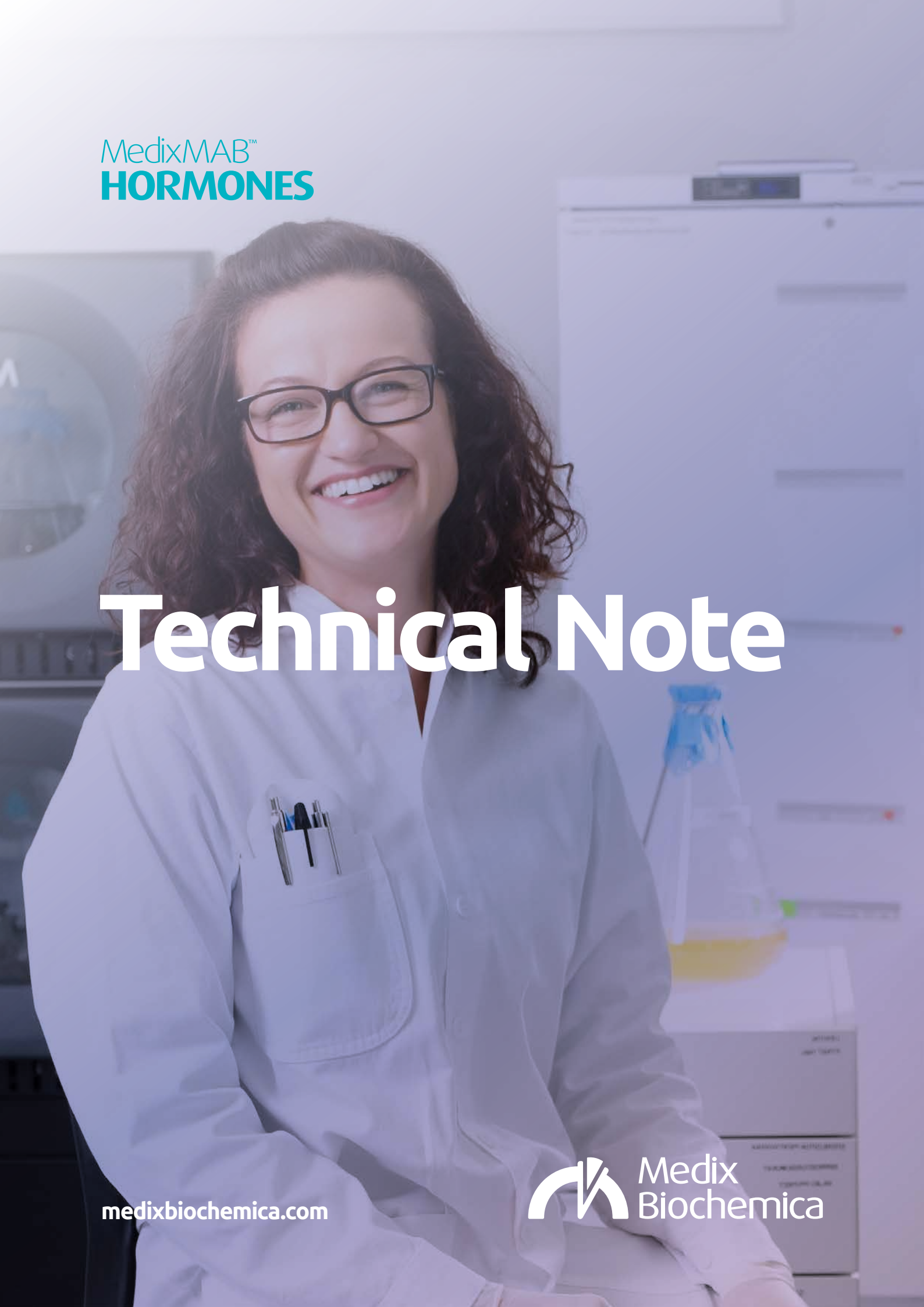
MedixMAB™
HORMONES

Technical Note



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Contents

Introduction

Hormones are a diverse group of signaling molecules produced mainly by the endocrine glands. They control a vast array of essential processes ranging from reproduction, sexual differentiation, development and growth to the regulation of metabolism and maintenance of cellular homeostasis. Due to the large diversity of cellular and bodily processes controlled by hormones, there are also various disorders related to defective endocrine functions. For example, several tumors, including thyroid, testicular and ovarian tumors, are assumed to be endocrine-dependent and have the potential to promote their own growth by excess hormone production.

