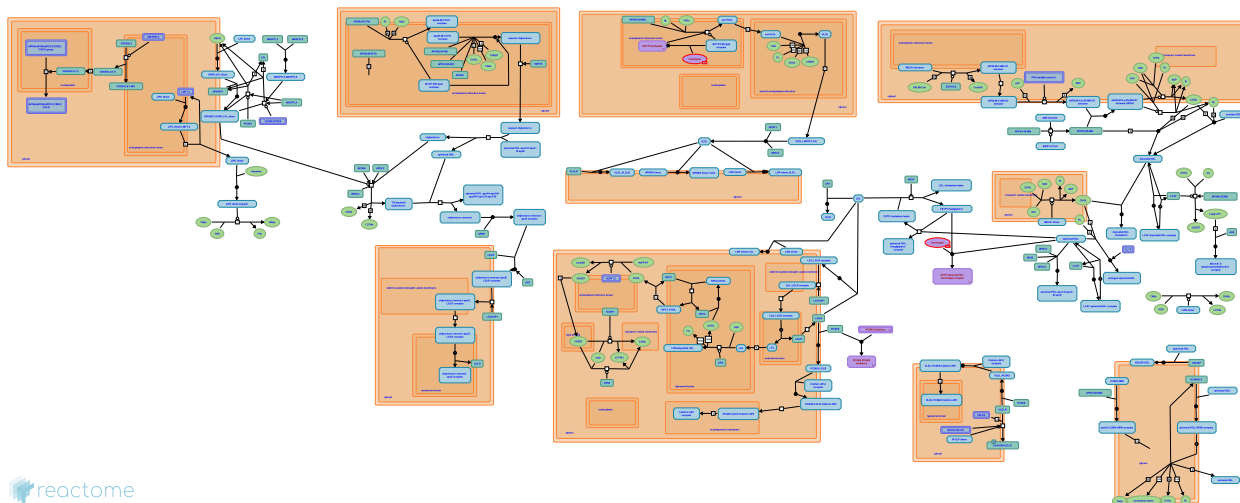


Plasma lipoprotein assembly, remodeling, and clearance



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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the [Reactome Textbook](https://reactome.org/textbook/).

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

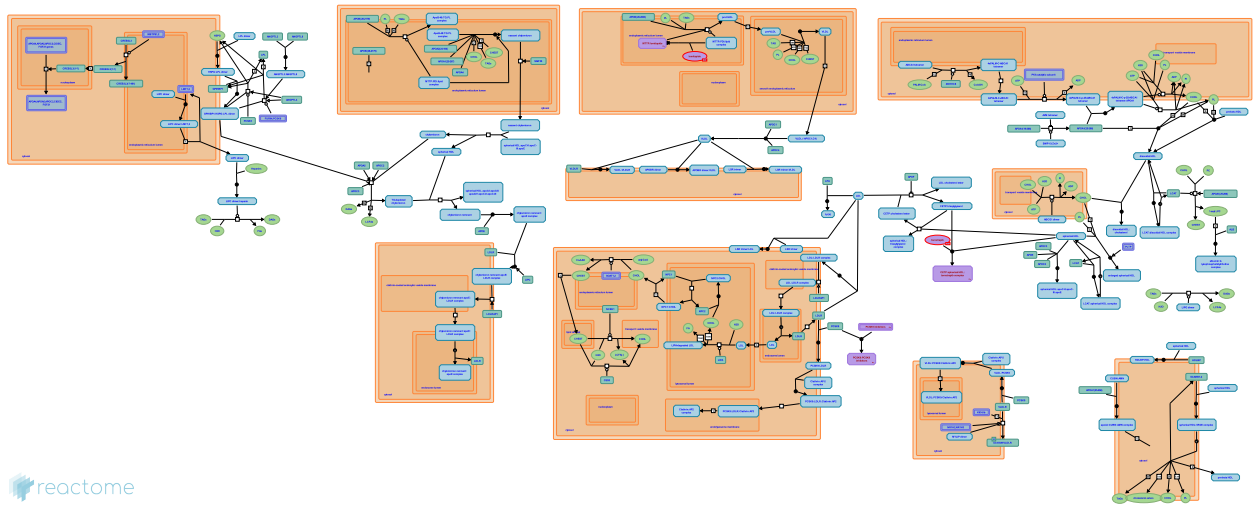
- Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics*, 18, 142. [↗](#)
- Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics*, 33, 3461-3467. [↗](#)
- Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res*, 46, D649-D655. [↗](#)
- Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology*, 14, e1005968. [↗](#)

