Lipase

A **lipase** (/ˈlaɪpeɪs/, /-peɪz/) is any enzyme that catalyzes the hydrolysis of fats (lipids).[1] Lipases are a subclass of the esterases.

Lipases perform essential roles in digestion, transport and processing of dietary lipids (e.g. triglycerides, fats, oils) in most, if not all, living organisms. Genes encoding lipases are even present in certain viruses.[2][3]

Most lipases act at a specific position on the glycerol backbone of a lipid substrate (A1, A2 or A3)(small intestine). For example, human pancreatic lipase (HPL),[4] which is the main enzyme that breaks down dietary fats in the human digestive system, converts triglyceride substrates found in ingested oils to monoglycerides and two fatty acids.

Several other types of lipase activities exist in nature, such as phospholipases [5] and sphingomyelinases;[6] however, these are usually treated separately from "conventional" lipases.

Some lipases are expressed and secreted by pathogenic organisms during an infection. In particular, *Candida albicans* has many different lipases, possibly reflecting broad-lipolytic activity, which may contribute to the persistence and virulence of *C. albicans* in human tissue.[7]

A computer-generated image of a type of pancreatic lipase (PLRP2) from the guinea pig. PDB: 1GPL (https://www.rcsb.org/structure/1GPL).

Contents

Structure and catalytic mechanism

A diverse array of genetically distinct lipase enzymes are found in nature, and they represent several types of protein folds and catalytic mechanisms. However, most are built on an alpha/beta hydrolase fold[8][9][10][11] and employ a chymotrypsin-like hydrolysis mechanism using a catalytic triad consisting of a serine nucleophile, a histidine base, and an acid residue, usually aspartic acid.[12][13]

Physiological distribution

Lipases are involved in diverse biological processes which range from routine metabolism of dietary triglycerides to cell signaling[14] and inflammation.[15] Thus, some lipase activities are confined to specific compartments within cells while others work in extracellular spaces.

- In the example of lysosomal lipase, the enzyme is confined within an organelle called the lysosome.
- Other lipase enzymes, such as pancreatic lipases, are secreted into extracellular spaces where they serve to process dietary lipids into more simple forms that can be more easily absorbed and transported throughout the body.
- Fungi and bacteria may secrete lipases to facilitate nutrient absorption from the external medium (or in examples of pathogenic microbes, to promote invasion of a new host).
- Certain wasp and bee venoms contain phospholipases that enhance the effects of injury and inflammation delivered by a sting.
- As biological membranes are integral to living cells and are largely composed of phospholipids, lipases play important roles in cell biology.
- *Malassezia globosa*, a fungus thought to be the cause of human dandruff, uses lipase to break down sebum into oleic acid and increase skin cell production, causing dandruff.[16]

Human lipases

The main lipases of the human digestive system are pancreatic lipase (PL) and pancreatic lipase related protein 2 (PLRP2), which are secreted by the pancreas. Humans also have several related enzymes, including hepatic lipase, endothelial lipase, and lipoprotein lipase. Not all of these lipases function in the gut (see table).

