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HMGB1 Protein (AA 2-215) (His tag)



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Overview	
Quantity:	1 mg
Target:	HMGB1
Protein Characteristics:	AA 2-215
Origin:	Human
Source:	Escherichia coli (E. coli)
Protein Type:	Recombinant
Purification tag / Conjugate:	This HMGB1 protein is labelled with His tag.
Application:	Western Blotting (WB), SDS-PAGE (SDS), ELISA, Crystallization (Crys)
Product Details	
Sequence:	GKGDPKKPRG KMSSYAFFVQ TCREEHKKKH PDASVNFSEF SKKCSERWKT MSAKEKGKFE
	DMAKADKARY EREMKTYIPP KGETKKKFKD PNAPKRPPSA FFLFCSEYRP KIKGEHPGLS

IGDVAKKLGE MWNNTAADDK QPYEKKAAKL KEKYEKDIAA YRAKGKPDAA KKGVVKAEKS KKKKEEEEDE EDEEDEEEE DEEDEDEEED DDDE

Sequence without tag. Tag location is at the discretion of the manufacturer. If you have a special request, please contact us.

Characteristics:

- Made in Germany from design to production by highly experienced protein experts.
- · Human HMGB1 Protein (raised in E. Coli) purified by multi-step, protein-specific process to ensure crystallization grade.
- State-of-the-art algorithm used for plasmid design (Gene synthesis).

This protein is a made to order protein and will be made for the first time for your order. Our experts in the lab will ensure that you receive a correctly folded protein.

The big advantage of ordering our made-to-order proteins in comparison to ordering custom made proteins from other companies is that there is no financial obligation in case the protein cannot be expressed or purified.

In the unlikely event that the protein cannot be expressed or purified we do not charge anything (other companies might charge you for any performed steps in the expression process for custom-made proteins, e.g. fees might apply for the expression plasmid, the first expression experiments or purification optimization).

When you order this made-to-order protein you will only pay upon receival of the correctly folded protein. With no financial risk on your end you can rest assured that our experienced protein experts will do everything to make sure that you receive the protein you ordered.

The protein's absorbance will be measured in several dilutions and is measured against its specific reference buffer.

The concentration of our recombinant proteins is measured using the absorbance at 280nm.

The concentration of the protein is calculated using its specific absorption coefficient. We use the Expasy's protparam tool to determine the absorption coefficient of each protein.

Purification:

Two step purification of proteins expressed in bacterial culture:

- In a first purification step, the protein is purified from the cleared cell lysate using three different His-tag capture materials: high yield, EDTA resistant, or DTT resistant. Eluate fractions are analyzed by SDS-PAGE.
- 2. Protein containing fractions of the best purification are subjected to second purification step through size exclusion chromatography. Eluate fractions are analyzed by SDS-PAGE and Western blot.

Purity:

>95 % as determined by SDS PAGE, Size Exclusion Chromatography and Western Blot.

Sterility:

0.22 µm filtered

Endotoxin Level:

Endotoxin has not been removed. Please contact us if you require endotoxin removal.

Grade:

Crystallography grade

Target Details

Target:	HMGB1	
Alternative Name:	HMGB1 (HMGB1 Products)	
Background:	Multifunctional redox sensitive protein with various roles in different cellular compartments. In the nucleus is one of the major chromatin-associated non-histone proteins and acts as a DNA	
	chaperone involved in replication, transcription, chromatin remodeling, V(D)J recombination,	

DNA repair and genome stability. Proposed to be an universal biosensor for nucleic acids. Promotes host inflammatory response to sterile and infectious signals and is involved in the coordination and integration of innate and adaptive immune responses. In the cytoplasm functions as sensor and/or chaperone for immunogenic nucleic acids implicating the activation of TLR9-mediated immune responses, and mediates autophagy. Acts as danger associated molecular pattern (DAMP) molecule that amplifies immune responses during tissue injury. Released to the extracellular environment can bind DNA, nucleosomes, IL-1 beta, CXCL12, AGER isoform 2/sRAGE, lipopolysaccharide (LPS) and lipoteichoic acid (LTA), and activates cells through engagement of multiple surface receptors. In the extracellular compartment fully reduced HMGB1 (released by necrosis) acts as a chemokine, disulfide HMGB1 (actively secreted) as a cytokine, and sulfonyl HMGB1 (released from apoptotic cells) promotes immunological tolerance (PubMed:23519706, PubMed:23446148, PubMed:23994764, PubMed:25048472). Has proangiogdenic activity (By similarity). May be involved in platelet activation (By similarity). Binds to phosphatidylserine and phosphatidylethanolamide (By similarity). Bound to RAGE mediates signaling for neuronal outgrowth (By similarity). May play a role in accumulation of expanded polyglutamine (polyQ) proteins such as huntingtin (HTT) or TBP (PubMed:23303669, PubMed:25549101). {ECO:0000250|UniProtKB:P10103,