Reactome database release: 88

This document contains 4 pathways ([see Table of Contents](#))

Plasma lipoprotein assembly, remodeling, and clearance ↗

Stable identifier: R-HSA-174824



 reactome

Because of their hydrophobicity, lipids are found in the extracellular spaces of the human body primarily in the form of lipoprotein complexes. **Chylomicrons** form in the small intestine and transport dietary lipids to other tissues in the body. **Very low density lipoproteins (VLDL)** form in the liver and transport triacylglycerol synthesized there to other tissues of the body. As they circulate, VLDL are acted on by lipoprotein lipases on the endothelial surfaces of blood vessels, liberating fatty acids and glycerol to be taken up by tissues and converting the VLDL first to **intermediate density lipoproteins (IDL)** and then to **low density lipoproteins (LDL)**. IDL and LDL are cleared from the circulation via a specific cell surface receptor, found in the body primarily on the surfaces of liver cells. **High density lipoprotein (HDL)** particles, initially formed primarily by the liver, shuttle several kinds of lipids between tissues and other lipoproteins. Notably, they are responsible for the so-called reverse transport of cholesterol from peripheral tissues to LDL for return to the liver.

Three aspects of lipoprotein function are currently annotated in Reactome: **chylomicron-mediated lipid transport**, **LDL endocytosis and degradation**, and **HDL-mediated lipid transport**, each divided into assembly, remodeling, and clearance subpathways.

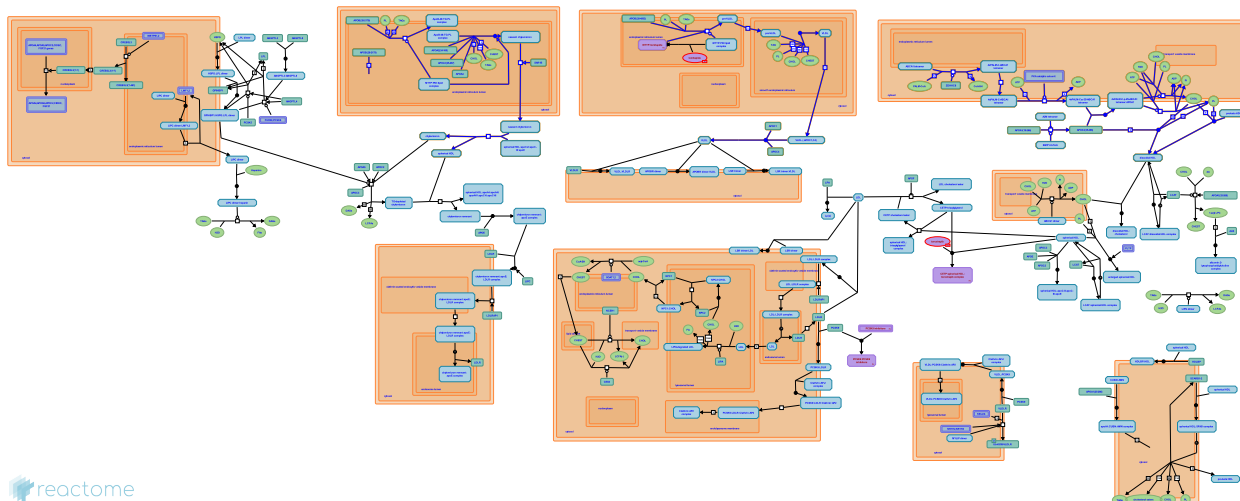
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2006-02-20	Authored, Edited	D'Eustachio, P.
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Plasma lipoprotein assembly ↗

Location: Plasma lipoprotein assembly, remodeling, and clearance

Stable identifier: R-HSA-8963898



 reactome

Because of their hydrophobicity, lipids are found in the extracellular spaces of the human body primarily in the form of lipoprotein complexes. Chylomicrons form in the small intestine and transport dietary lipids to other tissues in the body. Very low density lipoproteins (VLDL) form in the liver and transport triacylglycerol synthesized there to other tissues of the body. High density lipoprotein (HDL) particles are formed primarily by the liver and shuttle several kinds of lipids between tissues and other lipoproteins (Vance & Vance 1990). The assembly of these three classes of lipoproteins is annotated here.

