HF Canada
Hypercholestérolémie Familiale

FH Canada
Familial Hypercholesterolemia

Systems And Molecular Approach of Severe Hyperlipidemia (SMASH) Disorders

LDL Particles

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Homozygous Familial Hypercholesterolemia

- **OMIM:** #143890
- **Description:**
  - **Xanthomas in childhood**
  - **Vascular disease in adolescence and early adulthood**
  - **Corneal arcus**
- **Affected gene(s):** *LDLR*, *(APOB, PCSK9)*
- **PubMed additional information:** 25950706

http://omim.org/entry/143890?search=143890&highlight=143890

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Familial Defective ApoB-100

- **OMIM:** #144010
- **Description:**
  - A missense mutation which reduces the affinity of apoB-100 for the low-density lipoprotein receptor (LDL receptor)
  - This causes impairments in LDL catabolism, resulting in **increased levels of low-density lipoprotein in the blood.**
- **Affected gene(s):** *APOB*
- **Pubmed additional information:** 9777289

http://omim.org/entry/144010?search=%23144010&highlight=144010

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PCSK9 Gain of Function

- **OMIM:** #607786
- **Description:**
  - **High LDL in the blood**
  - **Significantly higher-than-average risk of developing heart disease.**
  - Decreased LDL-R receptors on cell surface
- **Affected gene(s):** *PCSK9*
- **Pubmed additional information: 26088304**

http://www.omim.org/entry/607786?search=PCSK9&highlight=pcsk9

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Autosomal Recessive Familial Hypercholesterolemia (ARH)

- **OMIM:** #603813
- **Description:**
  - **Very high levels of LDL in the plasma**
  - Complete loss of function of an adaptor protein (ARH protein) required for receptor-mediated hepatic uptake of LDL
  - Tuberous and tendon xanthomas
  - Premature atherosclerosis
- **Affected gene(s):** *LDLRAP1*
- **Pubmed additional information:** 2684433

http://omim.org/entry/603813?search=ARH&highlight=arh

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Abetalipoproteinemia

- **OMIM:** #200100
- **Alternate name(s):**
  - BASSEN-KORNZWEIG SYNDROME
  - MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN (MTTP) DEFICIENCY
- **Description:**
  - **Plasma concentrations of triglyceride and cholesterol will be very low**
  - **LDL and ApoB levels are very low or undetectable**
  - Malabsorption of lipid-soluble vitamins leading to retinal degeneration
  - Neuropathy
  - Coagulopathy
  - Hepatic steatosis
- **Affected gene(s):** *MTTP*
- **Pubmed additional information:** 24751931

http://omim.org/entry/200100?search=%23200100&highlight=200100

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Hypobetalipoproteinemia

- **OMIM:** #615558
- **Description:**
  - **Low ApoB**
  - Malabsorption of lipid-soluble vitamins leading to retinal degeneration, neuropathy, and coagulopathy
  - Abnormal buildup of fats in the liver called hepatic steatosis or fatty liver
  - Cirrhosis
  - Difficulty absorbing fats as well as fat-soluble vitamins such as vitamin E and vitamin A
  - Excess fat in the feces
- **Affected gene(s):** *APOB*, *ANGPTL3*
- **Pubmed additional information: 24751931**

http://omim.org/entry/615558?search=%23615558&highlight=615558

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Sitosterolemia

- **OMIM:** #210250
- **Alternate Name(s):**
  - PHYTOSTEROLEMIA
- **Description:**
  - Increased intestinal absorption of both cholesterol and plant-derived cholesterol-like molecules, such as sitosterol.
  - **Patients with this disorder have very high levels of plant sterols in the plasma**
  - Develop tendon and tuberous xanthomas
  - Accelerated atherosclerosis
  - Premature coronary artery disease
  - Do not respond to statins
  - Respond to ezetimibe
- **Affected gene(s):** *ABCG5, ABCG8*
- **Pubmed additional information:** **27104173**

http://omim.org/entry/210250?search=%23210250&highlight=210250

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Familial Lipoprotein(a) hyperlipoproteinemia

- **Description:**
  - Impaired fibrinolysis
  - **Increased cholesterol deposition in the Endothelium**
  - Enhanced oxidation of LDL particles
  - Detected in men and women with premature coronary atherosclerosis.
- **Affected Gene(s):** *APOA*
- **PubMed additional information:** 2144959

