



Metabolic Syndrome

Antibodies and antigens



Introduction

Metabolic syndrome is a cluster of conditions that increases the likelihood of cardiovascular heart diseases and diabetes. These metabolic risk factors include abdominal obesity, elevated blood pressure, insulin resistance, high blood sugar levels and abnormal blood cholesterol levels. Both genetic factors and the lifestyle of the individual, including limited physical activity and excess weight, are considered to be underlying causes of metabolic syndrome.

Estimates by the American Heart Association suggest that 20-25% of US adults have metabolic syndrome. It should be noted that there is currently no unified definition of metabolic syndrome. Instead, several organizations including the World Health Organization (WHO), the International Diabetes Federation (IDF) and the European Group for the study of Insulin Resistance (EGIR), have presented their own individual criteria for metabolic syndrome. These criteria have common features but also differing parameters and this inevitably complicates the comparisons of different studies. Nevertheless, as obesity rates grow it is expected to also result in an increase in the incidence of metabolic syndrome.

At HyTest, we provide immunological reagents — antibodies and antigens — that enable the development of quantitative immunoassays for the detection of various biomarkers, such as adiponectin, insulin and glycated hemoglobin.

Please note that in this brochure the monoclonal antibodies (MAbs) are only listed according to the analyte that they recognize. In most cases there are several different MAbs available under one catalogue number. More detailed information regarding the performance of our products, a full list of individual MAbs and recommendations for capture-detection antibody pairs (when available) can be found on our website — www.hytest.fi. You are also most welcome to contact our Tech Support Team directly by writing to support@hytest.fi.



Introduction	2
Adiponectin	4
Glycated hemoglobin (HbA1c)	6
Proinsulin, insulin and C-peptide	7
ADDITIONAL PRODUCTS	8
Leptin	
References	9

Adiponectin

CLINICAL UTILITY

- **Type 2 diabetes**

Adiponectin has been extensively studied as a prognostic and diagnostic marker of diabetes and cardiovascular diseases. It has been shown that the amount of adiponectin in blood reduces in cases of patients who suffer from Type 2 diabetes mellitus or coronary artery diseases, or who are insulin-resistant or obese (Arita et al., 1999, Kogan et al., 2013; Ouchi et al., 1999 and 2000, Weyer et al., 2001).

Adiponectin is an abundant hormone that is secreted by adipocytes. Adiponectin is an insulin-sensitizing hormone with anti-diabetic, anti-inflammatory and anti-atherogenic properties. Its main function is considered most likely to be the regulation of glucose metabolism. In blood, adiponectin is found in different oligomeric forms (Figure 1) as well as in complexes with several proteins.

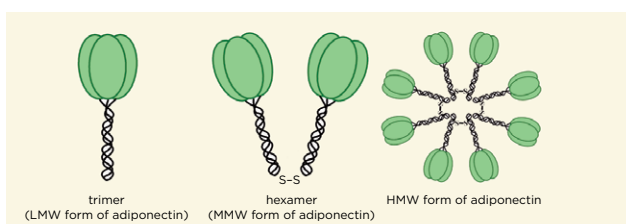


Figure 1. Schematic representation of the oligomeric forms of adiponectin.

Assays detecting total and LMW forms of human adiponectin

To establish an oligomer specificity of HyTest assays, serum proteins were separated according to their molecular masses by means of size-exclusion chromatography and immunoreactivity in fractions was measured. Assay Adn94-Adn63 recognizes all three adiponectin oligomeric forms (Figure 2).

Native purified adiponectin contains all three oligomeric forms

We offer native adiponectin purified from pooled human plasma. The preparation contains all oligomeric forms of adiponectin (Figure 3) and can be used as a calibrator in all types of adiponectin immunoassays.

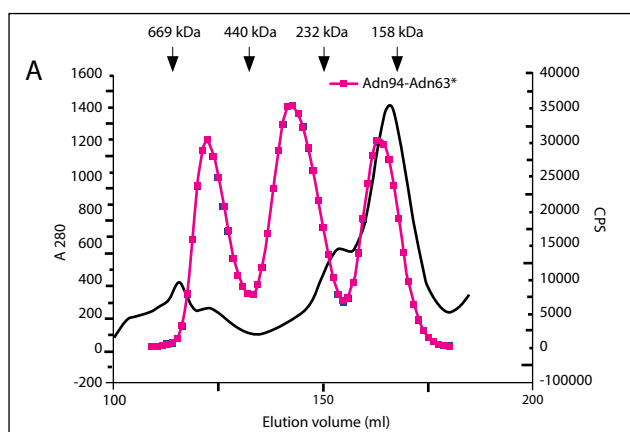


Figure 2. Sandwich ELISA in protein fractions after size-exclusion chromatography, measured by capture-detection antibody pair Adn94-Adn63. 1 ml of normal human serum was applied onto the column. Positions of oligomeric forms of adiponectin and molecular weight markers are depicted in the picture. The black line presents the optical density detected at 280 nm.

