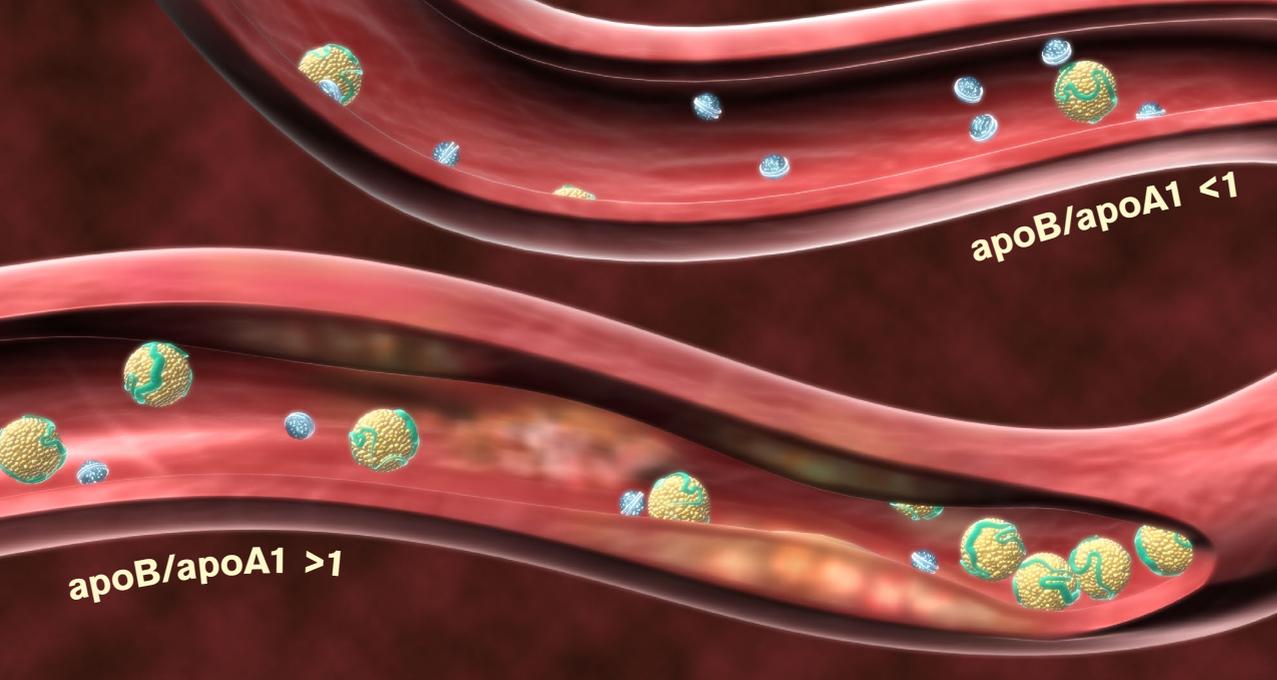


Apolipoproteins

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What is an apolipoprotein?

Apolipoproteins are a range of different proteins that can bind and thereby help to solubilize the hydrophobic lipids in water-based circulations such as blood. Apolipoproteins and phospholipids together form particles called lipoproteins into which a variety of lipids can be packed. The different apolipoproteins give the lipoprotein particles specific characteristics and are important in receptor recognition and regulation of specific enzymes.

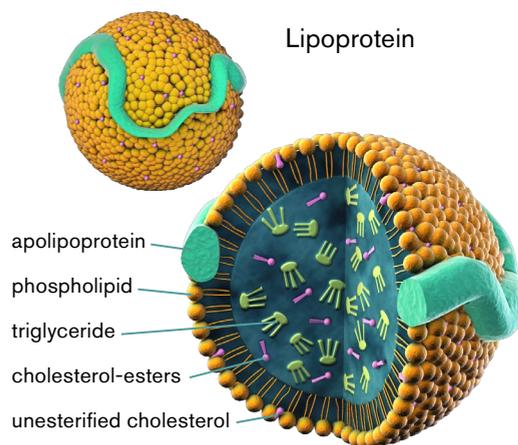
Apolipoproteins can be classified in two major types; the non-exchangeable and the exchangeable. Apolipoprotein B is non-exchangeable and is anchored in the lipoprotein particle whereas apolipoproteins A, E, D, J and H are exchangeable apolipoproteins that can be transferred between different lipoprotein particles and they may also acquire lipids in the circulation.