Name	Gene	Location	Description	Disorder
bile salt-dependent lipase	BSDL	pancreas, breast milk	aids in the digestion of fats	
pancreatic lipase	*PNLIP (https://www.genenames.org/tools/search/#!/genes?query=PNLIP)*	digestive juice	In order to exhibit optimal enzyme activity in the gut lumen, PL requires another protein, colipase, which is also secreted by the pancreas.[17]	
lysosomal lipase	*LIPA (https://www.genenames.org/tools/search/#!/genes?query=LIPA)*	interior space of organelle: lysosome	Also referred to as lysosomal acid lipase (LAL or LIPA) or acid cholesteryl ester hydrolase	Cholesteryl ester storage disease (CESD) and Wolman disease are both caused by mutations in the gene encoding lysosomal lipase.[18]
hepatic lipase	*LIPC (https://www.genenames.org/tools/search/#!/genes?query=LIPC)*	endothelium	Hepatic lipase acts on the remaining lipids carried on lipoproteins in the blood to regenerate LDL (low density lipoprotein).	–
lipoprotein lipase	*LPL (https://www.genenames.org/tools/search/#!/genes?query=LPL)* or "LIPD"	endothelium	Lipoprotein lipase functions in the blood to act on triacylglycerides carried on VLDL (very low density lipoprotein) so that cells can take up the freed fatty acids.	Lipoprotein lipase deficiency is caused by mutations in the gene encoding lipoprotein lipase.[19][20]
hormone-sensitive lipase	*LIPE (https://www.genenames.org/tools/search/#!/genes?query=LIPE)*	intracellular	–	–
gastric lipase	*LIPF (https://www.genenames.org/tools/search/#!/genes?query=LIPF)*	digestive juice	Functions in the infant at a near-neutral pH to aid in the digestion of lipids	–
endothelial lipase	*LIPG (https://www.genenames.org/tools/search/#!/genes?query=LIPG)*	endothelium	–	–
pancreatic lipase related protein 2	*PNLIPRP2 (https://www.genenames.org/tools/search/#!/genes?query=PNLIPRP2)* or "PLRP2" –	digestive juice	–	–
pancreatic lipase related protein 1	*PNLIPRP1 (https://www.genenames.org/tools/search/#!/genes?query=PNLIPRP1)* or "PLRP1"	digestive juice	Pancreatic lipase related protein 1 is very similar to PLRP2 and PL by amino acid sequence (all three genes probably arose via gene duplication of a single ancestral pancreatic lipase gene). However, PLRP1 is devoid of detectable lipase activity and its function remains unknown, even though it is conserved in other mammals.[21][22]	-
lingual lipase	?	saliva	Active at gastric pH levels. Optimum pH is about 3.5-6. Secreted by several of the salivary glands (Ebner's glands at the back of the tongue (lingua), the sublingual glands, and the parotid glands)	–

Other lipases include *LIPH (https://www.genenames.org/tools/search/#!/genes?query=LIPH)*, *LIPI (https://www.genenames.org/tools/search/#!/genes?query=LIPI)*, *LIPJ (https://www.genenames.org/tools/search/#!/genes?query=LIPJ)*, *LIPK (https://www.genenames.org/tools/search/#!/genes?query=LIPK)*, *LIPM (https://www.genenames.org/tools/search/#!/genes?query=LIPM)*, *LIPN (https://www.genenames.org/tools/search/#!/genes?query=LIPN)*, *MGLL (https://www.genenames.org/tools/search/#!/genes?query=MGLL)*, *DAGLA (https://www.genenames.org/tools/search/#!/genes?query=DAGLA)*, *DAGLB (https://www.genenames.org/tools/search/#!/genes?query=DAGLB)*, and *CEL (https://www.genenames.org/tools/search/#!/genes?query=CEL)*.

There also are a diverse array of phospholipases, but these are not always classified with the other lipases.

Industrial uses

Lipases serve important roles in human practices as ancient as yogurt and cheese fermentation. However, lipases are also being exploited as cheap and versatile catalysts to degrade lipids in more modern applications. For instance, a biotechnology company has brought recombinant lipase enzymes to market for use in applications such as baking, laundry detergents and even as biocatalysts[23] in alternative energy strategies to convert vegetable oil into fuel.[24][25] High enzyme activity lipase can replace traditional catalyst in processing biodiesel, as this enzyme replaces chemicals in a process which is otherwise highly energy intensive,[26] and can be more environmentally friendly and safe. Industrial application of lipases requires process intensification for continuous processing using tools like continuous flow microreactors at small scale.[27][28] Lipases are generally animal sourced, but can also be sourced microbially.

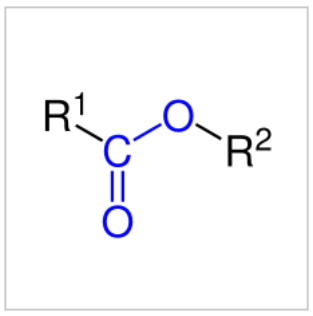
Diagnostic use

Blood tests for lipase may be used to help investigate and diagnose acute pancreatitis and other disorders of the pancreas.[29] Measured serum lipase values may vary depending on the method of analysis.