Clinical manifestations of endocrine disorders, however, are often indefinite and nonspecific. Accordingly, laboratory measurements are usually required to diagnose disease and to monitor therapeutic outcomes. Since hormone levels in bodily fluids are relatively low, reliable quantification of hormones often requires sensitive assays, which are usually immunoassays based on monoclonal antibodies that specifically recognize the target analyte. In addition to disorders and malignancies, hormone levels can also be used to monitor normal bodily processes. For example, immunoassays for human chorionic gonadotropin (hCG) are used for pregnancy detection and monitoring, while different hCG forms can also be used to detect trophoblastic tumors or pregnancy-related disorders. Human luteinizing hormone (LH) is often used for predicting ovulation, but it can also be used to investigate menstrual irregularities or to diagnose puberty-related disorders.

Medix Biochemica has over 30 years of experience in producing premium-quality monoclonal antibodies for detection of hCG, LH, and other hormones. The company's 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.

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). 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. Recently, the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) has initiated standardization and harmonization efforts, with very promising results.[3]

Medix Biochemica has been a leading provider of monoclonal antibodies recognizing human TSH for more than 30 years. We offer a wide selection of mouse monoclonal antibodies against both the alpha subunit and the full human TSH.

An independent laboratory conducted a large TSH study using 40 human clinical samples and all commercially available anti-TSH antibodies. Of all the tested antibodies, the best sensitivity was achieved with Medix Biochemica's TSH monoclonal antibodies (capture antibody 5405 or 5407 and label antibody: 5409, unpublished data).

Scientific publications: page 18

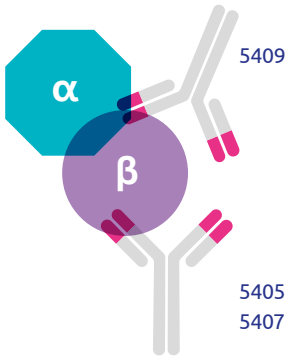
Anti-human TSH monoclonal antibodies

TSH antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
5401	100023	1	12	IgG_1	ELISA ,CLIA
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

Pair recommendations

Capture \ Detection	5401	5404	5405	5407	5408	5409*
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

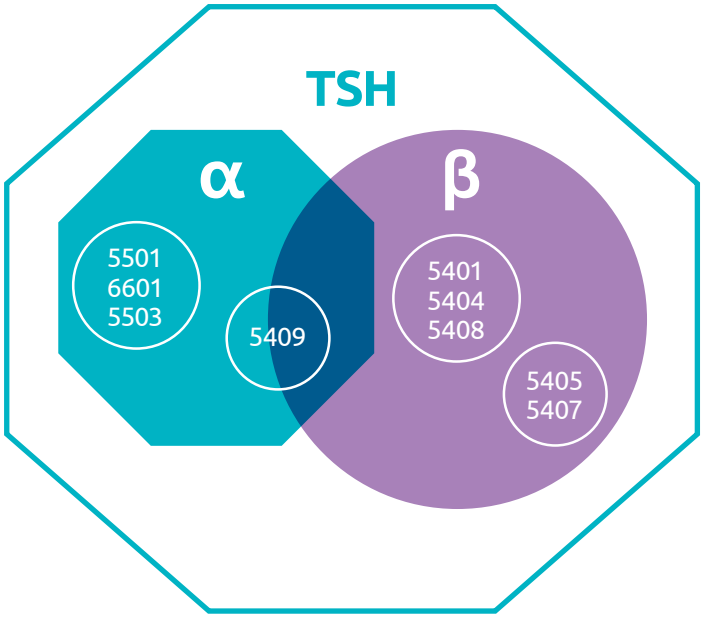


Kinetic parameters

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.



