

PRODUCT INFORMATION



PCSK9-DyLight™ 488

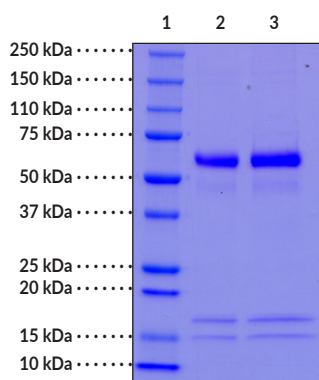
Item No. 30591

Overview and Properties

Synonyms: NARC-1, Proprotein Convertase Subtilisin Kexin 9
Source: Active recombinant N-terminal His-tagged enzyme expressed in *E. coli* cells. Conjugated to DyLight™ 488
Amino Acids: 1-692 (full length)
Uniprot No.: Q8NBP7
Molecular Weight: 13.8 kDa prodomain + 59 kDa mature form
Storage: -80°C (as supplied)
Stability: ≥6 months
Purity: ≥90% estimated by SDS-PAGE
Supplied in: Lyophilized from PBS, pH 7.4, with 30% sucrose
Protein
Activity: PCSK9 downregulates LDL uptake. See Figure 2.

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

Images



Lane 1: MW
Lane 2: PCSK9-DyLight™ 488 (2 µg)
Lane 3: PCSK9-DyLight™ 488 (4 µg)

Figure 1. PCSK9-DyLight™ 488 SDS-PAGE Analysis.
The observed MW of these bands is slightly higher due to post-translational modifications.

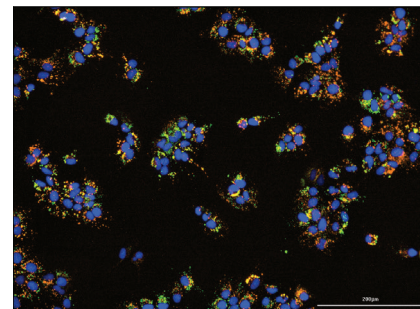
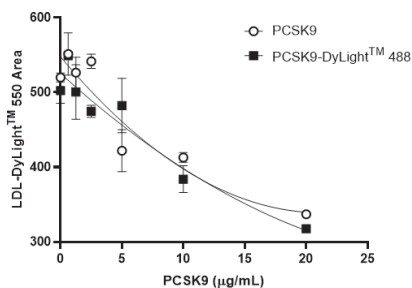


Figure 2. PCSK9 is taken up by hepatocytes, downregulating LDL uptake. Huh7 hepatocytes were plated in a 96-well plate at 5×10^3 cells/well and allowed to adhere. PCSK9-DyLight™ 488 (Item No. 30591) was added at the concentrations indicated for 16 hours in low serum media (2% FBS) followed by a four hour incubation with LDL-DyLight™ 550 (Item No. 10011229) at a 1:200 dilution. At the end of the experiment, the cells were stained with 5 µM Hoechst 33342 and then washed three times in PBS and resuspended in live cell imaging buffer. Imaging was performed using BioTek's Cytation 5 Multi-Mode Imaging Plate Reader and images were analyzed with Gen5 software for area per cell of LDL-DyLight™ 550 (plotted left). On the right, Hoechst-stained nuclei are blue, LDL-DyLight™ 550 is orange, and PCSK9-DyLight™ 488, which was added at 20 µg/ml, is green.

WARNING
THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA
This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

WARRANTY AND LIMITATION OF REMEDY
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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.²⁻⁴ 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.² 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.³ 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.³ 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-DyLight™ 488 is synthesized as a 75.8 kDa proprotein. After cleavage of the signal peptide (1-30 AA) PCSK9 autocatalytically cleaves to the 13.8 kDa prodomain (AA 31-152) and the 59 kDa mature form (AA 153-692 + 10x His-tag). It can be used for cell-based assays.

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. 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).
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. Seidah, N.G., Benjannet, S., Wickham, L., *et al.* The secretory proprotein convertase neural apoptosis-regulated convertase 1 (NARC-1): Liver regeneration and neuronal differentiation. *Proc. Natl. Acad. Sci. USA* **100(3)**, 928-933 (2003).

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