Function Tests. Available in: https://www.thyroid.org/wp-content/uploads/patients/brochures/FunctionTests_brochure.pdf (Accessed 06/2023).
4. Thienpont LM, van Uytfanghe K, van Houcke S et al. (2014). A progress report of the IFCC committee for standardization of thyroid function tests. Eur Thyroid J 3:109–116.
5. Vesper HW, Van Uytfanghe K, Hishinuma A et al. (2021). Implementing reference systems for thyroid function tests – A collaborative effort, Clinica Chimica Acta, 519:183-186.

T4:

1. Hulbert AJ (2000). Thyroid hormones and their effects: a new perspective. Biol Rev Camb Philos Soc 75:519–631.
2. Moreno M, de Lange P, Lombardi A et al. (2008). Metabolic effects of thyroid hormone derivatives. Thyroid 18:239–253
3. Pharoah P, Buttfield IH & Hetzel BS (2012). Neurological damage to the fetus resulting from severe iodine deficiency during pregnancy. Int J Epidemiol 41:589–592.
4. American Thyroid Association (2014). Thyroid Function Tests. Available in: https://www.thyroid.org/wp-content/uploads/patients/brochures/FunctionTests_brochure.pdf (Accessed 06/2023).

T3:

1. American Thyroid Association (2014). Thyroid Function Tests. Available in: https://www.thyroid.org/wp-content/uploads/patients/brochures/FunctionTests_brochure.pdf (Accessed 06/2023).
2. Hulbert AJ (2000). Thyroid hormones and their effects: a new perspective. Biol Rev Camb Philos Soc 75:519–631.

Medix Biochemica

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CPS = Counts per second
CLIA = Chemiluminescence immunoassay
ELISA = Enzyme-linked immunosorbent assay
FIA = Fluoroimmunoassay
IT = Immunoturbidimetry
LF = Lateral flow
N/A = Not Applicable
N/D = Not Determined
RLU = Relative Light Units

The results shown in this technical note are from prototype assays (unoptimized), indicating proof of concept with clinical samples. Further assay optimization may be required to obtain the best performance.