Lysosomal Acid Lipase Deficiency

- **OMIM:** #278000
- **Alternate name(s):**
  - LAL DEFICIENCY
  - CHOLESTERYL ESTER STORAGE DISEASE
  - WOLMAN DISEASE
- **Description:**
  - **Severe form in children : massive infiltration of the liver, spleen, and other organs by macrophages filled with cholesteryl esters and triglycerides**
  - Incomplete deficiency causes elevation of transaminases and elevated LDL cholesterol in adults
- **Affected gene(s):** *LIPA*
- **Pubmed additional information: 26225414**

http://omim.org/entry/278000?search=%23278000&highlight=278000

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Remnant Lipoproteins

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Type III Hyperlipoproteinemia

- **Alternate name(s):**
  - DYSBETALIPOPROTEINEMIA TYPE III
- **Description:**
  - Increased broadband beta VLDL
  - Palmar xanthomas
  - Premature CHD
  - Peripheral vascular disease
- **Affected gene(s):** *APOE2/2 + other genes*
- **Pubmed additional information: 25079293**

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Hepatic Lipase Deficiency

- **OMIM:** #614025
- **Description:**
  - **Increase in large, buoyant LDL particles**
  - **Triglyceride-rich LDL and HDL particles**
  - Beta-migrating very low density lipoproteins.
- **Affected gene(s):** *LIPC*
- **Pubmed additional information: 9885775**

http://omim.org/entry/614025?search=%23614025&highlight=614025

Zambon A, Hokanson JE, Brown BG, Brunzell JD. Evidence for a new pathophysiological mechanism for coronary artery disease regression: hepatic lipase-mediated changes in LDL density. Circulation 1999; 99:1959.

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Triglyceride-Rich Lipoproteins

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Familial Hypertriglyceridemia

- **OMIM:** #145750
- **Description:**
  - **Decreased lipoprotein lipase**
  - **Increased plasma VLDL**
  - Plasma Triglycerides are persistently increased
  - Plasma cholesterol and phospholipids are usually within normal limits.
  - Treated through diet
  - Xanthomas
  - Acute pancreatitis
  - Hypertriglyceridemia is commonly found in individuals with type II diabetes mellitus (125853).
- **Affected gene(s):** *LPL, APOC2*

http://omim.org/entry/145750?search=%23145750&highlight=145750

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Familial Hyperchylomicronemia

- **OMIM:** #144650
- **Alternate name(s):**
  - HYPERLIPOPROTEINEMIA, TYPE V
- **Description:**
  - **Increase number of chylomicrons and VLDL particles**
  - **Decreased number of LDL and HDL in plasma**
  - Treated through diet
  - Xanthomas
  - Acute pancreatitis
- **Affected gene(s):** *APOA5*
- **Pubmed additional information: 25732519**

http://omim.org/entry/144650?search=%23144650&highlight=144650

Chylomicron Retention Disease

- **OMIM:** #246700
- **Alternate name(s):**
  - ANDERSON DISEASE
  - LIPID TRANSPORT DEFECT OF INTESTINE
- **Description:**
  - **Disorder of fat absorption**
  - **Nutritional and developmental problems**
  - Fat-soluble vitamins vitamin D and vitamin E are not absorbed
- **Affected gene(s):** *SAR1B*
- **Pubmed additional information: 26868089**

http://omim.org/entry/246700?search=%23246700&highlight=246700

High Density Lipoproteins

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Apolipoprotein A1 Deficiency

- **OMIM :** #107680
- **Description:**
  - **Low levels of HDL**
  - Normal levels of triglycerides and LDL
  - Premature coronary heart disease
  - Can have planar xanthomas
- **Affected gene(s):** *APOA1*
- **Pubmed additional information: 20616715**

http://omim.org/entry/107680?search=107680&highlight=107680

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HDL Deficiency

- **OMIM:** #604091
- **Alternate name(s):**
  - HYPOALPHALIPOPROTEINEMIA
- **Description:**
  - Increased risk for cardiovascular disease
  - **Low levels of HDL**
- **Affected gene(s):** *APOA1*
- **Pubmed additional information: 20616715**

http://omim.org/entry/604091?search=%23604091&highlight=604091

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Tangier Disease

- **OMIM:** #205400
- **Alternate name(s):**
  - ANALPHALIPOPROTEINEMIA
- **Description:**
  - **Significantly reduced levels of HDL in the blood**
  - Neuropathy
  - Splenomegaly, hepatomegaly, corneal clouding, type 2 diabetes.
- **Affected gene(s):** *ABCA1*
- **Pubmed additional information: 16611066**

http://omim.org/entry/205400?search=%23205400&highlight=205400

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LECITHIN CHOLESTEROL ACYLTRANSFERASE (LCAT) Deficiency

