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Produktinformation

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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

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- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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PRODUCT INFORMATION

PCSK9-DyLight™ 633

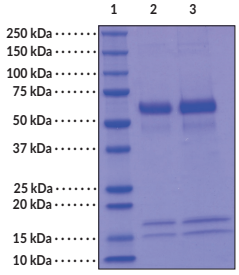
Item No. 30592

Overview and Properties

Synonyms:	NARC-1, Proprotein Convertase Subtilisin Kexin 9
Source:	Active recombinant N-terminal His-tagged enzyme expressed in HEK293 cells. Conjugated to DyLight™ 633
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 Markers
Lane 2: PCSK9-Dylight™ 633 (2 µg)
Lane 3: PCSK9-Dylight™ 633 (4 µg)

Figure 1. PCSK9-Dylight™ 633 SDS-PAGE Analysis
The observed MW of these bands is slightly higher due to post-translational modifications.

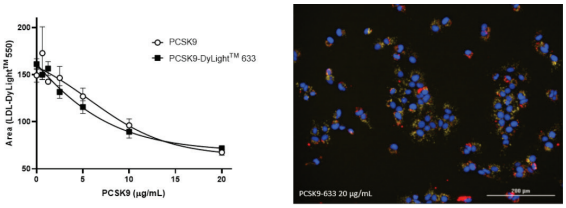


Figure 2. PCSK9 is taken up by hepatocytes, downregulating LDL uptake. Huh7 hepatocytes were plated in a 96-well plate at 5x10^3 cells/well and allowed to adhere. PCSK9-DyLight™ 633 (Item No. 30592) was added at the concentrations indicated for 16 hours in low serum media (2% FBS) followed by a four 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 yellow, and PCSK9-DyLight™ 633, which was added at 20 µg/ml, is red.

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PRODUCT INFORMATION

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.[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-DyLight™ 633 is synthesized as a 75.8 kDa proprotein. After cleavage of the signal peptide (1-30 aa) PCKS9 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. 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. 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).
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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