hCG

Human chorionic gonadotropin (hCG) is a glycoprotein hormone essential for the maintenance of pregnancy. Physiologically, this placental hormone is produced and secreted mainly by embryonic trophoblast cells. hCG has several roles at the interface between the mother and the placenta. These roles include stimulating the ovarian corpus luteum to secrete progesterone, maintaining myometrial quiescence, and contributing to maternal immunotolerance towards the embryo. In addition, small amounts of hCG are produced in other tissues, including pituitary, testis, and colon. hCG is also expressed to some extent by several tumors, such as germ cell tumors and trophoblastic cancers, but its exact role in these cancers remains unknown.[4–7]

hCG is a 37.5 kDa heterodimer consisting of two non-covalently linked subunits: hCGα, an alpha subunit identical in all glycoprotein hormones, and hCGβ, a 23.5 kDa subunit unique to hCG that confers its biological specificity. Both hCG subunits are highly glycosylated; the carbohydrate chains attached to the possible glycosylation sites of the molecule make up about 30 percent of the hCG mass. The carbohydrate content of hCG varies substantially between different cell types, with advancing pregnancy, and with tumor progression. Due to this heterogeneity, hCG occurs in biological fluids in different forms, including intact hCG, free hCGβ-subunit, free hCGα-subunit, and other nicked or truncated forms of the molecule. The biological effects of hCG are mediated through its binding to the receptor that recognizes hCGβ, LHCGR, which is also activated by luteinizing hormone (LH). Both subunits are required for the biological activity of hCG.[4,7–10]

The primary clinical use of hCG immunoassays is pregnancy detection. hCG can be detected from maternal blood already during the second week of pregnancy. Urine can also be used for hCG testing. Pregnancy tests are based on antibodies recognizing intact hCG, hCGβ, or both. Additionally, measurement of hCG or its different molecular forms can be utilized for various other clinical purposes, such as pregnancy monitoring, diagnosis of pregnancy-related disorders, prenatal screening (e.g. for Down syndrome), as well as screening for trophoblastic tumors.[4,7,8]

Medix Biochemica has more than three decades of experience in producing hCG mouse monoclonal antibodies for different diagnostic purposes. Currently, the company's products include eight anti-hCG antibodies recognizing either the hCG complex, free hCGβ, or both. The antigen epitopes of hCG recognized by Medix Biochemica antibodies have been extensively characterized.[8]

Scientific publications: page 18

Anti-human hCG monoclonal antibodies

hCG antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
5004	100004	1	36	IgG_1	ELISA, CLIA
5006	100005	5	24	IgG_1	ELISA, CLIA
5008	100006	5	36	IgG_1	ELISA, CLIA
5009	100008	5	18	IgG_1	ELISA
5011	100009	1	24	IgG_1	ELISA
5012	100368	5	36	IgG_1	ELISA, CLIA
5014	100011	5	36	IgG_1	ELISA
5016	100013	5	24	IgG_1	ELISA, CLIA

Pair recommendations

Capture \ Detection	hCG beta								alpha subunit		
	5004	5006	5008	5009*	5011	5012**	5014	5016	5501	5503	6601
5004	–	–	–	+	+	–	+	–	+	+[A]	+[A]
5006	–	–	–	–	–	–	+	–	+	+	+
5008	–	–	–	+	–	–	+[C]	–	+	+	+
5009*	+	+[A]	+	–	–	–	+[A]	+	–	–	+
5011	+	+	+	–	–	–	+	+	–	–	+
5012**	+	+[B]	+	–	–	–	+	+	–	–	–
5014	+	+	+	+	+	–	–	+	+	+	+
5016	–	–	–	–	–	–	+	–	+	+	+

* Recognizes an epitope at the junction of alpha and beta subunits in hCG
** Recognizes only free beta subunit of hCG
A) Recommendation for detecting intact hCG molecule (alpha/beta pair)
B) Recommendation for detecting free beta subunit of hCG
C) Recommendation for detecting total hCG (both intact and free beta subunit of hCG)

Antibodies recognizing alpha subunit are recommended only for detection antibodies, since they also recognize other gonadotropins (including hCG, FSH, LH, and TSH).