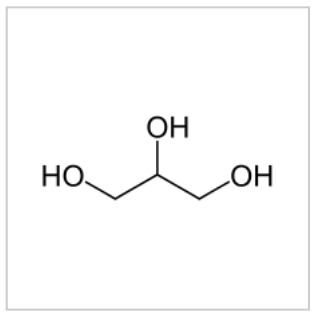
Medical use

Lipase can also assist in the breakdown of fats into lipids in those undergoing pancreatic enzyme replacement therapy (PERT). It is a key component in Sollpura (Liprotamase).[30][31]

Additional images



General formula of a carboxylate ester



Glycerol

See also

- Alpha toxin
- Pathology
- Lysosomal acid lipase deficiency
- Peripheral membrane proteins
- Phospholipase A
- Phospholipase C
- Triglyceride lipase
- Phospholipase A2
- Outer membrane phospholipase A1
- Patatin-like phospholipase

References

1. Svendsen A (2000). "Lipase protein engineering". *Biochim Biophys Acta*. **1543** (2): 223–228. doi:10.1016/S0167-4838(00)00239-9 (https://doi.org/10.1016%2FS0167-4838%2800%2900239-9). PMID 11150608 (https://pubmed.ncbi.nlm.nih.gov/11150608).
2. Afonso C, Tulman E, Lu Z, Oma E, Kutish G, Rock D (1999). "The Genome of Melanoplus sanguinipes Entomologists" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC103860). *J Virol*. **73** (1): 533–52. PMC 103860 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC103860). PMID 9847359 (https://pubmed.ncbi.nlm.nih.gov/9847359).
3. Girod A, Wobus C, Zádori Z, Ried M, Leike K, Tijssen P, Kleinschmidt J, Hallek M (2002). "The VP1 capsid protein of adeno-associated virus type 2 is carrying a phospholipase A2 domain required for virus infectivity" (https://doi.org/10.1099%2F0022-1317-83-5-973). *J Gen Virol*. **83** (Pt 5): 973–8. doi:10.1099/0022-1317-83-5-973 (https://doi.org/10.1099%2F0022-1317-83-5-973). PMID 11961250 (https://pubmed.ncbi.nlm.nih.gov/11961250).
4. Winkler FK; D'Arcy A; W Hunziker (1990). "Structure of human pancreatic lipase". *Nature*. **343** (6260): 771–774. doi:10.1038/343771a0 (https://doi.org/10.1038%2F343771a0). PMID 2106079 (https://pubmed.ncbi.nlm.nih.gov/2106079).
5. Diaz, B.L.; J. P. Arm. (2003). "Phospholipase A(2)". *Prostaglandins Leukot Essent Fatty Acids*. **69** (2–3): 87–97. doi:10.1016/S0952-3278(03)00069-3 (https://doi.org/10.1016%2FS0952-3278%2803%2900069-3). PMID 12895591 (https://pubmed.ncbi.nlm.nih.gov/12895591).
6. Goñi F, Alonso A (2002). "Sphingomyelinases: enzymology and membrane activity" (https://doi.org/10.1016%2FS0014-5793%2802%2903482-8). *FEBS Lett*. **531** (1): 38–46. doi:10.1016/S0014-5793(02)03482-8 (https://doi.org/10.1016%2FS0014-5793%2802%2903482-8). PMID 12401200 (https://pubmed.ncbi.nlm.nih.gov/12401200).
7. Hube B, Stehr F, Bossenz M, Mazur A, Kretschmar M, Schafer W (2000). "Secreted lipases of Candida albicans: cloning, characterisation and expression analysis of a new gene family with at least ten members". *Arch. Microbiol*. **174** (5): 362–374. doi:10.1007/s002030000218 (https://doi.org/10.1007%2Fs002030000218). PMID 11131027 (https://pubmed.ncbi.nlm.nih.gov/11131027).
8. Winkler FK; D'Arcy A; W Hunziker (1990). "Structure of human boob pancreatic lipase". *Nature*. **343** (6260): 771–774. doi:10.1038/343771a0 (https://doi.org/10.1038%2F343771a0). PMID 2106079 (https://pubmed.ncbi.nlm.nih.gov/2106079).