It is well known that apolipoproteins are associated with different diseases, e.g. apolipoprotein A1 and B with cardiovascular

diseases and apolipoprotein E with Alzheimer's disease. Apolipoproteins have therefore emerged as key risk markers to predict and diagnose different diseases and techniques measuring apolipoproteins are important tools of today's clinical work and research.

Function of apolipoproteins

Apolipoproteins (apo) have pivotal functions as structural components in lipoprotein particles, ligands to receptors and cofactors to enzymes. Lipoprotein particles are

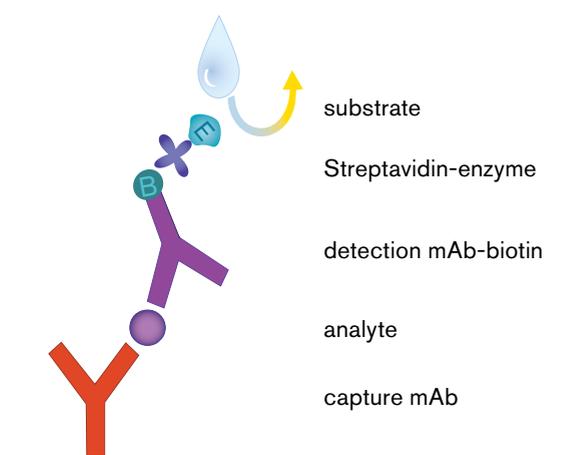


necessary in the transportation of lipids for energy supply and for synthesis of hormones, vitamins and bile acid. ApoB and apoE are important in the transport of dietary and endogenous lipids to peripheral tissues for energy supply, whereas apoA1 is crucial in returning excess cholesterol from peripheral tissues back to the liver.

Apolipoproteins such as apoE and apoJ are also important in the transportation of lipids in the brain. The system is complex and the right balance between different lipoproteins and apolipoproteins are of great importance. Disturbances in the balance could lead to detrimental diseases.

Measuring apolipoproteins

Enzyme-Linked ImmunoSorbent Assay (ELISA) has become a well-used method for detection and quantification of different analytes in many fields of life science. Mabtech offers highly sensitive and specific monoclonal antibodies and ELISA kits for measurement of apolipoproteins. All our kits are based on the sandwich ELISA technique and use well characterized monoclonal antibodies. The ELISAs are suitable for analysis of cell supernatants and samples from serum/plasma and are available as both ELISA^{PRO} kits and development kits. The specific monoclonal antibodies are also suitable for western blot and immunoprecipitation. For apoE Mabtech offers highly sensitive ELISpot kits, which enable detection of apoE secretion at the single cell level thereby facilitating studies of its regulation in immunocompetent cells such as macrophages and monocytes. For more information about our products, ELISA dilution guidelines and the ELISpot technique please visit our website www.mabtech.com.



Principle of the sandwich ELISA assay

ELISA^{PRO} kit



- Strip-plates pre-coated with capture mAb
- Biotinylated detection mAb
- Streptavidin-HRP
- TMB substrate
- ELISA standard
- Buffers, diluents, stop solution, adhesive plate covers