ECO:0000250|UniProtKB:P12682, ECO:0000250|UniProtKB:P63158,

ECO:0000250|UniProtKB:P63159, ECO:0000269|PubMed:23303669,

ECO:0000269|PubMed:25549101, ECO:0000305|PubMed:23446148,

ECO:0000305|PubMed:23519706, ECO:0000305|PubMed:23994764,

ECO:0000305|PubMed:25048472}., Nuclear functions are attributed to fully reduced HGMB1. Associates with chromatin and binds DNA with a preference to non-canonical DNA structures such as single-stranded DNA, DNA-containing cruciforms or bent structures, supercoiled DNA and ZDNA. Can bent DNA and enhance DNA flexibility by looping thus providing a mechanism to promote activities on various gene promoters by enhancing transcription factor binding and/or bringing distant regulatory sequences into close proximity (PubMed:20123072). May have an enhancing role in nucleotide excision repair (NER) (By similarity). However, effects in NER using in vitro systems have been reported conflictingly (PubMed:19446504, PubMed:19360789). May be involved in mismatch repair (MMR) and base excision repair (BER) pathways (PubMed:15014079, PubMed:16143102, PubMed:17803946). May be involved in double strand break repair such as non-homologous end joining (NHEJ) (By similarity). Involved in V(D)J recombination by acting as a cofactor of the RAG complex: acts by stimulating cleavage and RAG protein binding at the 23 bp spacer of conserved recombination signal sequences (RSS) (By similarity). In vitro can displace histone H1 from highly bent DNA (By similarity). Can restructure the canonical nucleosome leading to relaxation of structural

constraints for transcription factor-binding (By similarity). Enhances binding of sterol regulatory element-binding proteins (SREBPs) such as SREBF1 to their cognate DNA sequences and increases their transcriptional activities (By similarity). Facilitates binding of TP53 to DNA (PubMed:23063560). Proposed to be involved in mitochondrial quality control and autophagy in a transcription-dependent fashion implicating HSPB1, however, this function has been questioned (By similarity). Can modulate the activity of the telomerase complex and may be involved in telomere maintenance (By similarity). {ECO:0000250|UniProtKB:P10103, ECO:0000250|UniProtKB:P63158, ECO:0000250|UniProtKB:P63159, ECO:0000269|PubMed:15014079, ECO:0000269|PubMed:16143102, ECO:0000269|PubMed:17803946, ECO:0000269|PubMed:19446504, ECO:0000269|PubMed:23063560, ECO:0000305|PubMed:19360789, ECO:0000305|PubMed:20123072}., In the cytoplasm proposed to dissociate the BECN1:BCL2 complex via competitive interaction with BECN1 leading to autophagy activation (PubMed:20819940). Involved in oxidative stress-mediated autophagy (PubMed:21395369). Can protect BECN1 and ATG5 from calpain-mediated cleavage and thus proposed to control their proautophagic and proapoptotic functions and to regulate the extent and severity of inflammation-associated cellular injury (By similarity). In myeloid cells has a protective role against endotoxemia and bacterial infection by promoting autophagy (By similarity). Involved in

endosomal translocation and activation of TLR9 in response to CpG-DNA in macrophages (By similarity). {ECO:0000250|UniProtKB:P63158, ECO:0000269|PubMed:20819940, ECO:0000269|PubMed:21395369}., In the extracellular compartment (following either active secretion or passive release) involved in regulation of the inflammatory response. Fully reduced HGMB1 (which subsequently gets oxidized after release) in association with CXCL12 mediates the recruitment of inflammatory cells during the initial phase of tissue injury, the CXCL12:HMGB1 complex triggers CXCR4 homodimerization (PubMed:22370717). Induces the migration of monocyte-derived immature dendritic cells and seems to regulate adhesive and migratory functions of neutrophils implicating AGER/RAGE and ITGAM (By similarity). Can bind to various types of DNA and RNA including microbial unmethylated CpG-DNA to enhance the innate immune response to nucleic acids. Proposed to act in promiscuous DNA/RNA sensing which cooperates with subsequent discriminative sensing by specific pattern recognition receptors (By similarity). Promotes extracellular DNA-induced AIM2 inflammasome activation implicating AGER/RAGE (PubMed:24971542). Disulfide HMGB1 binds to transmembrane receptors, such as AGER/RAGE, TLR2, TLR4 and probably TREM1, thus activating their signal transduction pathways. Mediates the release of cytokines/chemokines such as TNF, IL-1, IL-6, IL-8, CCL2, CCL3, CCL4 and CXCL10 (PubMed:12765338, PubMed:18354232,

