Poster

Unravelling the mechanism of lipid – enzyme interactions in the limbus region of lipases at atomic resolution

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Å resolution [1]. Having the open and closed states at atomic resolution allows relating protonation to the conformation, indicating the role of Asp145 and Lys290 in the conformation alteration. Once positioned within the catalytic triad, substrates are then hydrolysed, and products released. However, the intermediate steps of substrate transfer from the lipidic-aqueous phase to the enzyme surface and then down to the catalytic site are still unclear. By inhibiting CALB with ethyl phosphonate and incubating with glyceryl tributyrate (2,3-di(butanoyloxy)propyl butanoate), the crystal structure of the lipid-enzyme complex, at 1.55 Å resolution, shows the tributyrin in the limbus region of active site [2]. The substrate is found above the catalytic Ser, with the glycerol backbone readily pre-aligned for further processing by key interactions via an extended water network with α-helix10 and α-helix5. These findings explain the lack of 'interfacial activation' of CALB and offer new elements to elucidate the mechanism of substrate recognition, transfer and catalysis of Candida antarctica Lipase B (CALB) and lipases in general.

[1] Stauch, B., Fisher, S. J., Cianci, M. (2015). Journal of Lipid Research, 56, 2348-2358.

[2] Silvestrini, L. & Cianci, M. (2020). International Journal of Biological Macromolecules, 158, 358-363.

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