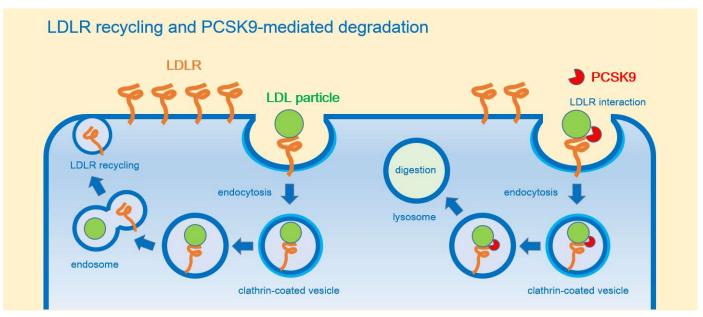


## LipoSEARCH® Applications in Studies of PCSK9 inhibition and reduction

**LipoSEARCH** ® is a cutting edge "lipoprotein profiling service" based on a GP-HPLC followed by a unique data analysis algorithm (patented).

Here are some articles *LipoSEARCH* ® has been used in studies of PCSK9 inhibition and reduction among many examples of *LipoSEARCH* ® applications. *LipoSEARCH* ® supply stable and sensitive measurement of cholesterol, triglycerides, and particle size of the four major classes (CM, VLDL, LDL, and HDL) from small blood sample volume, as well as more detailed subclass and particle number evaluations.



## PCSK9

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a protein that promotes degradation of the LDL receptor and is attracting attention as a new molecular target for the treatment of hypercholesterolemia and associated cardiovascular diseases. PCSK9 inhibitors has been reported potently lower blood LDL-C by increasing hepatocyte LDL receptors and two FDA/EMA-approved monoclonal antibodies: Alirocumab and Evolocumab showed its clinical efficacy. However, these monoclonal antibodies, the only currently available anti-PCSK9 therapies, have several disadvantages, such as high costs, subcutaneous administration (poor compliance and convenience), and potential immunogenicity with long term treatment. Recently, Inclisiran, a short interfering RNA (siRNA) targeting hepatic PCSK9 mRNA has developed and cheaper, orally available, small-molecule drugs are also greatly expected.

Evolocumab Effects on Lipoproteins, Measured by High-Performance Liquid Chromatography

Daisaku Masuda et al

J Atheroscler Thromb . 2020 Nov 1;27(11):1183-1207.



This post-hoc analysis reported the drug efficacy evaluation of Evolocumab used 404 patient blood samples from YUKAWA-2, a phase 3 trial evaluating the effectiveness of Evolocumab in Japanese adult patients with hyperlipidemia or mixed dyslipidemia and at high risk for cardiovascular disease. This research used *LipoSEARCH*® for detailed analysis of lipoprotein 4 major fractions, subclasses and particle numbers. From the result, Evolocumab may reduce atherogenicity by lowering lipid content and improving the lipid profile. This reduction is more accurately quantified by *LipoSEARCH*® than by conventional methods in the very low LDL-C range.

Development of vaccine for dyslipidemia targeted to a proprotein convertase subtilisin/kexin type 9 (PCSK9) epitope in mice

Ryo Kawakami et al

PLoS One. 2018 Feb 13;13(2):e0191895.



This study reported a development of anti-PCSK9 peptide vaccine targeting of the C-terminal domain and evaluated the efficacy using ApoE KO male mouse. *LipoSEARCH* ® is used to evaluate lipoproteins in a detailed assessment of lipid metabolism. Anti-PCSK9 peptide vaccine induced long-lasting anti-PCSK9 antibody production, increased LDL receptor expression significantly and improved lipoprotein profiles with sustained reductions in TCHO, VLDL, and CM. It concludes that anti-PCSK9 vaccination is an innovative approach and may become a new option for dyslipidemia as a long-acting therapeutic drug in the future.

Edible insect Locusta migratoria shows intestinal protein digestibility and improves plasma and hepatic lipid metabolism in male rats

Masaru Ochiai et al

Food Chem. 2022 Dec 1;396:133701.



Edible insects are expected to be one of the sustainable food resources and may be used as functional food materials if their nutritional physiological functions, active ingredients, and mechanisms are clarified. Migratory Locust is a representative edible insect among the approx. 2100 species of edible insects in the world, and contains protein and n-3 lipids. In this study, protein digestibility and dietary effects of the edible migratory locust powder (MLP) on growth and lipid metabolism in rats were investigated and *LipoSEARCH* ® is used for detail lipoprotein profiling. The results confirmed that MLP significantly improve lipid metabolism and prevent the onset and progression of dyslipidemia. Moreover, MLP suppressed plasma PCSK9 and LDL, so MBL may be a new useful approach to prevent cardiovascular diseases through the identification of the active ingredients and inhibitory mechanisms.

Deficiency of Nardilysin in the Liver Reduces Serum Cholesterol Levels Daisuke Yasuda et al *Biol Pharm Bull* . 2021;44(3):363-371.



Nardilysin (N-arginine dibasic convertase; NRDC) is a metalloendopeptidase belonging to M16 family and widely expressed throughout the body, particularly strongly expressed in the liver, heart, testis, and lungs. In this study, hepatic NRDC roles in regulation of lipid metabolism, especially lipoprotein cholesterol metabolism was investigated with liver-specific NRDC deficient mice and cultured murine hepatocytes. The results showed that serum T-CHO and LDL-C levels were significantly reduced by hepatic NRDC deficiency. It is suggested that the serum cholesterol reductions appeared due to increased uptake of circulating LDL into liver by increased LDLR recycling, from both enhanced LDLR expression and reduced PCSK9 secretion in hepatocytes.

Dietary D-allulose alters cholesterol metabolism in Golden Syrian hamsters partly by reducing serum PCSK9 levels Akane Kanasaki et al

J Funct Foods. 2019 Sep;60:103429.



In this paper, the effect of dietary D-allulose on lipid metabolism was evaluated with Golden Syrian hamsters, an animal model with lipid metabolism similar to humans. The results showed that D-allulose significantly decrease LDL/HDL ratio and serum PCSK9. D-allulose increased HDL-C levels in ND-fed hamsters and decreased LDL-C levels in HFD-fed hamsters, causing an overall decrease in the LDL/HDL ratio. It is suggested that Dietary D-allulose may modulate cholesterol metabolism by lowering serum PCSK9 levels and may reduce the risk of atherosclerosis.

## Learn More: *LipoSEARCH*® -

This service is for research purposes only. It cannot be used for clinical diagnostic purposes.







