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Apolipoproteins and metabolism in atherosclerosis
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The term "apolipoproteins" was initially coined by John Oncley in the 1940s to refer to the protein constituents of the plasma lipoproteins. Since then, we have learned a great deal about the structures, functions, and in some cases, the mechanisms of apolipoproteins.

One of the more important functions of apolipoproteins is to help bind and emulsify the water-insoluble lipids in lipoprotein packages. However, the apolipoproteins are not limited to structural functions. They also contribute to the regulation of lipoprotein metabolism.

With the exception of apolipoprotein B or apo B, the apolipoproteins are located on the surface of the lipoproteins. The apolipoproteins contain unique structures called amphipathic helices. These helices were first described by Segrest, et.al in 1974. Amphipathic helices allow the apolipoproteins to reside on the surface of the lipoprotein particle. Table 1 summarizes the apolipoproteins and some of their important properties.

Apo A's

Apo A is secreted by the liver and intestine. It is found in HDL and is also present in chylomicrons. Apo A-I is an activator of LCAT and is believed to play an important role in reverse cholesterol transport. Like Apo A-I, Apo A-II is secreted by the liver, but its intestinal origin is unclear. In addition to binding lipid, it has been suggested that apo A-II serves as an activator of the enzyme hepatic triglyceride lipase. Apo A-IV is secreted by the intestine and is present in chylomicrons and HDL. Some investigators have suggested that apo's A-I, A-IV and possibly A-II are involved in reverse cholesterol transport since these apolipoproteins are able to bind to 'HDL receptors' on the surface of cells and

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subsequently to promote cholesterol removal.

**Apo B's**

Apo B is the major protein constituent of LDL, but it is also found in chylomicrons and VLDL. Human apo B is a glycoprotein which occurs in two forms, apo B and apo B-100. In man, Apo B-48 is synthesized by the intestine, while apo B-100 is synthesized by the liver. The human gene for apo B contains 43 kilobases with 9.8 introns and is located on chromosome 2. Apo B-48 occurs because of the insertion of a stop codon in the editing of DNA. Most of the MRNA of the intestine is about 15 kilobases in size. This is the same as that for the MRNA for apo B-100. However, the stop codon is triggered by a CAA substitution for an UAA sequence. This substitution results in an aborted synthesis of the apolipoprotein and in the absence of the LDL receptor binding region.

**Apo C's**

Apo C-I, C-II and C-III are secreted by the liver. They are found in HDL and may also be transferred to VLDL and chylomicrons. Apo C-I can serve as an activator of LCAT; its other functions are unknown. Apo C-II is required to activate lipoprotein lipase. In certain kindreds, apo C-II is defective or deficient and is associated with a severe form of fasting chylomicronemia called Type I hyperlipoproteinemia. The clinical and lipoprotein abnormalities are very similar to those seen in familial lipoprotein lipase deficiency. Although the function of apo C-III is unknown, some investigators have suggested that apo C-III prevents a premature uptake of remnant particles by the liver.

**Apo D's**

Apo D is a minor protein which appears to be able to form complexes with HDL and the cholesteryl ester transfer protein (CETP), also called the lipid transfer protein (LTP). CETP catalyzes the exchange of cholesteryl ester and triglyceride between HDL and the lower-density lipoproteins.

**ApoE's**

Apo E is mainly synthesized in the liver, although a number of other tissues, including the brain, kidney and adrenal gland, are capable of making it. Synthesis and secretion of apo E has been shown in macrophages. Apo E serves as a ligand for the LDL or apo B/E receptor present on hepatic and extrahepatic tissues. Apo E also serves as a ligand recognized by liver receptors for chylomicron remnants.