- **OMIM:** #245900
- **Alternate name(s):**
  - FISH-EYE DISEASE
  - NORUM DISEASE
  - Familial LCAT deficiency
- **Description:**
  - Corneal opacities
  - Target cell hemolytic anemia
  - Proteinuria with renal failure
- **Affected gene(s):** *LCAT*
- **Pubmed additional information: 25172171**

http://omim.org/entry/245900?search=%23245900&highlight=245900

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Cholesteryl Ester Transfer Protein (CETP) Deficiency

- **OMIM:** #143470
- **Alternate name(s):**
  - HYPERALPHALIPOPROTEINEMIA
- **Description:**
  - Increased HDL levels
  - Decreased LDL levels
- **Affected gene(s):** *CETP*
- **Pubmed additional information: 25410905**

http://omim.org/entry/143470?search=%23143470&highlight=143470

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Niemann pick type A/B

- **OMIM:** #257200(A) #607616 (B)
- **Description:**
  - Infants affected by Niemann-Pick disease type A usually experience an enlarged liver and spleen (hepatosplenomegaly) by the age of 3 months and fail to gain weight and grow at the expected rate
  - Niemann-Pick disease types A and B are caused by an inherited deficiency of acid sphingomyelinase activity
  - Ranges from a severe infantile form with neurologic degeneration resulting in death usually by 3 years of age (type A) to a later-onset non-neurologic form (type B) that is compatible with survival into adulthood.
  - Low HDL cholesterol
  - Interstitial lung disease
- **Affected gene(s):** *SMPD1*
- **Pubmed additional Information (PMID): 25987176**

http://omim.org/entry/257200?search=%23257200&highlight=257200

http://omim.org/entry/607616?search=%23607616&highlight=607616

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Niemann pick type C

- **OMIM:** #257220
- **Description:**
  - **Progressive neurodegeneration**
  - Problems with speech and swallowing that worsen over time, eventually interfering with feeding.
  - Affected individuals often experience progressive decline in intellectual function and about one-third have seizures.
  - Other features include dystonia, vertical supranuclear gaze palsy, dementia, and psychiatric manifestations
  - Low HDL cholesterol
- **Affected gene(s):** *NPC1, NPC2*
- **Pubmed additional information: 27339554**

http://omim.org/entry/257220?search=%23257220&highlight=257220

Other

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Cerebrotendinous Xanthomatosis

- **OMIM:** #213700
- **Alternate name(s):**
  - CEREBRAL CHOLESTERINOSIS
- **Description:**
  - **Large deposits of cholesterol and cholestanol are found in virtually every tissue, particularly the Achilles tendons, brain, and lungs.**
  - Progressive neurologic dysfunction (cerebellar ataxia beginning after puberty, systemic spinal cord involvement and a pseudobulbar phase leading to death)
  - Premature atherosclerosis, and cataracts
  - Plasma cholesterol concentrations are low to normal in CTX patients.
- **Affected gene(s):** *CYP27A1*
- **Pubmed additional information: 20301583**

http://omim.org/entry/213700?search=Cerebrotendinous%20Xanthomatosis&highlight=cerebrotendinous%20xanthomatosi

Summary

DISORDER	GENE
LDL Particles	
• Homozygous familial hypercholesterolemia	LDLR
• Familial defective apo B100	Apo B
• Gain-of-function PCSK9 mutations	PCSK9
• Autosomal recessive hypercholesterolemia	LDLRAP1
• Abetalipoproteinemia	MTTP
• Hypobetalipoproteinemia	APOB
• Familial sitosterolemia	ABCG5/ABCG8
• Familial Lp(a) hyperlipoproteinemia	APOA
• Lysosomal Acid Lipase Deficiency	LIPA
Remnant Lipoproteins	
• Dysbetalipoproteinemia type III	APOE
• Hepatic lipase deficiency	LIPC
Triglyceride-Rich Lipoproteins	
• Familial hypertriglyceridemia	LPL, APOC2, Polygenic
• Familial Hyperchylomicronemia	APOA5
• Chylomicron Retention Disease	SAR1B
High Density Lipoproteins	
• Apo A-I deficiency	APOAI
• Tangier disease/familial HDL deficiency	ABCA1
• Familial LCAT deficiency syndromes	LCAT
• CETP deficiency	CETP
• Niemann-Pick disease types A and B	SMPD1
• Niemann-Pick disease type C	NPC1
Other	
• Cerebrotendinous xanthomatosis	CYP27A1

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