Kinetic parameters

hCG antibody	Association rate constant, k_{on} (1/Ms)		Dissociation rate constant, k_{off} (1/s)		Dissociation constant, K_D (M)	
5004	hCG: hCGß:	2.0×10^{6} 5.0×10^{5}	hCG: hCGß:	3.7×10^{-5} 1.2×10^{-4}	hCG: hCGß:	$1.9 \times 10^{-11} = 0.02$ nM $2.3 \times 10^{-10} = 0.23$ nM
5006	hCG: hCGß:	5.7×10^{6} 2.3×10^{6}	hCG: hCGß:	2.9×10^{-4} 4.8×10^{-4}	hCG: hCGß:	$5.0 \times 10^{-11} = 0.05$ nM $2.1 \times 10^{-10} = 0.21$ nM
5008	hCG: hCGß:	4.0×10^{6} 1.6×10^{6}	hCG: hCGß:	1.4×10^{-4} 3.6×10^{-4}	hCG: hCGß:	$3.4 \times 10^{-11} = 0.03$ nM $2.3 \times 10^{-10} = 0.23$ nM
5009	hCG: hCGß:	1.1×10^{6} N/A	hCG: hCGß:	3.1×10^{-4} N/A	hCG: hCGß:	$2.8 \times 10^{-10} = 0.28$ nM N/A
5011	hCG: hCGß:	2.4×10^{6} 1.9×10^{6}	hCG: hCGß:	4.4×10^{-4} 1.1×10^{-3}	hCG: hCGß:	$1.8 \times 10^{-10} = 0.18$ nM $5.7 \times 10^{-10} = 0.57$ nM
5012	hCG: hCGß:	N/A 2.1×10^{4}	hCG: hCGß:	N/A 1.7×10^{-4}	hCG: hCGß:	N/A $8.1 \times 10^{-10} = 0.81$ nM
5014	hCG: hCGß:	2.5×10^{5} 2.8×10^{5}	hCG: hCGß:	1.5×10^{-4} 2.8×10^{-4}	hCG: hCGß:	$6.1 \times 10^{-10} = 0.61$ nM $1.0 \times 10^{-9} = 1.0$ nM
5016	hCG: hCGß:	1.5×10^{6} 1.9×10^{6}	hCG: hCGß:	9.5×10^{-4} 5.2×10^{-3}	hCG: hCGß:	$6.4 \times 10^{-10} = 0.64$ nM $2.8 \times 10^{-9} = 2.8$ nM

Epitopes and specificity

Berger et al. 2013[8]

Product	Epitope	hCG	hCGβ	hCGβcf	hCGn	hCGβn	-CTP hCG	-CTP-hCGβ	ISOBM Ab codes
5004	β_2	✓	✓	✓	✓	✓	✓	✓	402
5006	β_2	✓	✓	✓	✓	✓	✓	✓	388
5008	β_2	✓	✓	✓	✓	✓	✓	✓	390
5016	β_2	✓	✓	✓	✓	✓	✓	✓	408
5012*	β_7		✓	✓					409
5014	β_9	✓	✓		✓	✓	✓	✓	394
5011	β	✓	✓		✓	✓	N/D	N/D	406
5009**	C_2	✓							387
5501	α	✓			✓		✓		383
5503	α	✓			✓		✓		385
6601	α	✓			✓		✓		391

The darker turquoise color indicates strong reactivity.

*) Free beta subunit specific Mab
**) αβ-heterodimer-specific Mab
N/D not determined

Nomenclature of hCG and hCG-related variants:

hCG	Intact αβ heterodimer, bioactive
hCGb	Intact noncombined free hCGβ-subunit, aa hCGβ1-145
hCGbcf	Core fragment of hCGβ; aa hCGβ6-40 linked to hCGβ55-92
hCGn	Nicked αβ heterodimer, nicks in the region of aa hCGβ44-48
hCGbn	Nicked hCGβ, nicks in the region of aa hCGβ44-48
-CTPhCG	hCGβ truncated core hCG, missing most of the hCGβCTP (aa hCGβ121-145)
-CTPhCGβ	hCGβ truncated core hCGβ (aa hCGβ1-120), missing most of the hCGβCTP

Epitope groups of hCG antibodies

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

LH

Human luteinizing hormone (LH), or lutropin, is a glycoprotein hormone produced by the anterior pituitary gland. LH is produced in a pulsatile manner in response to gonadotropin-releasing hormone from the hypothalamus. LH is essential for normal reproduction in both males and females.[11-12]

In females, LH together with follicle-stimulating hormone (FSH) regulates normal ovarian function. During the menstrual cycle, FSH initiates follicle growth leading to a rise in estrogen levels that triggers a peak in LH production, also known as the LH surge. The LH surge results in ovulation, and also stimulates corpus luteum formation and progesterone production, thus preparing the endometrium for possible pregnancy initiation. Furthermore, LH stimulates ovarian theca cells to produce androstenedione, which is converted to the female sex hormone estradiol. In males, LH stimulates testosterone production by the Leydig cells of the testis and is thus responsible for development of puberty, male secondary sexual characteristics, and spermatogenesis.[11–15]

