Shape and properties of lipase binding sites

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Lipases (EC 3.1.1.3) are widely used technical enzymes. They catalyze the cleavage of water-insoluble esters of fatty acids. Over the past 30 years, sequence and structure information on lipases accumulated abundantly, highly pure recombinant lipases have become available, and the number of patents and reports on their improvement by protein engineering is steadily increasing.

To assemble published information on lipases and to assist in analyzing sequence-structure-function relationship, the Lipase Engineering Database (LED) has been established. By aligning and classifying sequences, superimposing structures and a consistent annotation, shape of substrate binding sites were compared and related to properties of lipases. Two important properties, the specificity profile toward scissile fatty acids and enantioselectvity toward chiral alcohols, were investigated by molecular modeling.

To understand the fatty acid chain length profile of lipases, schematic shapes were generated. Residues which mediate chain length specificity were identified and the experimentally observed effect of mutations could be understood.

To investigate the enantioselectivity of lipases toward chiral alcohols, various substrates were docked using molecular dynamics simulations and geometric parameters were extracted, which correlate with experimentally observed enantioselectivities. Thus, comparing and analyzing shape and properties of lipase binding sites and studying enzyme-substrate complexes, intermolecular interactions were identified which mediate specificity and selectivity.