PRODUCT INFORMATION

PCSK9 (human, recombinant)

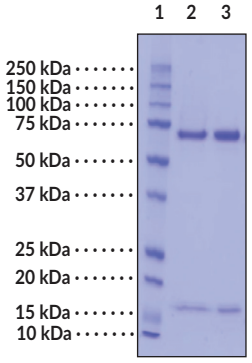
Item No. 20631

Overview and Properties

Synonyms:	NARC-1, Proprotein Convertase Subtilisin Kexin 9
Source:	Active recombinant C-terminal 10x-His-tagged enzyme isolated from a HEK293 overexpression system
Amino Acids:	31-692
Uniprot No.:	Q8NBP7
Molecular Weight:	76 kDa (17 kDa prodomain + 59 kDa mature form)
Storage:	-20°C (as supplied); avoid freeze/thaw cycles by aliquoting protein
Stability:	≥9 months
Purity:	≥95% estimated by SDS-PAGE
Supplied in:	Lyophilized from PBS, pH 7.4, with 30% sucrose
Protein Concentration:	Recommended reconstitution in serum-free media or sterile buffer to 200 µg/ml
Activity:	***batch specific*** Qualitative biological assay - reduces uptake of LDL-DyLight™ by >30% in Huh7 cells at concentrations above 5 µg/ml

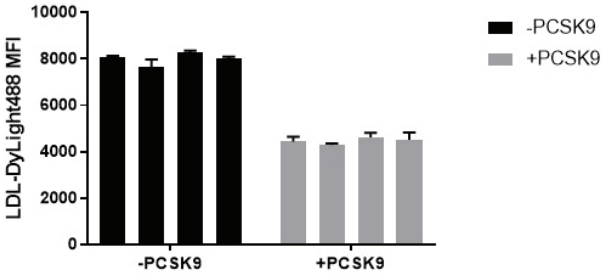
Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Images



Lane 1: MW Markers
Lane 2: PCSK9 (1 µg)
Lane 3: PCSK9 (2 µg)

Representative gel image shown; actual purity may vary between each batch.



PCSK9 inhibits LDL uptake. On four separate plates Huh7 cells were plated and treated with or without 5 µg/ml PCSK9 in media. Sixteen hours later, LDL-DyLight™ 488 was added. After a four-hour incubation the cells were washed, trypsanized, and analyzed by flow cytometry.

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Description

Proprotein convertase subtilisin kexin 9 (PCSK9) is a zymogen and member of the subtilisin serine protease family that reduces protein levels of LDL receptors (LDLRs), the receptor for LDL-cholesterol (LDL-C).[1,2] It is primarily expressed in the liver and is composed of an N-terminal prodomain that regulates PCSK9 maturation, a catalytic domain containing a catalytic aspartic acid-histidine-serine triad, and a C-terminal domain that contains the LDLR binding site.[2,3,4] PCSK9 is synthesized as a proprotein that is autocatalytically cleaved to generate the 63 kDa mature protein in which the N-terminal prodomain remains non-covalently bound to the catalytic domain to inhibit further activity.[4] The mature PCSK9 is secreted and circulates in the plasma where it binds to cell surface-expressed LDLRs, triggering endocytosis and lysosomal degradation of the PCSK9-LDLR complex.[2] This action decreases LDLR expression and reduces cellular LDL-C uptake. Gain-of-function and loss-of-function *PCSK9* mutations have been associated with autosomal dominant hypercholesterolemia and decreased plasma LDL-C levels, respectively, in humans.[2] Reducing the activity of circulating PCSK9 with monoclonal antibodies or small molecule inhibitors decreases LDL-C levels and reduces the risk of adverse cardiovascular events in individuals with hypercholesterolemia. Cayman's PCSK9 (human, recombinant) protein is synthesized as a 76 kDa proprotein. After cleavage of the signal peptide PCKS9 autocatalytically cleaves to the ~15 kDa prodomain and the ~60 kDa mature form and can be used for ELISA, flow cytometry (FC), and Western blot (WB) applications.

References

1. Maxwell, K.N., Fisher, E.A., and Breslow, J.L. Overexpression of PCSK9 accelerates the degradation of the LDLR in a post-endoplasmic reticulum compartment. *Proc. Natl. Acad. Sci. USA* **102(6),** 2069-2074 (2005).
2. Schulz, R., Schlüter, K.-D., and Laufs, U. Molecular and cellular function of the proprotein convertase subtilisin/kexin type 9 (PCSK9). *Basic Res. Cardiol.* **110(2),** 4 (2015).
3. Schulz, R., Schlüter, K.-D., and Laufs, U. Molecular and cellular function of the proprotein convertase subtilisin/kexin type 9 (PCSK9). *Basic Res. Cardiol.* **110(2),** 4 (2015).
4. Burke, A.C., Dron, J.S., Hegele, R.A., *et al.* PCSK9: Regulation and target for drug development for dyslipidemia. *Annu. Rev. Pharmacol. Toxicol.* **57,** 223-244 (2017).

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