Like other glycoprotein hormones, LH is a heterodimer composed of a common 14 kDa alpha subunit, as well as a unique beta subunit that defines the hormone's functional specificity. The subunits of the 28 kDa LH are non-covalently linked to each other, and both subunits are highly glycosylated. Similar to hCG, the biological functions of LH are mediated through LHCGR binding. However, although LH and hCG activate the same receptor, their molecular properties and expression patterns differ significantly due to their different physiological roles. For example, the serum half-life of LH is less than 120 minutes, while it is several hours for hCG.[13,16]

The clinical indications of assaying LH levels in blood or urine include predicting the timing of ovulation, investigating menstrual irregularities, and diagnosing early or delayed puberty. The LH test is often used in conjunction with other hormonal tests, such as tests for FSH or TSH levels.[17–20]

Medix Biochemica has over three decades of experience in producing high-quality monoclonal anti-LH antibodies. Currently, the company offers four different mouse monoclonal antibodies for LH detection. Two have no cross-reactivity with hCG, TSH, or FSH (clones 5303 and 5304), one has negligible cross-reactivity with TSH and FSH (clone 5301), and one has cross-reactivity to hCG (clone 5302). The association and dissociation constants of the antibodies have been measured using SPR.

Scientific publications: page 18

Anti-human LH monoclonal antibodies

LH antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
5301	100016	5	24	IgG_1	ELISA
5302	100018	1	36	IgG_1	ELISA
5303	100588	5	36	IgG_1	ELISA
5304	100022	5	36	IgG_1	ELISA

Pair recommendations

		Detection				
		LH				alpha subunit
		5301	5302	5303	5304	5501
Capture	5301	–	+	+	+	+
	5302	+	–	–	–	+
	5303	+	–	–	–	–
	5304	+	–	–	–	–

Kinetic parameters

LH antibody	Association rate constant, k_{on} (1/Ms)	Dissociation rate constant, k_{off} (1/s)	Dissociation constant, K_D (M)
5301	5.8×10^{6}	1.3×10^{-5}	2.3×10^{-12} = 2.3 pM
5302	1.3×10^{6}	2.6×10^{-5}	2.1×10^{-11} = 21 pM
5303	5.4×10^{6}	3.4×10^{-5}	6.3×10^{-12} = 6.3 pM
5304	4.7×10^{6}	1.6×10^{-5}	3.4×10^{-12} = 3.4 pM

FSH

Similar to LH, follicle-stimulating hormone (FSH) is a glycoprotein hormone secreted from the anterior pituitary gland under the control of gonadotropin-releasing hormone. FSH is an α/β heterodimer consisting of the glycoprotein hormone alpha subunit and a hormone-specific FSHβ chain. FSHβ is a 119 amino acid peptide with two N-linked glycosylation sites. FSH mediates its biological functions by binding to the FSH receptor (FSHR), which is expressed mainly by ovarian granulosa cells and testicular Sertoli cells, but also by osteoclasts and certain tumor cells.[11,21–23]

FSH has several essential functions related to mammalian development and reproduction. In both sexes, FSH stimulates germ cell maturation. During male development, FSH promotes spermatogonia mitosis and ensures normal testes development by activating proliferation of Sertoli cells. In adult males, FSH maintains normal spermatogenesis and Sertoli cell activities important for testis function and maintenance of male fertility. In females, FSH drives follicle growth and granulosa cell estrogen production. FSH also prevents granulosa cell apoptosis and stimulates their proliferation. Furthermore, there is a small rise in FSH levels at the end of the menstrual cycle luteal phase; this seems to be relevant for the initiation of the next ovulatory cycle. Besides its reproductive roles, FSH has also been associated with postmenopausal bone loss and neovascularization surrounding malignant tumors; however, these functions require further investigation.[11,15,22,24]

Clinically, FSH is commonly used for ovarian stimulation in women who are undergoing infertility treatment or oocyte retrieval. FSH can also be used for treating anovulatory infertility in women or hypogonadotropic hypogonadism in men. LH is often used as a supportive treatment with FSH therapy. FSH tests are often carried out together with an LH test. Assaying serum or urine FSH levels can be used to investigate female infertility, menstrual irregularities, or to diagnose conditions related to ovarian or testicular dysfunction.[15,22,25]

Medix Biochemica offers one FSH-specific mouse monoclonal antibody (6602) that can be used as a pair with an alpha subunit antibody (6601) in diagnostic tests.

