Pacific Biomarkers
The Value of Expertise

Preß$_1$-HDL

Key marker in Reverse Cholesterol Transport

SAMPLE REQUIREMENTS

Optimum volume: 2 mL
Sample Type: Stabilized EDTA Plasma
Method: ELISA

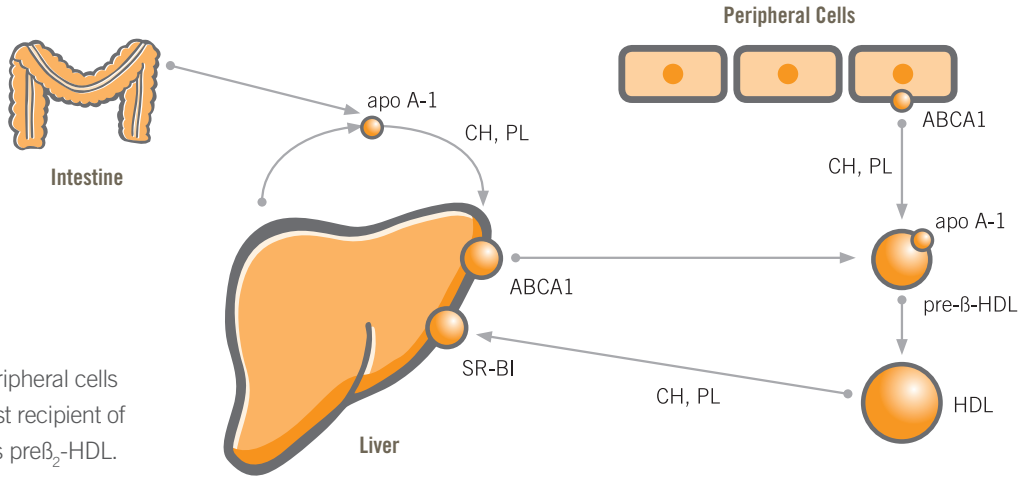
BACKGROUND

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 preß$_1$-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 preß$_1$-HDL. Preß$_1$-HDL accepts cholesterol at the cell membrane through the binding of ATP-binding cassette AI (ABCA1) transporter to apo AI. The resulting complex is then converted to a larger particle, preß$_2$-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 preß$_1$-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 preß$_1$-HDL. A disturbance in this HDL cycle can lead to the inhibition of RCT.

While preß$_1$-HDL is the first recipient of peripheral cholesterol, its concentration does not appear to be rate limiting for RCT.

FIGURE 1: Reverse Cholesterol Transport (RCT)



Cholesterol cycles from peripheral cells to the liver via RCT. The first recipient of cholesterol from the cells is preß$_2$-HDL.

Individuals with CVD, obesity and hyperlipidemia have all been shown to have elevated preß$_1$-HDL levels. The cause of this increase is unknown. One hypothesis is the preß$_1$-HDL is unable to bind the cholesterol and convert to ß$_2$ or α$_3$ particles, thus increasing preß$_1$ particle levels and decreasing RCT.

Until recently, the method for determining preß$_1$-HDL was cumbersome native 2-D gel electrophoresis. With the development of a monoclonal antibody to apo AI present in preß$_1$-HDL, a sandwich ELISA assay is now available. This assay allows for much easier detection and quantification of the preß$_1$ form of HDL in plasma (3). Because of the particle nature of the preß$_1$-HDL, the complex must be protected from modification. It has been shown that freezing plasma results in an increase, over time, in the detected preß$_1$-HDL. This is possibly because other forms of HDL are converted to the preß$_1$ 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).

PRE ß$_1$-HDL AT A GLANCE

- Preß$_1$-HDL is a small, lipid-poor, discoid particle.
- Preß$_1$-HDL accepts cholesterol at peripheral cells during reverse cholesterol transport (RCT).
- Preß$_1$-HDL levels are elevated in obesity and CVD.
- Plasma samples must be treated with stabilization buffer to insure stability of the particles.
- Preß$_1$-HDL can be detected in stabilized plasma by an ELISA assay that has been established at Pacific Biomarkers (PacBio).

RELATED INFORMATION

Preß$_1$-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)

Preß$_1$-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 Precipitation
- HDL Cholesterol
  - Chemical Precipitation (Dextran Sulfate or Hep Manganese)
  - Direct Homogeneous Methods
- ICAM and VCAM
- IL-6
- Insulin
- Leptin
- LDL Cholesterol
  - Beta Quantification
  - Direct Homogeneous Methods
  - Friedewald Estimation
  - Small Dense LDL
- 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
- TNFα
- Triglycerides, Glycerol Blanked and Total
- Ultracentrifugation for chylo, VLDL, IDL, LDL & 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.