Lactate dehydrogenase

**Lactate dehydrogenase** (**LDH** or **LD**) is an [enzyme](https://en.wikipedia.org/wiki/Enzyme) found in nearly all living cells. LDH catalyzes the conversion of [lactate](https://en.wikipedia.org/wiki/Lactic_acid) to [pyruvate](https://en.wikipedia.org/wiki/Pyruvic_acid%22%20%5Co%20%22Pyruvic%20acid) and back, as it converts NAD+ to [NADH](https://en.wikipedia.org/wiki/NADH) and back. A [dehydrogenase](https://en.wikipedia.org/wiki/Dehydrogenase%22%20%5Co%20%22Dehydrogenase) is an enzyme that transfers a [hydride](https://en.wikipedia.org/wiki/Hydride) from one molecule to another.

LDH exists in four distinct enzyme classes. This article is specifically about the [NAD(P)](https://en.wikipedia.org/wiki/NAD%28P%29)-dependent L-lactate dehydrogenase. Other LDHs act on D-lactate and/or are dependent on [cytochrome c](https://en.wikipedia.org/wiki/Cytochrome_c%22%20%5Co%20%22Cytochrome%20c): [D-lactate dehydrogenase (cytochrome)](https://en.wikipedia.org/wiki/D-lactate_dehydrogenase_%28cytochrome%29) and [L-lactate dehydrogenase (cytochrome)](https://en.wikipedia.org/wiki/L-lactate_dehydrogenase_%28cytochrome%29).

LDH is expressed extensively in body tissues, such as blood cells and heart muscle. Because it is released during tissue damage, it is a marker of common injuries and disease such as heart failure.

Reaction



Reaction catalyzed by lactate dehydrogenase

Lactate dehydrogenase catalyzes the interconversion of [pyruvate](https://en.wikipedia.org/wiki/Pyruvate%22%20%5Co%20%22Pyruvate) and [lactate](https://en.wikipedia.org/wiki/Lactic_acid) with concomitant interconversion of NADH and [NAD+](https://en.wikipedia.org/wiki/Nicotinamide_adenine_dinucleotide). It converts pyruvate, the final product of [glycolysis](https://en.wikipedia.org/wiki/Glycolysis%22%20%5Co%20%22Glycolysis), to lactate when oxygen is absent or in short supply, and it performs the reverse reaction during the [Cori cycle](https://en.wikipedia.org/wiki/Cori_cycle) in the [liver](https://en.wikipedia.org/wiki/Liver). At high concentrations of lactate, the enzyme exhibits feedback inhibition, and the rate of conversion of pyruvate to lactate is decreased. It also catalyzes the dehydrogenation of [2-hydroxybutyrate](https://en.wikipedia.org/wiki/2-hydroxybutyrate), but it is a much poorer substrate than lactate.

Active site[[edit](https://en.wikipedia.org/w/index.php?title=Lactate_dehydrogenase&action=edit&section=2" \o "Edit section: Active site)]



Arrow pushing mechanism for the reaction catalyzed by lactate dehydrogenase

LDH in humans uses [His](https://en.wikipedia.org/wiki/Histidine)(193) as the proton donor, and works in unison with the [coenzyme](https://en.wikipedia.org/wiki/Cofactor_%28biochemistry%29) ([Arg](https://en.wikipedia.org/wiki/Arginine)99 and [Asn](https://en.wikipedia.org/wiki/Asparagine)138), and substrate (Arg106; Arg169; [Thr](https://en.wikipedia.org/wiki/Threonine)248) binding residues. The His(193) active site, is not only found in the human form of LDH, but is found in many different animals, showing the convergent evolution of LDH. The two different subunits of LDH (LDHA, also known as the M subunit of LDH, and LDHB, also known as the H subunit of LDH) both retain the same active site and the same amino acids participating in the reaction. The noticeable difference between the two subunits that make up LDH's tertiary structure is the replacement of [alanine](https://en.wikipedia.org/wiki/Alanine%22%20%5Co%20%22Alanine) (in the M chain) with a [glutamine](https://en.wikipedia.org/wiki/Glutamine) (in the H chain). This tiny but notable change is believed to be the reason the H subunit can bind faster, and the M subunit's catalytic activity isn't reduced when subjected to the same conditions as the H subunit, whereas the H subunit's activity is reduced fivefold.

