PRODUCT INFORMATION

PAD4 (human, recombinant; His- and GST-tagged)

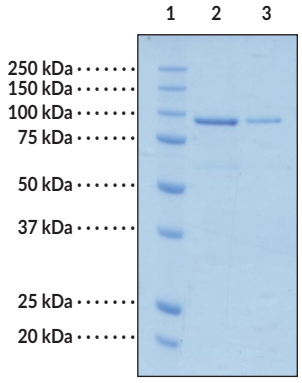
Item No. 25915

Overview and Properties

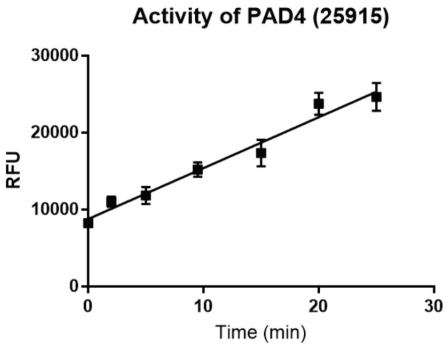
Synonyms:	PADI4, PADI5, Peptidylarginine Deiminase 4, Protein Arginine Deiminase Type 4, Protein Arginine Deiminase Type IV
Source:	Active recombinant N-terminal His-GST-tagged PAD4 expressed in *E. coli*
Amino Acids:	2-663 (full length)
Uniprot No.:	Q9UM07
Molecular Weight:	103.2 kDa
Storage:	-80°C (as supplied)
Stability:	≥1 year
Purity:	***batch specific*** (≥80% estimated by SDS-PAGE)
Supplied in:	50 mM HEPES, pH 8.0, 300 mM sodium chloride, 1mM DTT, and 10% glycerol
Protein Concentration:	***batch specific***
Activity:	***batch specific***
Specific Activity:	***batch specific***
Unit Definition:	One unit is defined as the amount of enyme required to produce 1 nmol of NH_4^+ per minute at 37°C in 50 mM HEPES, pH 8.0, containing 10 mM calcium chloride, 5 mM DTT, and 2 mM N-α-Benzoyl-L-Arginine Ethyl Ester (BAEE).

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

Images



Lane 1: MW Markers
Lane 2: PAD4 (His- and GST-tagged; 4 µg)
Lane 3: PAD4 (His- and GST-tagged; 2 µg)



PAD4 activity was determined using Cayman's PAD4 Inhibitor Screening Assay Kit (Item No. 700560) with 0.25 µg PAD4 and 2 mM BAEE substrate.

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Description

Protein arginine deiminase 4 (PAD4) catalyzes the conversion of arginine residues to citrulline within cellular protein substrates, resulting in the loss of a positive charge, which can alter protein structure and/or function.[1] It is expressed in neutrophils, as well as a variety of tissues, including the brain, liver, lung, and kidney.[1-3] PAD4 has a key role in NETosis, a lytic form of cell death characterized by the release of neutrophil extracellular traps (NETs).[1] Upon neutrophil activation, PAD4 translocates to the nucleus where it citrullinates histones, initiating chromatin decondensation and the release of NETs.[2-4,5] Neutrophils isolated from *Pad4*$^{-/-}$ mice exhibit decreased citrullination of histone H3 under both basal and LPS-stimulated conditions and are defective for NET formation in response to stimulation with LPS, phorbol 12-myristate 13-acetate (PMA; Item No. 10008014), or hydrogen peroxide.[4] *Pad4*$^{-/-}$ mice exhibit larger lesions than wild-type mice in a model of necrotizing fasciitis induced by M1 group A *S. pyogenes* lacking the extracellular DNase Sda1. *Pad4*-deficient mice also exhibit reduced infarct size in a model of myocardial ischemia-reperfusion injury and reduced tumor growth in a Lewis lung carcinoma model.[2,6] Serum PAD4 autoantibodies have been found in patients with rheumatoid arthritis and are associated with disease severity.[7] Cayman's PAD4 (human, recombinant; His- and GST-tagged) protein can be used for enzyme activity assays. This protein contains two types of affinity tags, His and GST, that allow for flexibility in the removal of PAD4 following citrullination reactions and an enterokinase cleavage site that facilitates removal of both the His and GST tags.

References

1. van Beers, J.J.B.C., Zendman, A.J.W., Raijmakers, R., *et al.* Peptidylarginine deiminase expression and activity in PAD2 knock-out and PAD4-low mice. *Biochimie* **95(2)**, 299-308 (2013).
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3. Jones, J.E., Causey, C.P., Knuckley, B., *et al.* Protein arginine deiminase 4 (PAD4): Current understanding and future therapeutic potential. *Curr. Opin. Drug Discov. Devel.* **12(5)**, 616-627 (2009).
4. Li, P., Li, M., Lindberg, M.R., *et al.* PAD4 is essential for antibacterial innate immunity mediated by neutrophil extracellular traps. *J. Exp. Med.* **207(9)**, 1853-1862 (2010).
5. Thiam, H.R., Wong, S.L., Qiu, R., *et al.* NETosis proceeds by cytoskeleton and endomembrane disassembly and PAD4-mediated chromatin decondensation and nuclear envelope rupture. *Proc. Natl. Acad. Sci. USA* **117(13)**, 7326-7337 (2020).
6. Savchenko, A.S., Borissoff, J.I., Martinod, K., *et al.* VWF-mediated leukocyte recruitment with chromatin decondensation by PAD4 increases myocardial ischemia/reperfusion injury in mice. *Blood* **123(1)**, 141-148 (2014).
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