

Pre β ₁-HDL at a Glance

- Pre β ₁-HDL is a small, lipid-poor, discoid particle.
- Pre β ₁-HDL accepts cholesterol at peripheral cells during reverse cholesterol transport (RCT).
- Pre β ₁-HDL levels are elevated in obesity and CVD.
- Plasma samples must be treated with stabilization buffer to insure stability of the particles.
- Pre β ₁-HDL can be detected in stabilized plasma by an ELISA assay that has been established at PBI.

Related Information

Pre β ₁-HDL is frequently requested in conjunction with:

- Apo AI
- CETP Activity
- CETP Mass
- Cholesterol Efflux
- LCAT Activity (Lecithin – Cholesterol Acyltransferase Activity)
- LCAT Mass (Lecithin – Cholesterol Acyltransferase Mass)

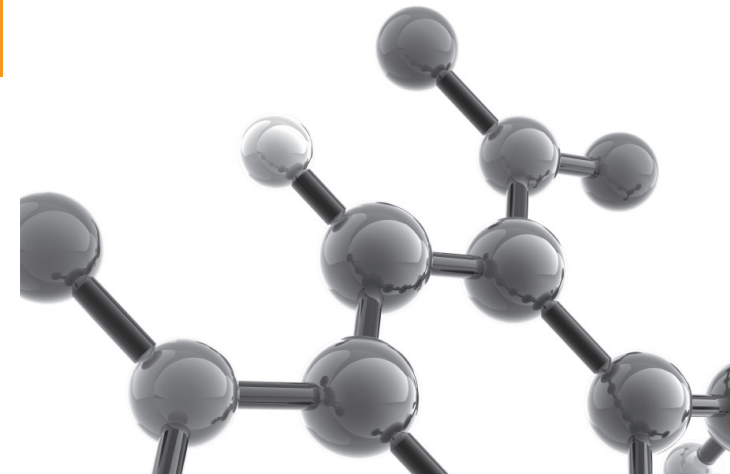
Pre β ₁-HDL analysis is a useful efficacy biomarker in the following drug development programs:

- CETP inhibitors
- MTP inhibitors (Microsomal triglyceride transfer protein)
- DGAT (Diacylglycerol Acyltransferase)
- HDL modifiers

Frequently Requested Tests

Cardiovascular Risk – Diabetes, Dyslipidemia, Metabolic Syndrome & Obesity

- Adiponectin
- Apolipoproteins (i.e. AI, B, B48, E, etc.)
- CETP (Cholesterol Ester Transfer Protein: Activity and Mass)
- Cholesterol (Total, Esterified, and Free)
- C-Peptide
- C-Reactive Protein
- E-Selectin
- Fibrinogen
- Glycerol, Free
- Ghrelin, Acylated and Total
- GLP-1, Active and Total
- Glucagon
- GIP
- HDL Subclasses by ppt. or GGE
- HDL Cholesterol
 - Chemical Precipitation (e.g. Hep Mn, DS)
 - Direct Homogeneous Methods
- ICAM and VCAM
- IL-6
- Insulin
- Leptin
- LDL Cholesterol
 - Beta Quantification
 - Direct Homogeneous Methods
 - Friedewald Estimation
 - small dense LDL
- LDL Subclasses by GGE
- Lp (a) [Lipoprotein (a)]
- LpPLA2
- Myeloperoxidase
- Non-Esterified Fatty Acids (NEFA or FFA)
- Oxidized LDL (antigen)
- PAI-1 (plasminogen activator inhibitor)
- Paraoxonase
- Phospholipids, Total
- Pre-beta-1 HDL
- Proinsulin
- PYY
- RLP-C and RLP-TG
- TNF α
- Triglycerides, Glycerol Blanked and Total
- Ultracentrifugation for chylo, VLDL, IDL, LDL & HDL



FEATURED ASSAY:

pre β ₁-HDL

Key marker in Reverse Cholesterol Transport

SAMPLE REQUIREMENTS

Optimum volume: 2 mL

Sample Type: Stabilized EDTA Plasma

Method: ELISA

Background Information

Increased levels of high density lipoprotein cholesterol, HDL-C, have been shown to be a negative risk factor for atherothrombotic cardiovascular disease (CVD) outcomes. The HDL particle itself has been shown to participate in anti-oxidative, anti-inflammatory, anti-apoptotic, anti-thrombotic and anti-infectious capacities. HDL is a complex mixture of particles that vary in size, shape, lipid and protein contents and biological activity, with some forms having negative CVD impact, some a neutral influence, and others, perhaps, a positive effect. One form of HDL is pre β_1 -HDL, so called because of its electrophoretic migration in native 2-dimensional (2-D) agarose gels. It is a lipid-poor, discoid HDL species containing apolipoprotein (apo) AI, but lacking apo AII and other apolipoproteins (1,2).