9. Schrag J, Cygler M (1997). "Lipases and alpha/beta hydrolase fold". *Methods Enzymol*. Methods in Enzymology. **284**: 85–107. doi:10.1016/S0076-6879(97)84006-2 (https://doi.org/10.1016%2FS0076-6879%2897%2984006-2). ISBN 978-0-12-182185-2. PMID 9379946 (https://pubmed.ncbi.nlm.nih.gov/9379946).
10. Egmond, M. R.; C. J. van Bemmel (1997). "Impact of Structural Information on Understanding of Lipolytic Function". *Methods Enzymol*. Methods in Enzymology. **284**: 119–129. doi:10.1016/S0076-6879(97)84008-6 (https://doi.org/10.1016%2FS0076-6879%2897%2984008-6). ISBN 978-0-12-182185-2. PMID 9379930 (https://pubmed.ncbi.nlm.nih.gov/9379930).
11. Withers-Martinez C; Carriere F; Verger R; Bourgeois D; C Cambillau (1996). "A pancreatic lipase with a phospholipase A1 activity: crystal structure of a chimeric pancreatic lipase-related protein 2 from guinea pig" (https://doi.org/10.1016%2FS0969-2126%2896%2900143-8). *Structure*. **4** (11): 1363–74. doi:10.1016/S0969-2126(96)00143-8 (https://doi.org/10.1016%2FS0969-2126%2896%2900143-8). PMID 8939760 (https://pubmed.ncbi.nlm.nih.gov/8939760).
12. Brady, L.; A. M. Brzozowski; Z. S. Derewenda; E. Dodson; G. Dodson; S. Tolley; J. P. Turkenburg; L. Christiansen; B. Huge-Jensen; L. Norskov; et al. (1990). "A serine protease triad forms the catalytic centre of a triacylglycerol lipase". *Nature*. **343** (6260): 767–70. doi:10.1038/343767a0 (https://doi.org/10.1038%2F343767a0). PMID 2304552 (https://pubmed.ncbi.nlm.nih.gov/2304552).
13. Lowe ME (1992). "The catalytic site residues and interfacial binding of human pancreatic lipase". *J Biol Chem*. **267** (24): 17069–73. PMID 1512245 (https://pubmed.ncbi.nlm.nih.gov/1512245).
14. Spiegel S; Foster D; R Kolesnick (1996). "Signal transduction through lipid second messengers". *Current Opinion in Cell Biology*. **8** (2): 159–67. doi:10.1016/S0955-0674(96)80061-5 (https://doi.org/10.1016%2FS0955-0674%2896%2980061-5). PMID 8791422 (https://pubmed.ncbi.nlm.nih.gov/8791422).
15. Tjoelker LW; Eberhardt C; Unger J; Trong HL; Zimmerman GA; McIntyre TM; Stafforini DM; Prescott SM; PW Gray (1995). "Plasma platelet-activating factor acetylhydrolase is a secreted phospholipase A2 with a catalytic triad" (https://doi.org/10.1074%2Fjbc.270.43.25481). *J Biol Chem*. **270** (43): 25481–7. doi:10.1074/jbc.270.43.25481 (https://doi.org/10.1074%2Fjbc.270.43.25481). PMID 7592717 (https://pubmed.ncbi.nlm.nih.gov/7592717).
16. Genetic Code of Dandruff Cracked – BBC News (http://news.bbc.co.uk/2/hi/health/7080434.stm)
17. Lowe ME (2002). "The triglyceride lipases of the pancreas" (https://doi.org/10.1194%2Fjlr.R200012-JLR200). *J Lipid Res*. **43** (12): 2007–16. doi:10.1194/jlr.R200012-JLR200 (https://doi.org/10.1194%2Fjlr.R200012-JLR200). PMID 12454260 (https://pubmed.ncbi.nlm.nih.gov/12454260).
18. Omim – Wolman Disease (https://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=278000)
19. Familial lipoprotein lipase deficiency – Genetics Home Reference (http://ghr.nlm.nih.gov/condition=lipoproteinlipasedeficiencyfamilial)