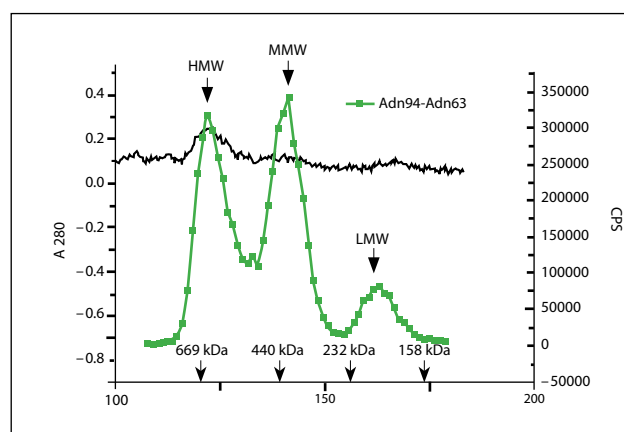


Figure 3. Native purified adiponectin contains all oligomeric forms. 3 µg of adiponectin was applied onto a gel-filtration column and immunoreactivity in fractions was measured by the sandwich ELISA using Adn94 and Adn63 as capture and detection antibodies respectively. Molecular weight markers are depicted by arrows on the x-axis. The black curve represents the optical density measured at 280 nm.

MONOCLONAL ANTIBODIES

Cat.#	Product	Tested applications
2AN6*	Monoclonal mouse anti-human adiponectin	Enzyme immunoassays Western blotting

* Please note: Several MAbs are available under one catalogue number. Please see www.hytest.fi for more information.

ANTIGEN

Cat.#	Product	Source	Purity
8AN7	Adiponectin, human, native	Pooled human plasma	>95%

Glycated hemoglobin HbA1c

CLINICAL UTILITY

- **Chronic hyperglycemia**
- **Type 2 diabetes**

Many proteins, including hemoglobin, become glycated during their life cycle. Glycation, in contrast to glycosylation, is a non-enzymatic process that takes place in the bloodstream. The concentration of glycated hemoglobin (HbA1c) provides information regarding the average concentration of blood glucose during the previous 2-3 months. The higher the amount of HbA1c, the higher the blood glucose concentration has been over a longer period of time. HbA1c concentration is the most widely used index of chronic hyperglycemia (Weykamp et al., 2008) and routine measurements are important in the management of Type 2 diabetes. HbA1c measurement is also recommended to be used to diagnose diabetes.

Sandwich immunoassay for detecting HbA1c

We provide monoclonal antibodies that detect both HbA1c and HbA10, which is the non-glycated hemoglobin, as well as one antibody that only detects HbA1c. A calibration curve of native HbA1c for the MAb combination Hb6-75C9 is provided in Figure 4.

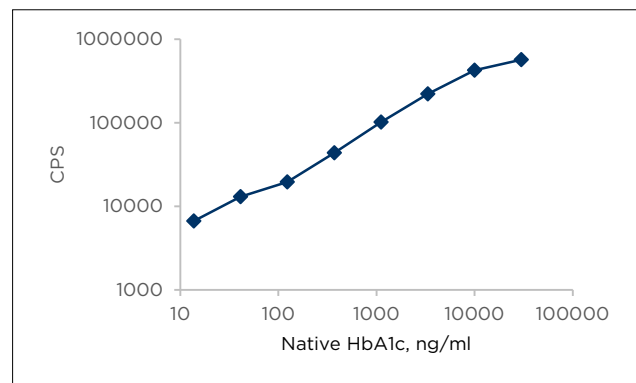


Figure 4. Calibration curve for the Hb6-75C9 fluoroimmunoassay. MAb Hb6 was used as a coating antibody (1 µg/well), while MAb 75C9 was labeled with stable Eu³⁺ chelate and served as a detection antibody (0.4 µg/well). Native HbA1c was utilized as an antigen.

MONOCLONAL ANTIBODIES

Cat.#	Product	Tested applications
4HH0*	Monoclonal mouse anti-hemoglobin, human, HbA ₁₀	Enzyme immunoassays
4HA1	Monoclonal mouse anti-glycated hemoglobin, human, HbA _{1c}	Enzyme immunoassays

* Please note: A few MAbs are available under one catalogue number. Please see www.hytest.fi for more information.

Proinsulin, insulin and C-peptide

CLINICAL UTILITY

- **Diabetes mellitus**
- **Hypoglycemia**

Assays for proinsulin, insulin and C-peptide are widely used in the monitoring of hypoglycemia, pathogenesis and the treatment of diabetes mellitus. Insulin is synthesized in the pancreas from