The negative association of HDL-C with CVD outcomes is predominantly because of its role in reverse cholesterol transport (RCT). This is a process whereby extra-hepatic cholesterol is incorporated into HDL and transported to the liver for excretion after uptake primarily by the SR-BI receptor. The first HDL particle involved in RCT appears to be pre β_1 -HDL. Pre β_1 -HDL accepts cholesterol at the cell membrane through the binding of ATP-binding cassette A1 (ABCA1)

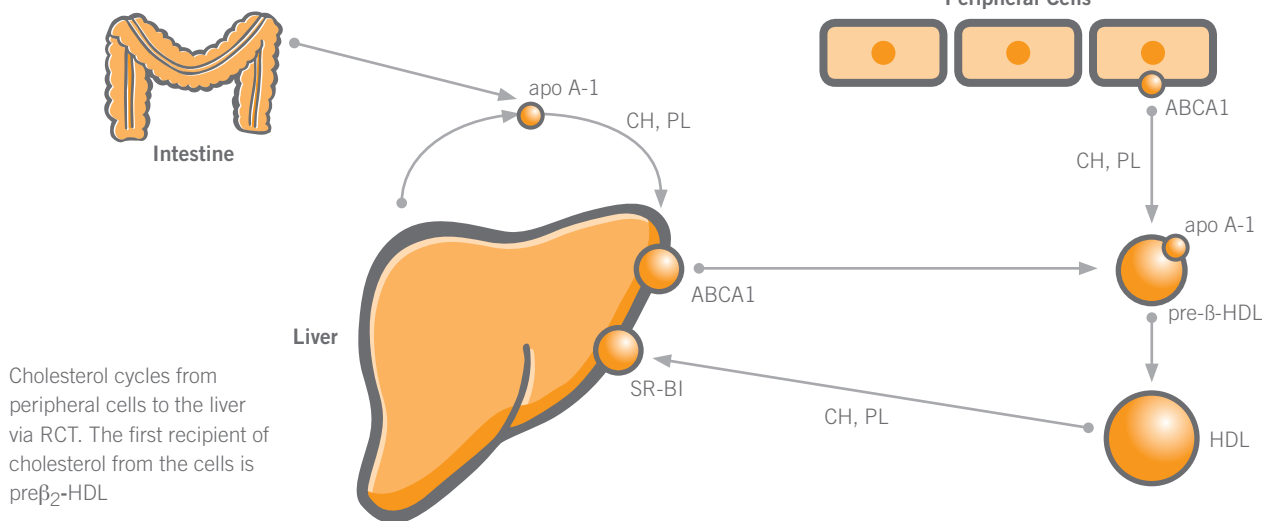
transporter to apo AI. The resulting complex is then converted to a larger particle, pre β_2 -HDL, by incorporation of cholesterol. The cholesterol is esterified via the action of LCAT (lecithin:cholesterol acyltransferase) converting the particle into the larger, spherical α_3 -HDL particle. The α_3 -HDL particle acquires more cholesterol from pre β_1 -HDL, converting the particle to α_2 - and α_1 -HDL. The cholesterol is exchanged for triglycerides via cholesterol ester transfer protein (CETP) and remodeled back to α_3 -HDL and free apo AI. The apo AI is rapidly converted back to pre β_1 -HDL. A disturbance in this HDL cycle can lead to the inhibition of RCT.

While pre β_1 -HDL is the first recipient of peripheral cholesterol, its concentration does not appear to be rate limiting for RCT. Individuals with CVD, obesity and hyperlipidemia have all been shown to have elevated pre β_1 -HDL levels. The cause of this increase is unknown. One hypothesis is the pre β_1 -HDL is unable to bind the cholesterol and convert to β_2 or α_3 particles, thus increasing pre β_1 particle levels and decreasing RCT.

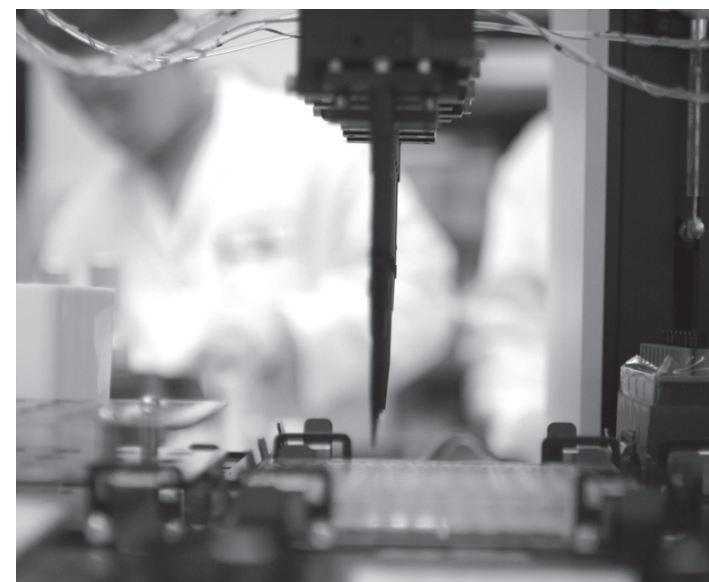
Until recently, the method for determining pre β_1 -HDL was cumbersome native 2-D gel electrophoresis. With the development of

a monoclonal antibody to apo AI present in pre β_1 -HDL, a sandwich ELISA assay is now available. This assay allows for much easier detection and quantification of the pre β_1 form of HDL in plasma (3). Because of the particle nature of the pre β_1 -HDL, the complex must be protected from modification. It has been shown that freezing plasma results in an increase, over time, in the detected pre β_1 -HDL. This is possibly because other forms of HDL are converted to the pre β_1 form. To prevent this conversion, plasma samples are frozen in the presence of 10-20 volumes of a 50% sucrose stabilization buffer. This ensures that the particles can be stored at -70°C without significant change (4).

REVERSE CHOLESTEROL TRANSPORT (RCT)



Cholesterol cycles from peripheral cells to the liver via RCT. The first recipient of cholesterol from the cells is pre β_2 -HDL



References: 1. Kapur NK, Ashen D, Blumenthal RS. Vasc Health Risk Manag. 2008;4:39-57. 2. Movva R, Rader DJ. Clin Chem. 2008;54:788-800. 3. Miyazaki O, et al. J Lip Res. 2000;41:2083-2088. 4. Miiada T, et al. J Lip Res. 2003;44:645-650.