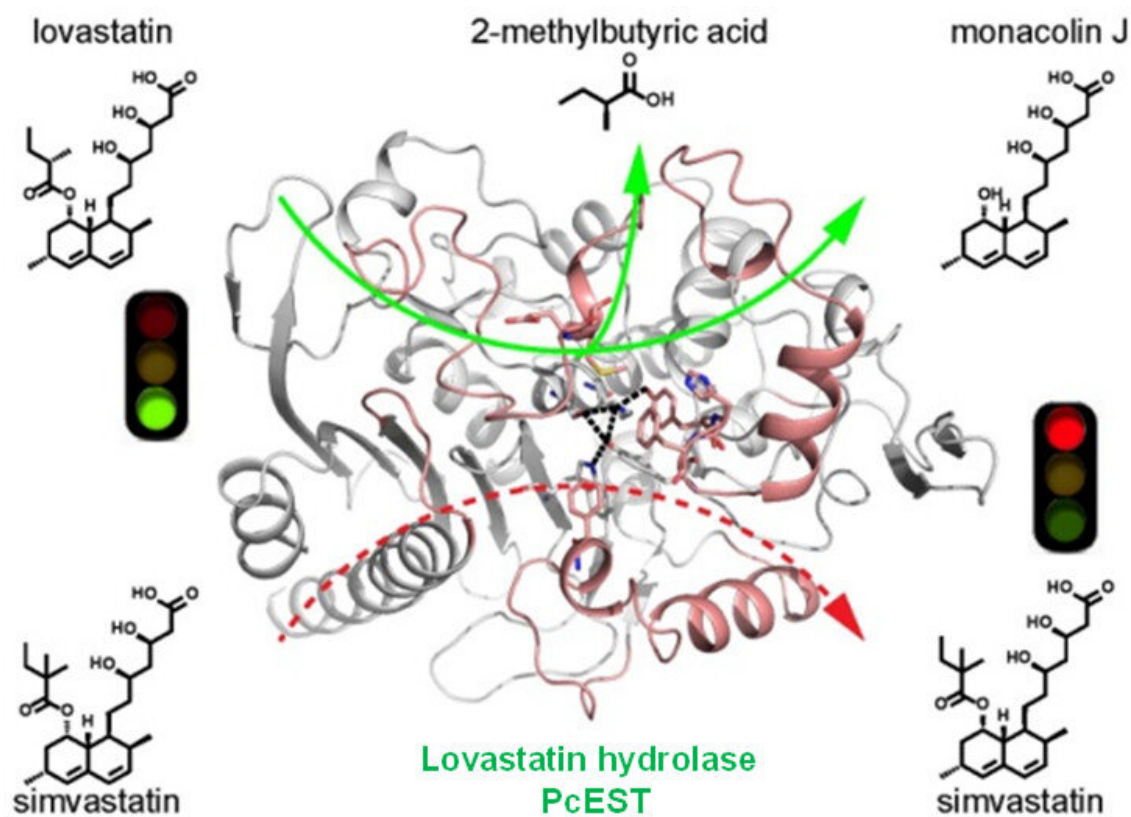


Scientists reveal catalytic mechanism of lovastatin hydrolase

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Lovastatin hydrolase PcEST specifically and efficiently catalyzes the conversion of lovastatin to monacolin J, but cannot hydrolyze simvastatin Credit: LIANG Yajing

Hyperlipidemia, one of the most common threats to human health, refers

to an abnormal increase of cholesterol and/or triglycerides in the blood. One effective method for prevention and treatment of the disease is cholesterol-lowering therapy, such as the drug simvastatin.

Alkaline hydrolysis of lovastatin to produce monacolin J is an intermediate step to obtain simvastatin. Enzymatic synthesis using a specific and efficient lovastatin hydrolase is one of the alternative methods for green production of monacolin J.

Recently, the research team led by Prof. Lu Xuefeng from the Qingdao Institute of Bioenergy and Bioprocess Technology (QIBEBT), Chinese Academy of Sciences (CAS), revealed the [catalytic mechanism](#) and structure-function relationship of the specific and efficient lovastatin hydrolase PcEST.

It is the first report describing the mechanism and structure-function relationship of lovastatin hydrolase and provides insights about further lovastatin hydrolase screening, engineering, and commercial applications. The results were published in the *Journal of Biological Chemistry*.

Structure-based biochemical analyses and mutagenesis assays revealed that the Ser-57 (nucleophile)-Tyr-170 (general base)-Lys-60 (general acid) catalytic triad, together with the hydrogen-bond network around the [active site](#) and the specific substrate-binding tunnel determine the efficient and specific [lovastatin](#) hydrolysis by PcEST.

Furthermore, using structure-guided enzyme engineering, the researchers developed a PcEST variant, D106A, which improved solubility and thermostability, suggesting a promising application of this variant in industrial processes.

More information: Yajing Liang et al, Structural insights into the

catalytic mechanism of lovastatin hydrolase, *Journal of Biological Chemistry* (2019). [DOI: 10.1074/jbc.RA119.011936](https://doi.org/10.1074/jbc.RA119.011936)

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