PubMed:19264983, PubMed:20547845, PubMed:24474694). Promotes secretion of interferon-

gamma by macrophage-stimulated natural killer (NK) cells in concert with other cytokines like IL-2 or IL-12 (PubMed:15607795). TLR4 is proposed to be the primary receptor promoting macrophage activation and signaling through TLR4 seems to implicate LY96/MD-2 (PubMed:20547845). In bacterial LPS- or LTA-mediated inflammatory responses binds to the endotoxins and transfers them to CD14 for signaling to the respective TLR4:LY96 and TLR2 complexes (PubMed:18354232, PubMed:21660935, PubMed:25660311). Contributes to tumor proliferation by association with ACER/RAGE (By similarity). Can bind to IL1-beta and signals through the IL1R1:IL1RAP receptor complex (PubMed:18250463). Binding to class A CpG activates cytokine production in plasmacytoid dendritic cells implicating TLR9, MYD88 and AGER/RAGE and can activate autoreactive B cells. Via HMGB1-containing chromatin immune complexes may also promote B cell responses to endogenous TLR9 ligands through a B-cell receptor (BCR)-dependent and ACER/RAGE-independent mechanism (By similarity). Inhibits phagocytosis of apoptotic cells by macrophages, the function is dependent on poly-ADPribosylation and involves binding to phosphatidylserine on the cell surface of apoptotic cells (By similarity). In adaptive immunity may be involved in enhancing immunity through activation of effector T cells and suppression of regulatory T (TReg) cells (PubMed:15944249, PubMed:22473704). In contrast, without implicating effector or regulatory T-cells, required for tumor infiltration and activation of T-cells expressing the lymphotoxin LTA:LTB heterotrimer thus promoting tumor malignant progression (By similarity). Also reported to limit proliferation of T-cells (By similarity). Released HMGB1:nucleosome complexes formed during apoptosis can signal through TLR2 to induce cytokine production (PubMed:19064698). Involved in induction of immunological tolerance by apoptotic cells, its pro-inflammatory activities when released by apoptotic cells are neutralized by reactive oxygen species (ROS)-dependent oxidation specifically on Cys-106 (PubMed:18631454). During macrophage activation by activated lymphocyte-derived self apoptotic DNA (ALD-DNA) promotes recruitment of ALD-DNA to endosomes (By similarity). {ECO:0000250|UniProtKB:P10103, ECO:0000250|UniProtKB:P63158, ECO:0000250|UniProtKB:P63159, ECO:0000269|PubMed:12765338, ECO:0000269|PubMed:15607795, ECO:0000269|PubMed:15944249, ECO:0000269|PubMed:18250463, ECO:0000269|PubMed:18354232, ECO:0000269|PubMed:18631454, ECO:0000269|PubMed:19064698, ECO:0000269|PubMed:19264983, ECO:0000269|PubMed:20547845, ECO:0000269|PubMed:21660935, ECO:0000269|PubMed:22370717, ECO:0000269|PubMed:22473704, ECO:0000269|PubMed:24474694, ECO:0000269|PubMed:24971542, ECO:0000269|PubMed:25660311, ECO:0000269|Ref.8}.

Target Details

Molecular Weight:	25.7 kDa Including tag.	
UniProt:	P09429	
Pathways:	p53 Signaling, Regulation of Muscle Cell Differentiation, Skeletal Muscle Fiber Development, Positive Regulation of Endopeptidase Activity, Regulation of Carbohydrate Metabolic Process, Toll-Like Receptors Cascades, Smooth Muscle Cell Migration, Inflammasome	

Application Details

Application Notes:	In addition to the applications listed above we expect the protein to work for functional studies
	as well. As the protein has not been tested for functional studies yet we cannot offer a gurantee
	though.
Comment:	In cases in which it is highly likely that the recombinant protein with the default tag will be
	insoluble our protein lab may suggest a higher molecular weight tag (e.g. GST-tag) instead to
	increase solubility. We will discuss all possible options with you in detail to assure that you
	receive your protein of interest.
Restrictions:	For Research Use only

Handling

Format:	Liquid
1 omiat.	Elquid
Buffer:	100 mM NaCL, 20 mM Hepes, 10% glycerol. pH value is at the discretion of the manufacturer.
Handling Advice:	Avoid repeated freeze-thaw cycles.
Storage:	-80 °C
Storage Comment:	Store at -80°C.
Expiry Date:	Unlimited (if stored properly)



Image 1. "Crystallography Grade" protein due to multi-step, protein-specific purification process