

Chymosin

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Chymosin or **rennin** is an enzyme found in rennet. It is produced by newborn ruminant animals in the lining of the fourth stomach to curdle the milk they ingest, allowing a longer residence in the bowels and better absorption. It used widely in the production of cheese. Bovine chymosin is now produced recombinantly in *E. coli*, *Aspergillus niger var awamori*, and *K. lactis* as alternative resource.

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Occurrence

Chymosin is produced by ruminant animals in the lining of the abomasum. Chymosin is produced by gastric chief cells in young ruminants and some other newborn animals^[2] to curdle the milk they ingest, allowing a longer residence in the bowels and better absorption.

Some other non-ruminant species, including pigs, cats, and seals, produce it.^[3]

Humans have a pseudogene for chymosin that does not generate a protein, found on chromosome 1.^{[3][4]} Humans have other proteases to digest milk, such as pepsin and lipase.^{[5]:262}

Enzymatic reaction

Chymosin causes cleavage of a specific linkage — the peptide bond between 105 and 106, phenylalanine and methionine, in K-casein, the native substrate of this enzyme.^[6] Preceding the uneven cleavage of kappa-casein, the opposite charges on the substrate can interact with the enzyme; histidines on the kappa-casein are attracted to glutamates and aspartate on chymosin.^[6] When chymosin is not binding substrate, a beta-hairpin, sometimes referred to as "the flap," can hydrogen bond with the active site, therefore covering it and not allowing further binding of substrate.^[1]

When chymosin acts on milk, the specific linkage between the hydrophobic (para-casein) and hydrophilic (acidic glycopeptide) groups of casein is broken, since they are joined by phenylalanine and methionine.^[citation needed] The

Chymosin



Crystal structure of bovine chymosin complex with the inhibitor CP-113972.^[1]

Identifiers

EC number 3.4.23.4 (<http://www.chem.qmul.ac.uk/iubmb/enzyme/EC3/4/23/4.html>)

CAS number 9001-98-3 (<http://tools.wmflabs.org/magnustools/cas.php?language=en&cas=9001-98-3&title=>)

Databases

IntEnz IntEnz view (<http://www.ebi.ac.uk/intenz/query?cmd=SearchEC&ec=3.4.23.4>)

BRENDA BRENDA entry (http://www.brenda-enzymes.org/php/result_flat.php4?ecno=3.4.23.4)

ExPASy NiceZyme view (<http://www.expasy.org/enzyme/3.4.23.4>)

KEGG KEGG entry (http://www.genome.ad.jp/dbget-bin/www_bget?enzyme+3.4.23.4)

MetaCyc metabolic pathway (<http://biocyc.org/META/substring-search?type=NIL&object=3.4.23.4>)

PRIAM profile (http://priam.prabi.fr/cgi-bin/PRIAM_profiles_CurrentRelease.pl?EC=3.4.23.4)

PDB structures RCSB PDB (http://www.rcsb.org/pdb/search/smartSubquery.do?smartSearchSubtype=EnzymeClassificationQuery&Enzyme_Classification=3.4.23.4) PDBe (<http://www.ebi.ac.uk/pdbe-srv/PDBeXplore/enzyme/?ec=3.4.23.4>) PDBsum (http://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/enzymes/GetPage.pl?ec_number=3.4.23.4)

Gene AmiGO (<http://amigo.geneontology.org/cgi-bin/amigo>)

Ontology /go.cgi?query=GO:0030602&view=details) / EGO (<http://www.ebi.ac.uk/ego/DisplayGoTerm?id=GO:0030602&format=normal>)

Search

PMC articles (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&term=3.4.23.4%5BEC/RN%20Number%5D%20AND%20pubmed%20pmc%20local%5Bsb%5D>)


PubMed articles (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&term=3.4.23.4%5BEC/RN%20Number%5D>)

NCBI proteins (<http://www.ncbi.nlm.nih.gov/protein?term=3.4.23.4%5BEC/RN%20Number%5D>)

hydrophobic group unites and forms a 3D network that traps the aqueous phase of the milk. The resultant product is calcium phosphocaseinate. Due to this reaction, rennin is used to bring about the extensive precipitation and curd formation in cheese-making.

Examples

Listed below are the ruminant *Cym* gene and corresponding human pseudogene:

Chymosin [Precursor] (<i>B.taurus</i> or <i>C.dromedarius</i>)	
	
<small>Imol</small> X-ray analysis of calf chymosin ^[7]	
Identifiers	
Symbol	Cym
Alt.	CPC
symbols	
Entrez	529879 (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=retrieve&dopt=default&list_uids=529879&rn=1)
PDB	4CMS (RCSB PDB (http://www.pdb.org/pdb/cgi/explorer.cgi?pdbId=4CMS) PDBe (http://www.ebi.ac.uk/pdbe-srv/view/entry/4CMS) PDBj (http://pdbj.org/pdb/4CMS))
RefSeq	NP_851337.1 (http://genome.ucsc.edu/cgi-bin/hgTracks?Submit=Submit&position=NP_851337.1&rn=1)
UniProt	Q9GK11 (http://www.uniprot.org/uniprot/Q9GK11)

chymosin pseudogene (<i>H.sapiens</i>)	
Identifiers	
Symbol	CYMP
Entrez	643160 (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=retrieve&dopt=default&list_uids=643160&rn=1)
HUGO	2588 (http://www.genenames.org/data/hgnc_data.php?hgnc_id=2588)
OMIM	118943 (http://www.omim.org/118943)
RefSeq	NR_003599 (http://genome.ucsc.edu/cgi-bin/hgTracks?Submit=Submit&position=NR_003599&rn=1)
Other data	
Locus	Chr. 1 <i>p13.3</i> (http://omim.org/search?index=geneMap&search=1p13.3)

Recombinant Chymosin

Because of the imperfections and scarcity of microbial and animal rennets, producers sought replacements. With the development of genetic engineering, it became possible to extract rennet-producing genes from animal stomach and insert them into certain bacteria, fungi or yeasts to make them produce chymosin during fermentation.^{[8][9]} The genetically-modified microorganism is killed after fermentation and chymosin isolated from the fermentation broth, so that the Fermentation-Produced Chymosin (FPC) used by cheese producers does not contain any GM component or ingredient.^[10] FPC contains the identical chymosin as the animal source, but produced in a more efficient way. FPC products have been on the market since 1990 and have been considered in the last 20 years the ideal

milk-clotting enzyme.^[11]

FPC was the first artificially produced enzyme to be registered and allowed by the US Food and Drug Administration. In 1999, about 60% of US hard cheese was made with FPC^[12] and it has up to 80% of the global market share for rennet.^[13]

By 2008, approximately 80% to 90% of commercially made cheeses in the US and Britain were made using FPC.^[10] Today, the most widely used Fermentation-Produced Chymosin (FPC) is produced either by the fungus *Aspergillus niger* and commercialized under the trademark CHY-MAX®^[14] by the Danish company Chr. Hansen, or produced by *Kluyveromyces lactis* and commercialized under the trademark MAXIREN®^[15] by the Dutch company DSM.

FPC contains only chymosin B, achieving a high degree of purity compared with animal rennet. FPC can deliver several benefits to the cheese producer compared with animal or microbial rennet, such as higher production yield, better curd texture and reduced bitterness.^[11]

References

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Further reading

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External links

- The MEROPS online database for peptidases and their inhibitors: A01.006 (<http://merops.sanger.ac.uk/cgi-bin/merops.cgi?id=A01.006>)

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Categories: Genes on chromosome 1

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