ELISA development kit



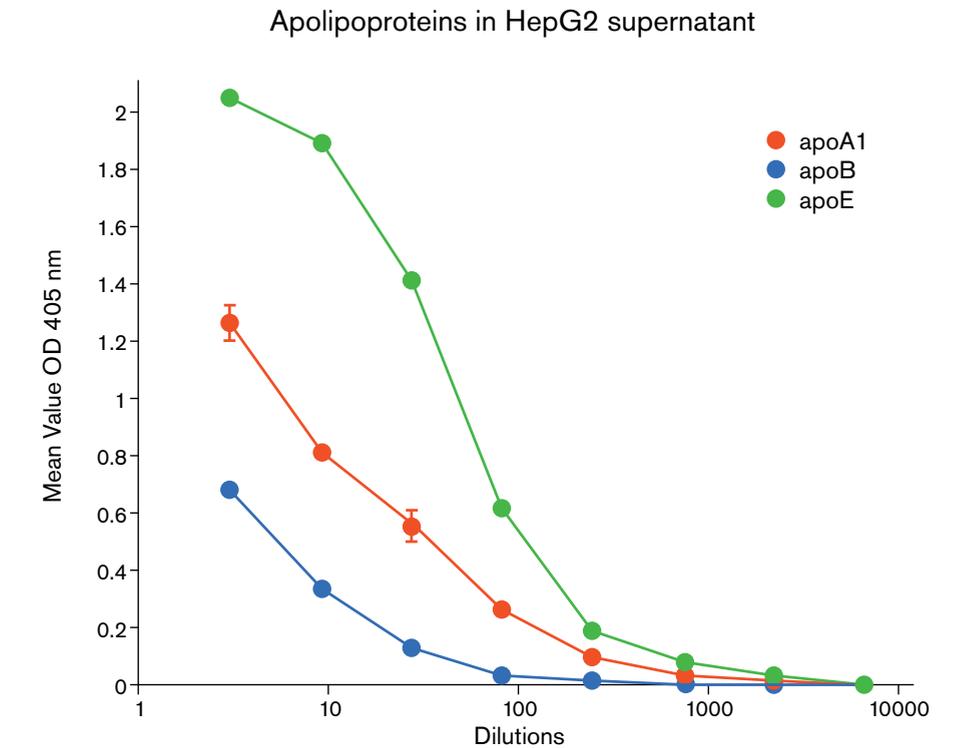
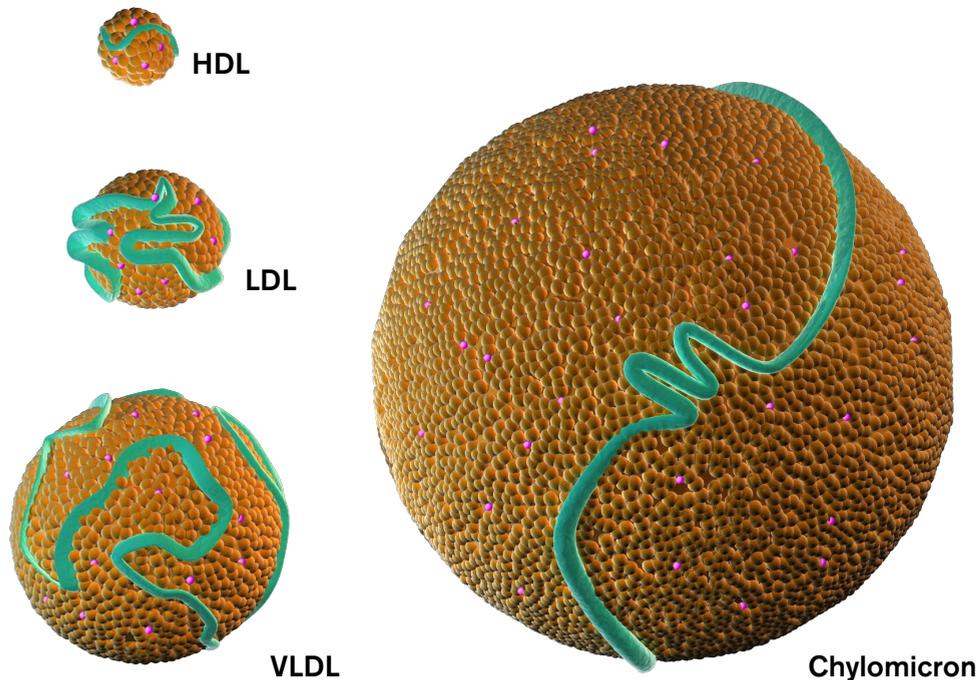
- Capture mAb
- Biotinylated detection mAb
- Streptavidin-ALP or -HRP
- ELISA standard

Please note that the products are sold for research use only.