Isozymes

Lactate dehydrogenase is composed of four subunits (tetramer). The two most common subunits are the LDH-M and LDH-H protein, encoded by the *LDHA* and *LDHB* genes, respectively. These two subunits can form five possible tetramers (isoenzymes): 4H, 4M, and the three mixed tetramers (3H1M, 2H2M, 1H3M). These five isoforms are enzymatically similar but show different tissue distribution: The major isoenzymes of skeletal muscle and liver, M4, has four muscle (M) subunits, while H4 is the main isoenzymes for heart muscle in most species, containing four heart (H) subunits.

* LDH-1 (4H)—in the [heart](https://en.wikipedia.org/wiki/Heart) and in RBC ([red blood cells](https://en.wikipedia.org/wiki/Red_blood_cells)), as well as the [brain](https://en.wikipedia.org/wiki/Brain)
* LDH-2 (3H1M)—in the [reticuloendothelial system](https://en.wikipedia.org/wiki/Reticuloendothelial_system%22%20%5Co%20%22Reticuloendothelial%20system)
* LDH-3 (2H2M)—in the [lungs](https://en.wikipedia.org/wiki/Lung)
* LDH-4 (1H3M)—in the [kidneys](https://en.wikipedia.org/wiki/Kidney), [placenta](https://en.wikipedia.org/wiki/Placenta), and [pancreas](https://en.wikipedia.org/wiki/Pancreas)
* LDH-5 (4M)—in the [liver](https://en.wikipedia.org/wiki/Liver) and [striated muscle](https://en.wikipedia.org/wiki/Striated_muscle)[[4]](https://en.wikipedia.org/wiki/Lactate_dehydrogenase#cite_note-4)

LDH-2 is usually the predominant form in the [serum](https://en.wikipedia.org/wiki/Blood_serum). An LDH-1 level higher than the LDH-2 level (a "flipped pattern") suggests [myocardial infarction](https://en.wikipedia.org/wiki/Myocardial_infarction) (damage to heart tissues releases heart LDH, which is rich in LDH-1, into the bloodstream). The use of this phenomenon to diagnose infarction has been largely superseded by the use of [Troponin](https://en.wikipedia.org/wiki/Troponin%22%20%5Co%20%22Troponin) I or T measurement.

There are two more mammalian LDH subunits that can be included in LDH tetramers: LDHC and LDHBx. LDHC is a testes-specific LDH protein, that is encoded by the LDHC gene. LDHBx is a [peroxisome](https://en.wikipedia.org/wiki/Peroxisome%22%20%5Co%20%22Peroxisome)-specific LDH protein. LDHBx is the readthrough-form of LDHB. LDHBx is generated by [translation](https://en.wikipedia.org/wiki/Translation) of the LDHB [mRNA](https://en.wikipedia.org/wiki/MRNA), but the [stop codon](https://en.wikipedia.org/wiki/Stop_codon) is interpreted as an [amino acid](https://en.wikipedia.org/wiki/Amino_acid)-encoding [codon](https://en.wikipedia.org/wiki/Codon%22%20%5Co%20%22Codon). In consequence, [translation](https://en.wikipedia.org/wiki/Translation) continues to the next stop codon. This leads to the addition of seven amino acid residues to the normal LDH-H protein. The extension contains a [peroxisomal targeting signal](https://en.wikipedia.org/wiki/Peroxisomal_targeting_signal%22%20%5Co%20%22Peroxisomal%20targeting%20signal), so that LDHBx is imported into the peroxisome.