

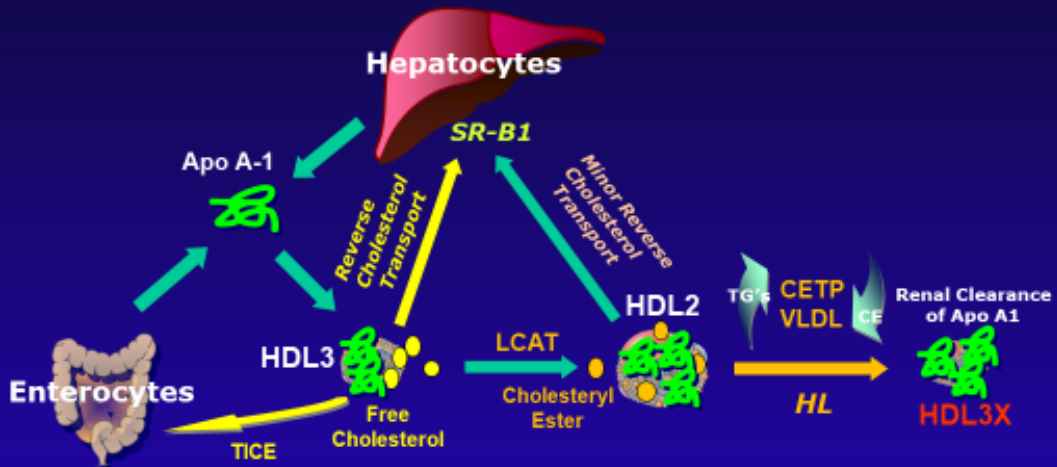
The Tale of Two HDL3s

Scholarly articles suggest that either high or low HDL3-C/HDL3-P is atherogenic creating uncertainty on the functionality of HDL3. Recent articles have also focused on the importance of HDL3 over HDL2 in reverse cholesterol transport (RCT), anti-oxidant and cardioprotective function. HDL3 is usually identified by analytical methods measuring either size or density and two types of HDL3 have been identified with the same size and density.

Newly formed HDL3 particles contain two Apo A-1s, phospholipids and unesterified cholesterol with the two Apo A-1 molecules arranged in an antiparallel orientation. These particles have a short life completing RCT in $t_{1/2} = 7-8$ minutes and can be measured by the postprandial response in the HDL3-P Activation Index™ assay.

A second path to HDL3 particles (HDL3X) is the action of CETP transferring triacylglycerol (TG) to HDL2 particles; followed by hepatic lipase TG reduction; thereby shrinking the size to that of HDL3s. HDL2 and HDL3X particles have three Apo A-1s with two outer Apo A-1 strands antiparallel to the center Apo A-1. Metabolic Syndrome patients, with high TGs, produce small HDL3X particles that have an Apo A-1 configuration of HDL2 particles. These patients show poor postprandial HDL3-P Activation. Small HDL3X particles participate in RCT with $t_{1/2} = 0.92$ days, like HDL2, or lose their Apo A-1s through renal clearance reducing total HDL.

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Sorci-Thomas et al., *J. Lipid Research* (2012) 53: 1890-1909.

Brewer HB et al. *Am J Cardiol* 2003;92:10K-16K.

Gillard et al., Rethinking reverse cholesterol transport and dysfunctional high-density lipoproteins. *J. Clinical Lipidology* (2018) 12, 849-856

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