Literature references

Vance, JE., Vance, DE. (1990). The assembly of lipids into lipoproteins during secretion. *Experientia*, 46, 560-9. ↗

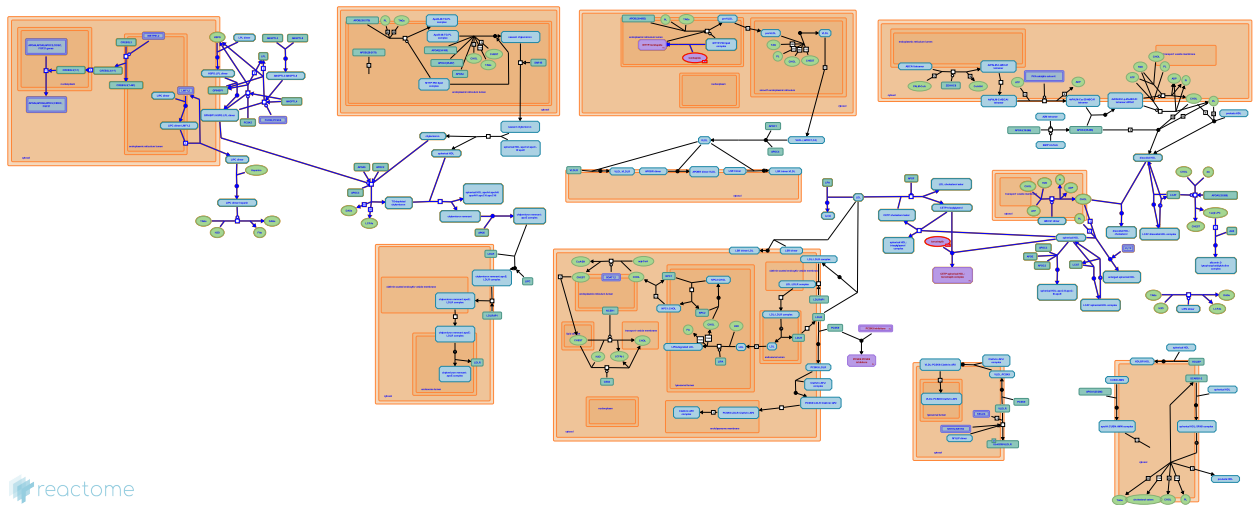
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Plasma lipoprotein remodeling ↗

Location: Plasma lipoprotein assembly, remodeling, and clearance

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 reactome

As chylomicrons circulate in the body, they acquire molecules of apolipoproteins C and E, and through interaction with endothelial lipases can lose a large fraction of their triacylglycerol. These changes convert them to chylomicron remnants which bind to LDL receptors, primarily on the surfaces of liver cells, clearing them from the circulation. This whole sequence of events is rapid: the normal lifespan of a chylomicron is 30 - 60 minutes (Redgrave 2004).

As they circulate, VLDL are acted on by lipoprotein lipases on the endothelial surfaces of blood vessels, liberating fatty acids and glycerol to be taken up by tissues and converting the VLDL first to intermediate density lipoproteins (IDL) and then to low density lipoproteins (LDL) (Gibbons et al. 2004).

HDL remodeling includes the conversion of HDL-associated cholesterol to cholesterol esters (remodeling of spherical HDL), the transfer of HDL lipids to target cells with the regeneration of pre-beta HDL (lipid-poor apoA-I), and the conversion of pre-beta HDL to discoidal HDL (Rye et al. 1999).

Literature references

Brown, AM., Gibbons, GF., Hebbachi, AM., Wiggins, D. (2004). Synthesis and function of hepatic very-low-density lipoprotein. *Biochem. Soc. Trans.*, 32, 59-64. ↗

Redgrave, TG. (2004). Chylomicron metabolism. *Biochem. Soc. Trans.*, 32, 79-82. ↗

Barter, PJ., Clay, MA., Rye, KA. (1999). Remodelling of high density lipoproteins by plasma factors. *Atherosclerosis*, 145, 227-38. ↗