20. Gilbert B, Rouis M, Griglio S, de Lumley L, Laplaud P (2001). "Lipoprotein lipase (LPL) deficiency: a new patient homozygote for the preponderant mutation Gly188Glu in the human LPL gene and review of reported mutations: 75 % are clustered in exons 5 and 6". *Ann Genet*. **44** (1): 25–32. doi:10.1016/S0003-3995(01)01037-1 (https://doi.org/10.1016%2FS0003-3995%2801%2901037-1). PMID 11334614 (https://pubmed.ncbi.nlm.nih.gov/11334614).
21. Crenon I, Foglizzo E, Kerfelec B, Verine A, Pignol D, Hermoso J, Bonicel J, Chapus C (1998). "Pancreatic lipase-related protein type I: a specialized lipase or an inactive enzyme" (https://doi.org/10.1093%2Fprotein%2F11.2.135). *Protein Eng*. **11** (2): 135–42. doi:10.1093/protein/11.2.135 (https://doi.org/10.1093%2Fprotein%2F11.2.135). PMID 9605548 (https://pubmed.ncbi.nlm.nih.gov/9605548).
22. De Caro J, Carriere F, Barboni P, Giller T, Verger R, De Caro A (1998). "Pancreatic lipase-related protein 1 (PLRP1) is present in the pancreatic juice of several species". *Biochim Biophys Acta*. **1387** (1–2): 331–41. doi:10.1016/S0167-4838(98)00143-5 (https://doi.org/10.1016%2FS0167-4838%2898%2900143-5). PMID 9748646 (https://pubmed.ncbi.nlm.nih.gov/9748646).
23. Guo Z, Xu X (2005). "New opportunity for enzymatic modification of fats and oils with industrial potentials". *Org Biomol Chem*. **3** (14): 2615–9. doi:10.1039/b506763d (https://doi.org/10.1039%2Fb506763d). PMID 15999195 (https://pubmed.ncbi.nlm.nih.gov/15999195).
24. Gupta R, Gupta N, Rathi P (2004). "Bacterial lipases: an overview of production, purification and biochemical properties". *Appl Microbiol Biotechnol*. **64** (6): 763–81. doi:10.1007/s00253-004-1568-8 (https://doi.org/10.1007%2Fs00253-004-1568-8). PMID 14966663 (https://pubmed.ncbi.nlm.nih.gov/14966663).
25. Ban K, Kaieda M, Matsumoto T, Kondo A, Fukuda H (2001). "Whole cell biocatalyst for biodiesel fuel production utilizing Rhizopus oryzae cells immobilized within biomass support particles". *Biochem Eng J*. **8** (1): 39–43. doi:10.1016/S1369-703X(00)00133-9 (https://doi.org/10.1016%2FS1369-703X%2800%2900133-9). PMID 11356369 (https://pubmed.ncbi.nlm.nih.gov/11356369).
26. Harding, K.G; Dennis, J.S; von Blottnitz, H; Harrison, S.T.L (2008). "A life-cycle comparison between inorganic and biological catalysis for the production of biodiesel". *Journal of Cleaner Production*. **16** (13): 1368–78. doi:10.1016/j.jclepro.2007.07.003 (https://doi.org/10.1016%2Fj.jclepro.2007.07.003).
27. Bhangale, Atul S; Beers, Kathryn L; Gross, Richard A (2012). "Enzyme-Catalyzed Polymerization of End-Functionalized Polymers in a Microreactor". *Macromolecules*. **45** (17): 7000–8. doi:10.1021/ma301178k (https://doi.org/10.1021%2Fma301178k).
28. Kundu, Santanu; Bhangale, Atul S; Wallace, William E; Flynn, Kathleen M; Guttman, Charles M; Gross, Richard A; Beers, Kathryn L (2011). "Continuous Flow Enzyme-Catalyzed Polymerization in a Microreactor". *Journal of the American Chemical Society*. **133** (15): 6006–11. doi:10.1021/ja111346c (https://doi.org/10.1021%2Fja111346c). PMID 21438577 (https://pubmed.ncbi.nlm.nih.gov/21438577).
29. "Lipase – TheTest" (http://labtestsonline.org/understanding/analytes/lipase/tab/test/). *Lab Tests Online*. Retrieved 12 May 2014.
30. "Anthera Pharmaceuticals – Sollpura." Anthera Pharmaceuticals – Sollpura. N.p., n.d. Web. 21 July 2015. <http://www.anthera.com/pipeline/science/sollpura.html Archived (https://web.archive.org/web/20150718042137/http://www.anthera.com/pipeline/science/sollpura.html) 2015-07-18 at the Wayback Machine>.
31. Bustanji, Yasser; Al-Masri, Ihab M; Mohammad, Mohammad; Hudaib, Mohammad; Tawaha, Khaled; Tarazi, Hamada; Alkhatib, Hatim S (2010). "Pancreatic lipase inhibition activity of trilactone terpenes of *Ginkgo biloba*". *Journal of Enzyme Inhibition and Medicinal Chemistry*. **26** (4): 453–9. doi:10.3109/14756366.2010.525509 (https://doi.org/10.3109%2F14756366.2010.525509). PMID 21028941 (https://pubmed.ncbi.nlm.nih.gov/21028941).

25. Gulzar, Bio-degradation of hydrocarbons using different bacterial and fungal species. Published in international conference on biotechnology and neurosciences. CUSAT (cochin university of science and technology), 2003

External links

- Lipase (https://meshb.nlm.nih.gov/record/ui?name=Lipase) at the US National Library of Medicine Medical Subject Headings (MeSH)