Specific apolipoproteins

ApoA1 (28kDa) is the principal protein component of HDL (high density lipoprotein) and the concentration in human plasma is approximately 1.3 g/L. HDL is often referred to as “the good cholesterol particle” since it transports cholesterol from blood vessels back to the liver for degradation, thereby counteracting atherosclerosis. ApoA1 is essential for this reverse cholesterol transport and low plasma apoA1 levels are associated with increased risk for cardiovascular diseases. Therefore, apoA1 is often used as a biomarker for prediction of cardiovascular diseases and more recently apoA1 has been proposed also as a biomarker for prediction of vaccine-induced immunity and overall survival¹.

ApoB (512 kDa) is the main protein component of LDL (low density lipoprotein), often referred to as the “bad cholesterol particle”. The concentration of apoB in human plasma is approximately 1.0 g/L, dependent upon gender and age. ApoB-100 (the full size of the protein) mediates a ligand-receptor uptake of LDL-particles, and dysfunctional apoB leads to impaired ligand-receptor interaction and premature cardiovascular diseases. Since each LDL-particle carries one apoB-100, the amount of plasma apoB-100 reflects the number of LDL-particles in plasma. LDL particles can penetrate vessel walls, promoting the progress of atherosclerosis. The balance between the plasma concentration of apoA1 and apoB is of great importance², and the ratio apoB-100/apoA1 has been reported as a stronger



The high sensitivity of Mabtech's ELISAs for apoA1, apoB and apoE is demonstrated using an overnight HepG2 cell culture supernatant.

predictor for the risk of myocardial infarction than any other lipid measurement for all ethnicities, ages and sexes³. ApoB is also produced in the intestine where it is targeted to mRNA-editing, resulting in 48% of the full protein length and hence is referred to as apoB-48. ApoB-48 is incorporated into chylomicrons for transportation of dietary lipids. Chylomicrons are rapidly removed from the circulation and are not normally present in human fasting blood samples. The human/monkey apoB ELISA from Mabtech is specific for apoB-100.

ApoE (34 kDa) is a polymorphic, heparin-binding glycoprotein involved in many biological processes. Many cell types including hepatocytes, macrophages and endothelial cells produce apoE. It is present

in chylomicrons, VLDL and HDL and the concentration in fasting human plasma is approximately 25 mg/L. ApoE is important for facilitating receptor-mediated uptake of large lipoproteins and is considered to be anti-atherogenic. ApoE is regarded as the primary carrier of lipids in the brain where it is locally produced by astrocytes and is important for functional neurophysiology. It is associated with both cardiovascular diseases and neurological diseases such as Alzheimer's. Dysfunctional apoE in the apoE2 isoform can lead to hyperlipoproteinemia while dysfunctional apoE in the isoform apoE4 contributes to neurodegeneration and increased risk for development of Alzheimer's disease. The human and monkey apoE ELISAs from Mabtech recognize all three isoforms.

Apolipoprotein H (50 kDa), also known as beta-2-glycoprotein I (β 2GPI), binds to negatively charged molecules such as phospholipids, cardiolipids, heparin and lipoproteins, but can also circulate in its free form. The apoH concentration in plasma is approximately 200-300 mg/L^{4, 5}. ApoH has been reported to be involved in several different physiological pathways but its function has not yet been fully elucidated. Apart from being involved in lipoprotein metabolism, apoH inhibits blood coagulation and thrombosis, binds to platelets and is involved in autoimmune diseases, such as antiphospholipid syndrome (APS)⁶ and systemic lupus erythematosus (SLE). ApoH has been shown to interact with oxidized LDL (but not native LDL) and inhibit macrophage uptake of oxidized LDL⁷, and thereby having potential anti-atherogenic properties.