Anti-human FSH monoclonal antibody

FSH antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
6602	100067	5	24	IgG_1	ELISA

Pair recommendations

		Detection
		6601 *
Capture	6602	+

* alpha subunit

Kinetic parameters

FSH antibody	Dissociation constant, K_D (M)
6602	$3.0 \times 10^{-11} = 0.03$ nM

Alpha subunit

The alpha subunit is common to all glycoprotein hormones, also known as gonadotropins. The glycoprotein hormones are specific to vertebrates and include hCG, FSH, LH, and TSH. In humans, the alpha subunit consists of 92 amino acids and has an average molecular weight of 14 kDa. In all gonadotropins, the alpha subunit binds non-covalently to the beta subunit forming a heterodimer; each beta subunit is hormone-specific and mediates receptor binding and the specific functions of the glycoprotein hormones. However, the alpha subunit is also required for the biological activity of these hormones.[5,10,26]

Medix Biochemica offers three mouse monoclonal antibodies (5501, 5503, and 6601) for the detection of the human glycoprotein hormone alpha subunit. The association and dissociation characteristics of the binding reaction between the alpha subunit antibodies and the alpha subunit have been measured using multiplexed SPR technology. Anti-human alpha subunit specific antibodies are recommended only as detection antibodies with human glycoprotein hormone (hCG, LH, FSH and TSH) beta subunit specific antibodies. Anti-human alpha subunit antibodies bind to several glycoprotein hormones and therefore are not recommended to be used as capture antibodies.

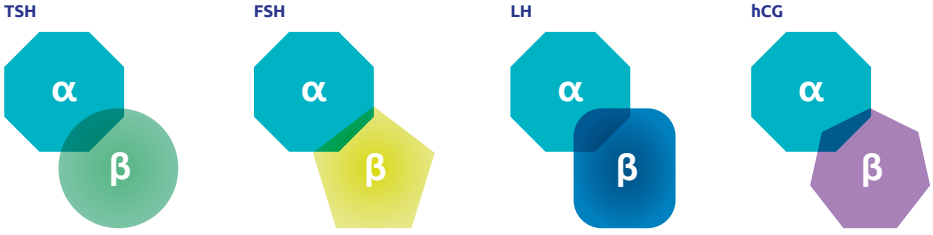
Anti-human alpha subunit monoclonal antibodies

Alpha subunit antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
5501	100035	1	36	IgG_1	ELISA
5503	100037	1	6	IgG_1	ELISA
6601	100066	5	36	IgG_{2a}	ELISA

Kinetic parameters

Alpha subunit antibody	Association rate constant, k_{on} (1/Ms)	Dissociation rate constant, k_{off} (1/s)	Dissociation constant, K_D (M)
5501	1.9×10^{6}	1.1×10^{-3}	5.7×10^{-10} = 0.57 nM
5503	1.7×10^{6}	5.3×10^{-4}	3.2×10^{-10} = 0.32 nM
6601	8.9×10^{5}	3.8×10^{-5}	4.2×10^{-11} = 0.04 nM

Binding of glycoprotein hormones



Glycoprotein hormones (TSH, FSH, LH, and hCG) have an identical alpha subunit (α) and a hormone-specific beta subunit (β).

SHBG

Sex hormone binding globulin (SHBG) is a steroid-binding serum glycoprotein synthesized in the liver. Synthesized SHBG is secreted into the circulation, where it binds the sex hormones testosterone and estradiol with high affinity and specificity. Thus, SHBG regulates sex hormone bioavailability and affects steroid responses by inhibiting their function. Some SHBG is also expressed by testicular germ cells, suggesting that the protein may have influence on sperm function. SHBG serum levels are regulated primarily by sex hormone blood levels, but also e.g. by nutritional factors.[27,28]

SHBG is an approximately 90 kDa homodimeric glycoprotein that is present in blood only as dimer. Dimerization occurs automatically upon synthesis and secretion of the molecule, and is promoted by high-affinity steroid ligands of the hormone. Upon dimerization, eight hydrogen bonds form between β-sheets of the monomers. This leads to an elongated, cylinder-shaped mature dimer.[27,28]

SHBG immunoassays are often used to assess patient testosterone status, such as in male infertility treatment or female hirsutism. In addition, several conditions affect SHBG plasma levels either by increasing or decreasing it. For example, low SHBG levels can indicate diabetes, hypothyroidism, or polycystic ovary syndrome. High SHBG levels may be associated with pregnancy, hyperthyroidism, or anorexia nervosa. Furthermore, recent research has also linked high SHBG levels with breast and testicular cancer. Epidemiological studies indicate that low serum SHBG levels predict a higher risk for metabolic syndrome.[27-29]

Medix Biochemica's selection of mouse monoclonal anti-SHBG antibodies includes three products (6001, 6002, and 6007).

