# **PRODUCT** INFORMATION



Human Fibrinogen (PAD4 Citrullinated)

Item No. 400076

## **Overview and Properties**

Source:	Fibrinogen, purified from human plasma, that has been shown by certified tests to be negative for HBsAg and for antibodies to HIV and HCV. Citrullinated with human recombinant PAD4.
Uncitrullinated Fibrinogen	
Molecular Weight:	$\alpha$ chain isoform 1 (95 kDa), $\alpha$ chain isoform 2 (69.8 kDa), $\beta$ chain (55.9 kDa), and isoform $\gamma\text{-B}$ chain (51.5 kDa)
Storage:	-80°C (as supplied); avoid clotting by thawing the protein slowly on ice and flash freeze in liquid nitrogen if needed
Stability:	≥1 year
Purity:	Homogeneous by SDS-PAGE. Clottable proteins: ≥90%
Supplied in:	Frozen solution with 50 mM Tris-HCl, pH 7.4, 150 mM sodium chloride, and 10% glycerol.
Special Conditions	This product has a propensity to clot; avoid agitation and warm to room temperature after thawing on ice. Freeze/thaws are not recommended as concentration may vary.

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

#### Images



Lane 2: Pre-Citrullination (5 µg) Lane 3: Post-Citrullination (5 µg)

10	20		40	50
MKRMVSWSFH	KLKTMKHLLL	LLLCVFLVKS	QGVNDNEEGF	FSA <b>R</b> GH <b>R</b> PLD
60	70	80	90	100
KKREEAPSLR	PAPPPISGGG	Y <b>R</b> A <b>R</b> PAKAAA	TQKKVE <b>R</b> KAP	DAGGCLHADP
110	120	130	140	150
DLGVLCPTGC	QLQEALLQQE	RPIRNSVDEL	NNNVEAVSQT	SSSSFQYMYL
160	170	180	190	200
LKDLWQKRQK	QVKDNENVVN	EYSSELEKHQ	LYIDETVNSN	IPTNLRVLRS
210	220	230	240	250
ILENLRSKIQ	KLESDVSAQM	EYCRTPCTVS	CNIPVVSGKE	CEEIIRKGGE
260	270	280	290	300
TSEMYLIQPD	SSVKPYRVYC	DMNTENGGWT	VIQNRQDGSV	DFG <b>R</b> KWDPYK
310	320	330	340	350
QGFGNVATNT	DGKNYCGLPG	EYWLGNDKIS	QLTRMGPTEL	LIEMEDWKGD
360	370	380	390	400
KVKAHYGGFT	VQNEANKYQI	SVNKYRGTAG	NALMDGASQL	MGENRTMTIH
410	420	430	440	450
NGMFFSTYD <b>R</b>	DNDGWLTSDP	<b>R</b> KQCSKEDGG	GWWYNRCHAA	NPNG <b>R</b> YYWGG
460	470	480	490	
OVTWDMAKHG	TODGWWMNW	KGSWYSMRKM	SMKIRPEEPO	0

Identification of modified sites in Human Fibrinogen (PAD4 Citrullinated) (Item No. 400076). The β-chain of Human Fibrinogen (PAD4 Citrullinated) was detected by LC-MS/MS and analyzed using Mascot and Scaffold PTM software. Deiminated arginines are indicated in teal.

Citrullination sites shown are representative of typical results. Batch-to-batch variations may occur

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.

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### Description

Fibrinogen is a plasma clotting factor composed of three different polypeptide chains ( $\alpha$ ,  $\beta$  and  $\gamma$ ). Under chronic inflammatory conditions, fibrinogen can be acted upon by the enzyme peptidylarginine deiminase 4 (PAD4), converting specific arginine residues to citrulline. Patients with rheumatoid arthritis (RA) produce antibodies that bind citrullinated human fibrinogen.<sup>1</sup> The citrullinated fibrinogen and reactive antibodies form immune complexes in RA patients, and these immune complexes can stimulate macrophages.<sup>2,3</sup> Recently, it has been discovered that immunizing certain strains of mice with citrullinated human fibrinogen can induce the production of anti-citrullinated human fibrinogen antibodies and the development of arthritis that shares many pathophysiological features of the human disease.<sup>4,5</sup>

### References

- 1. Hill, J.A., Al-Bishri, J., Gladman, D.D., *et al.* Serum autoantibodies that bind citrullinated fibrinogen are frequently found in patients with rheumatoid arthritis. *J. Rheumatol.* **33(11)**, 2115-2119 (2006).
- 2. Zhao, X., Okeke, N.L., Sharpe, O., *et al.* Circulating immune complexes contain citrullinated fibrinogen in rheumatoid arthritis. *Arthritis Res. Ther.* **10(4)**, (2008).
- 3. Sokolove, J., Zhao, X., Chandra, P.E., *et al.* Immune complexes containing citrullinated fibrinogen costimulate macrophages via toll-like receptor 4 and Fcγ receptor. *Arthritis Rheum.* **63(1)**, 53-62 (2011).
- Hill, J.A., Bell, D.A., Brintnell, W., et al. Arthritis induced by posttranslationally modified (citrullinated) fibrinogen in DR4-IE transgenic mice. J. Exp. Med. 205(4), 967-979 (2008).
- 5. Yue, D., Brintnell, W., Mannik, L.A., *et al.* CTLA-4lg blocks the development and progression of citrullinated fibrinogen-induced arthritis in DR4-transgenic mice. *Arthritis Rheum.* **62(10)**, 2941-2952 (2010).

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