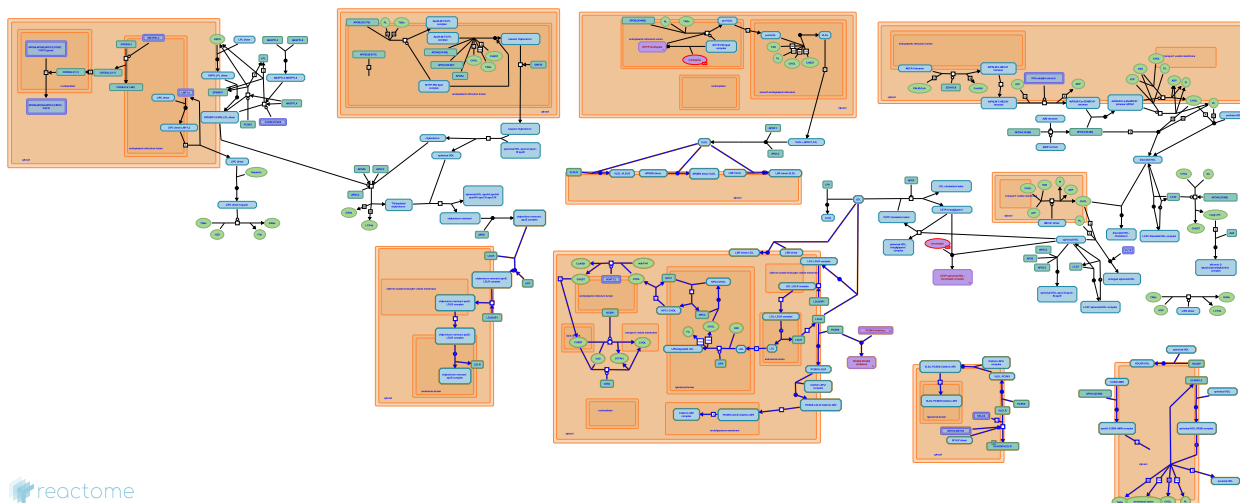
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Plasma lipoprotein clearance ↗

Location: Plasma lipoprotein assembly, remodeling, and clearance

Stable identifier: R-HSA-8964043



 reactome

Circulating chylomicrons acquire molecules of apolipoproteins C and E and through interaction with endothelial lipases lose a large fraction of their triacylglycerol. These changes convert them to chylomicron remnants which bind to LDL receptors, primarily on the surfaces of liver cells, clearing them from the circulation (Redgrave 2004).

Most very-low-density lipoproteins (VLDL) are converted to low-density lipoproteins (LDL) (VLDL remodeling pathway). A small fraction are taken up by VLDL receptors on extrahepatic cells, as annotated here. Clearance of LDL from the blood involves binding to LDL receptors associated with coated pits at the cell surface, forming complexes that are internalized and passed via clathrin-coated vesicles to endosomes, where they dissociate. The LDL particles move into lysosomes and are degraded while the LDL receptors are returned to the cell surface. This process occurs in most cell types but is especially prominent in hepatocytes. It plays a major role in returning cholesterol from peripheral tissues to the liver (Hobbs et al. 1990).

Clearance of circulating HDL particles involves particle binding to cell-surface SR-BI receptors, particle disassembly with release of pre-beta HDL (Silver & Tall 2001), and uptake of the latter mediated by cell-surface CUBN:AMN complex (Kozyraki et al. 1999).

VLDLR internalization plays a clinically significant role in determining the efficiency of lipoprotein clearance from the blood (Poirier et al. 2008).

Literature references

Mayer, G., Nimpf, J., Benjannet, S., Poirier, S., Prat, A., Seidah, NG. et al. (2008). The proprotein convertase PCSK9 induces the degradation of low density lipoprotein receptor (LDLR) and its closest family members VLDLR and ApoER2. *J. Biol. Chem.*, 283, 2363-72. ↗

Hobbs, HH., Goldstein, JL., Brown, MS. (1990). The LDL receptor locus in familial hypercholesterolemia: mutational analysis of a membrane protein. *Annu Rev Genet*, 24, 133-70. ↗

Fyfe, JC., Krahe, R., Kozyraki, R., Kristiansen, M., Moestrup, SK., Aminoff, M. et al. (1999). The intrinsic factor-vitamin B12 receptor, cubilin, is a high-affinity apolipoprotein A-I receptor facilitating endocytosis of high-density lipoprotein. *Nat Med*, 5, 656-61. ↗

Tall, AR., Silver, DL. (2001). The cellular biology of scavenger receptor class B type I. *Curr Opin Lipidol*, 12, 497-504. ↗

Redgrave, TG. (2004). Chylomicron metabolism. *Biochem. Soc. Trans.*, 32, 79-82. ↗

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Table of Contents

- Introduction 1
- ❖ Plasma lipoprotein assembly, remodeling, and clearance 2
 - ❖ Plasma lipoprotein assembly 3
 - ❖ Plasma lipoprotein remodeling 4
 - ❖ Plasma lipoprotein clearance 5
- Table of Contents 6