Anti-human SHBG monoclonal antibodies

SHBG antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
6001	100539	5	24	IgG_1	ELISA
6002	100540	5	24	IgG_1	ELISA
6007	100569	5	24	IgG_1	ELISA

Pair recommendations

		Detection		
		6001	6002	6007
Capture	6001	–	+	+
	6002	–	–	–
	6007	+	–	–

Kinetic parameters

SHBG antibody	Association rate constant, k_{on} (1/Ms)	Dissociation rate constant, k_{off} (1/s)	Dissociation constant, K_D (M)
6001	4.1×10^5	4.7×10^{-5}	1.2×10^{-10} = 0.12 nM
6002	1.5×10^5	1.0×10^{-4}	6.8×10^{-10} = 0.68 nM
6007	2.9×10^5	1.1×10^{-4}	3.7×10^{-10} = 0.37 nM

Progesterone

Progesterone (PR) is a steroid hormone produced in the corpus luteum after ovulation and in the placenta during pregnancy. Progesterone is also produced in the adrenal glands. The main functions of progesterone include induction of endometrial transition from a proliferative to a secretory stage during the menstrual cycle, facilitating blastocyst nesting, as well as maintenance of pregnancy. Progesterone also promotes insulin release and may have some neuroprotective effects, including slowing down Alzheimer's disease progression.[30-32]

In women, progesterone levels are generally low (approximately <1 ng/mL) before ovulation and rise thereafter up to 10 to 35 ng/mL. During pregnancy, progesterone levels may reach 100 to 300 ng/mL. In early pregnancy, progesterone measurements are used in addition to hCG measurements for more precise diagnosis of an ectopic or otherwise dysfunctional pregnancy. As low progesterone levels can lead to pregnancy termination, progesterone levels are often monitored during high-risk pregnancies to evaluate and ensure fetal health.[30-31]

Medix Biochemica offers four anti-progesterone mouse monoclonal antibodies (1801, 1802, 1803, and 1805). Due to the small size of the analyte, competitive immunoassay is recommended for progesterone level determination. Progesterone conjugated to BSA from C6 has been used as the immunogen for the production of Medix Biochemica anti-progesterone antibodies.

Anti-human progesterone monoclonal antibodies

PR antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
1801	100248	5	24	IgG_1	ELISA
1802	100249	5	36	IgG_{2a}	ELISA
1803	100250	5	24	IgG_{2a}	ELISA
1805	100252	5	36	IgG_{2a}	ELISA

Prolactin

Prolactin (PRL) is a peptide hormone secreted primarily by the lactotroph cells of the pituitary gland. PRL is also produced by various extrapituitary cells and sites, including immune cells, neurons, prostate, mammary epithelium, and skin. During pregnancy, PRL acts in concert with other hormones, including progesterone and insulin, to promote mammary gland growth and development. In the postpartum period, PRL stimulates lactation by initiating milk synthesis and maintaining its secretion. PRL production reduces the secretion of gonadotropin-releasing hormone, thereby suppressing LH and FSH secretion and inhibiting ovulation. Besides its effects on pituitary-gonadal processes, PRL is involved in various other processes. These include regulating osmotic balance, increasing bile and insulin secretion, and regulating the immune system, for example via stimulation of T and NK cell cytokine expression.[33,34]

PRL is a 23 kDa hormone that consists of 199 amino acids. Structurally, PRL resembles members of cytokine family molecules and consists of a single polypeptide chain with three intramolecular disulfide bonds. The various effects of PRL are mediated by its binding to a specific PRL receptor (PRLR), a type I cytokine receptor family member expressed in various tissues and as several different isoforms. PRL secretion is controlled mainly by dopamine, which inhibits the release of PRL. There are also several other molecules that influence PRL secretion either by stimulation (e.g. thyrotropin-releasing hormone, serotonin, oxytocin) or by inhibition (e.g. serotonin, histamine, noradrenaline).[34,35]

PRL blood levels are generally relatively low, but high PRL levels are expected during pregnancy and nursing. High PRL levels in other situations may indicate a potential disorder. For example, high PRL levels may be related to pituitary or other PRL-releasing tumors, certain kidney or liver diseases, or hypothalamus diseases. PRL levels are often measured in cases of infertility or irregular menstrual periods, testicular dysfunction, or symptoms suggesting prolactinoma, including visual impairment. PRL levels vary significantly during the day, which should be taken into account when using them as a diagnostic tool.[34,36-38]

Medix Biochemica offers two anti-PRL mouse monoclonal antibodies (5601 and 5602), which can be used as a pair in diagnostic tests.