ApoD (29kDa) is a multifunctional protein present in adrenal glands, kidneys, pancreas, placenta, spleen, lungs, ovaries, testes, brain, peripheral nerves and cerebrospinal fluid. It is also expressed in the liver and intestine but at a low degree⁸. The exact role of apoD has not been established although it has been shown to be involved in several physiological and pathophysiological processes such as growth regulation of tumors, maintenance or repair within the central nervous system and as a co-enzyme in the catabolism of lipoprotein particles. ApoD gene polymorphisms have been associated with obesity, hyperinsulinemia and type 2 diabetes. ApoD is a lipocalin that can bind lipids and steroid hormones such as progesterone. Plasma-circulating apoD is mainly present in HDL and to a lesser extent in VLDL and LDL⁹. The human plasma concentration is approximately 120 mg/L¹⁰.

ApoJ (70kDa), also called clusterin, is a multifunctional glycoprotein with chaperon function. It is associated with several pathological conditions such as atherosclerosis, diabetes, inflammation, cancer and Alzheimer's, and is also involved in apoptosis. ApoJ is expressed in almost all mammalian cells and most biological fluids. The plasma concentration has been reported to range from 35-300 mg/L, a variance that more likely reflects differences in methodology and standards than real concentration differences. However, the concentration will also depend upon subjects' health and age. Circulating ApoJ is primarily associated to HDL particles but also to LDL¹¹ and platelets.

There are many other important apolipoproteins like apoA2-5, apoC1-3, apoL, apoM, apolipoprotein(a) and paroxonase that in different ways are associated with lipid metabolism.

Apolipoprotein	Lipoprotein
ApoA1	HDL, chylomicrons
ApoB100	LDL, VLDL
ApoB48	Chylomicrons
ApoE	Chylomicrons, VLDL, HDL
ApoH	HDL, chylomicrons, VLDL, LDL
ApoD	HDL, LDL, VLDL
ApoJ	HDL, LDL, VLDL
ApoC	VLDL, chylomicrons, HDL
ApoM	HDL, LDL
ApoL	HDL
Paroxonase	HDL
Apolipoprotein (a)	LDL

References

- Walter S, *et al.* Muropeptide immune response to cancer vaccine IMA901 after single-dose cyclophosphamide associates with longer patient survival. *Nature Med.* (Epub ahead of print), 2012
- Walldius G and Jungner I. Apolipoprotein B and apolipoprotein A-I: risk indicators of coronary heart disease and targets for lipid-modifying therapy. *J. Intern. Med.* 255: 2, 2004
- McQueen MJ, *et al.* Lipids, lipoproteins, and apolipoproteins as risk markers of myocardial infarction in 52 countries (the INTERHEART study): a case-control study. *Lancet* 372: 9634, 2008
- Zahedi RG, *et al.* The response of serum apolipoprotein H to an oral fat load. *Ann. Clin. Biochem.* 41: 4, 2004
- Mehdi H, *et al.* Genetic variation in the apolipoprotein H (beta2-glycoprotein I) gene affects plasma apolipoprotein H concentrations. *Hum. Genetics* 105: 1-2, 1999
- McNeil HP, *et al.* Anti-phospholipid antibodies are directed against a complex antigen that includes a lipid-binding inhibitor of coagulation: beta 2-glycoprotein I (apolipoprotein H). *PNAS* 87: 11, 1990
- Hasunuma Y, *et al.* Involvement of beta 2-glycoprotein I and anticardiolipin antibodies in oxidatively modified low-density lipoprotein uptake by macrophages. *Clin. Exp. Immunology* 107: 3, 1997
- Drayna D, *et al.* Cloning and expression of human apolipoprotein D cDNA. *J. Biol. Chemistry* 261: 35, 1986
- Bancells C, *et al.* Proteomic analysis of electronegative low-density lipoprotein. *J. Lipid Res.* 51: 12, 2010
- Rassart E, *et al.* Apolipoprotein D. *Biochim. Biophys. Acta* 1482: 1-2, 2000
- Pettersson C, *et al.* LDL-associated apolipoprotein J and lysozyme are associated with atherogenic properties of LDL found in type 2 diabetes and the metabolic syndrome. *J. Intern. Med.* 269: 3, 2011



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