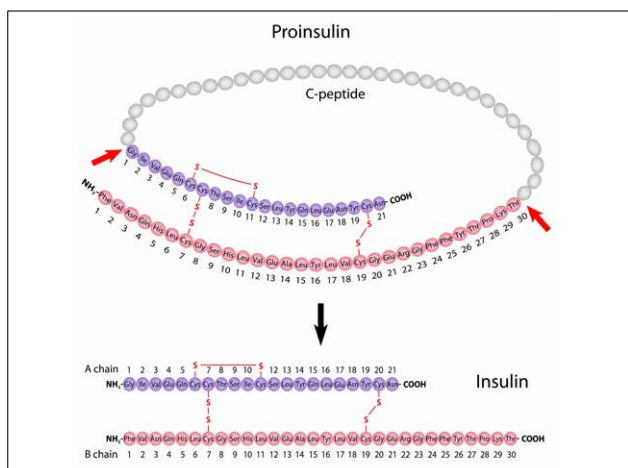


Figure 5. Proinsulin is enzymatically cleaved into C-peptide and mature insulin.

its precursor proinsulin and during this process proinsulin is proteolytically cleaved into three peptides: A- and B-chains and C-peptide. A- and B-chains are covalently linked by disulfide bonds to form mature insulin (Figure 5).

The analysis of proinsulin synthesis and processing, as well as insulin and C-peptide clearance, is very important for the improved understanding of carbohydrate metabolism abnormalities. Assays for insulin, proinsulin and C-peptide are widely used in the monitoring of hypoglycemia, pathogenesis and the treatment of diabetes mellitus.

Monoclonal antibodies specific to human and rat proteins

We provide over 30 monoclonal antibodies that enable the development of immunoassays for the detection of human and rat proinsulin, insulin and C-peptide molecules. By choosing the right antibody combinations it is possible to detect C-peptide with no cross-reaction to proinsulin.

MONOCLONAL ANTIBODIES

Cat.#	Product	Tested applications
2P9*	Monoclonal mouse anti-human proinsulin	Enzyme immunoassays Immunohistochemistry
2PR8	Monoclonal mouse anti-rat proinsulin	Enzyme immunoassays
2I1*	Monoclonal mouse anti-human insulin	Enzyme immunoassays Immunohistochemistry
2IP10cc*	Monoclonal mouse anti-rat-mouse insulin/proinsulin	Enzyme immunoassays Immunohistochemistry
2I3*	Monoclonal mouse anti-rat C-peptide	Enzyme immunoassays

* Please note: Several MAbs are available under one catalogue number. Please see www.hytest.fi for more information.

Additional products

Leptin

Leptin is a hormone that is secreted by adipocytes. It crosses the blood-brain barrier and binds to receptors in the brain. When the level of leptin increases, it tells the brain that the energy reservoirs are full and that there is no need for food intake. This signaling route is often impaired in obese people as a result of leptin resistance.

We provide monoclonal antibodies that are specific to leptin for research purposes. They have been tested in sandwich immunoassays and Western blotting.

MONOCLONAL ANTIBODIES

Cat.#	Product	Tested applications
2LE1*	Monoclonal mouse anti-human leptin	Enzyme immunoassays Western blotting

* Please note: A few MAbs are available under one catalogue number. Please see www.hytest.fi for more information.

References

- Arita Y. et al.** Paradoxical decrease of an adipospecific protein, adiponectin, in obesity. *Biochem. Biophys. Res. Commun.* 1999, 257:79-83.
- Blaner W.S.** Retinol-binding protein: the serum transport protein for vitamin A. *Endocr. Rev.* 1989, 10:308-316.
- Hara K. et al.** Measurement of the high-molecular weight form of adiponectin in plasma is useful for the prediction of insulin resistance and metabolic syndrome. *Diabetes Care* 2006, 29:1357-1362.
- Jaconi S.** Characterization of two post-translationally processed forms of human serum retinol-binding protein: altered ratios in chronic renal failure. *J. Lip. Res.* 1995, 36:1247-1253.
- Klotnik P. et al.** RBP4: a controversial adipokine. *Eur. J. Endocrinol.* 2011, 165:703-711
- Kogan A.E. et al.** Oligomeric adiponectin forms and their complexes in the blood of healthy donors and patients with Type 2 Diabetes Mellitus. *J. Immunoassay Immunochem.* 2013, 34(2):180-196.
- Lara-Castro C. et al.** Adiponectin multimeric complexes and the metabolic syndrome trait cluster. *Diabetes.* 2006, 55(1):249-59.
- Norden A.G. et al.** Urine retinol-binding protein 4: a functional biomarker of the proximal renal tubule. *Adv. Clin. Chem.* 2014, 63:85-122.
- Ouchi N. et al.** Novel modulator for endothelial adhesion molecules: Adipocyte-derived plasma protein adiponectin. *Circulation* 1999, 100:2473-2476.
- Ouchi N. et al.** Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. *Circulation* 2000, 102:1296-1301.
- Weyer C. et al.** Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. *J. Clin. Endocrinol. Metab.* 2001, 86:1930-1935.
- Weykamp C. et al.** The IFCC Reference Measurement System for HbA1c: a 6-year progress report. *Clin. Chem.* 2008, 54:240-248.



Together. Today and Tomorrow.

www.hytest.fi



Intelligate 1, 6th floor, Joukahaisenkatu 6
FI-20520 Turku, FINLAND
Tel. +358 2 512 0900
E-mail: hytest@hytest.fi