Anti-human prolactin monoclonal antibodies

PRL antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
5601	100038	1	36	IgG_1	ELISA
5602	100360	5	24	IgG_1	ELISA

Pair recommendations

		Detection
		5602
Capture	5601	+

Kinetic parameters

PRL antibody	Dissociation constant, K_D (M)
5601	$3.8 \times 10^{-11} = 0.04$ nM
5602	$1.05 \times 10^{-10} = 0.1$ nM

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.[39-42]

Medix Biochemica offers two anti-T4 mouse monoclonal antibodies (6901 and 6902), which can be used for a competitive immunoassay for T4 detection.

Anti-human T4 monoclonal antibodies

T4 antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
6901	100348	5	36	IgG_1	ELISA
6902	100801	5	N/D	IgG_1	ELISA

Kinetic parameters

T4 antibody	Dissociation constant, K_D (M)
6901	$1.0 \times 10^{-10} = 0.1$ nM
6902	N/D

Thyroglobulin

Thyroglobulin is the predominant protein produced by the thyroid gland. This homodimeric 660 kDa glycoprotein protein acts as a substrate for the synthesis of the thyroid hormones triiodothyroxine (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.[43]

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.[42-45]

Medix Biochemica's antibody selection contains four anti-thyroglobulin mouse monoclonal antibodies (2802, 2803, 2804, and 2805).

Anti-human thyroglobulin monoclonal antibodies

Thyroglobulin antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
2802	100331	5	18	IgG_1	ELISA
2803	100332	5	36	IgG_{2b}	ELISA
2804	100333	5	36	IgG_1	ELISA
2805	100334	5	36	IgG_1	ELISA

Pair recommendations

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

Kinetic parameters

Thyroglobulin 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}	$1.4 \times 10^{-9} = 1.4$ nM
2803	1.7×10^{5}	3.7×10^{-5}	$2.2 \times 10^{-10} = 0.22$ nM
2804	7.2×10^{4}	7.9×10^{-4}	$1.1 \times 10^{-8} = 11$ nM
2805	6.2×10^{5}	1.3×10^{-5}	$2.1 \times 10^{-11} = 0.02$ nM

Growth hormone

Human growth hormone (GH) is a single-chain 22 kDa peptide hormone synthesized and secreted by the anterior pituitary gland. In accordance with its name, GH stimulates various bodily processes related mostly to growth and regeneration. Besides stimulating longitudinal bone growth, GH regulates cell growth and differentiation, as well as metabolic processes in various tissues, such as liver, adipose tissue, muscle, and bone. GH release is regulated primarily by growth hormone releasing hormone (GHRH), which induces GH secretion, and by somatostatin, which inhibits it. While males secrete GH in a pulsatile manner, females have been reported to exhibit more continuous GH secretion. GH function is mediated by its binding to the GH receptor, a type I cytokine receptor expressed primarily in the liver. Clinically, GH testing is mainly used for identifying growth hormone deficiency or, less commonly, excess GH related to acromegaly and gigantism.[46-49]

Medix Biochemica's selection of mouse monoclonal antibodies includes two anti-GH antibodies (5801 and 5802). These can be used as a pair in diagnostic tests.

Anti-human growth hormone monoclonal antibodies

GH antibody	Product code	Concentration (mg/mL)	Shelf life (months at +2–8°C)	Subclass	Applications tested
5801	100041	1	36	IgG_1	ELISA
5802	100042	1	36	IgG_1	ELISA

Pair recommendations

		Detection
		5801
Capture	5802	+

Kinetic parameters

GH antibody	Dissociation constant, K_D (M)
5801	$5.0 \times 10^{-11} = 0.05$ nM
5802	$1.0 \times 10^{-10} = 0.1$ nM

Page 3

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

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

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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