Cation–π and hydrophobic interaction controlled PET recognition in double mutated cutinase – identification of a novel binding subsite for better catalytic activity

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Accelerated hydrolysis of polyethylene terephthalate (PET) by enzymatic surface modification of various hydrolases, which would not degrade the building blocks of PET in order to retain the quality of recycled PET, is a promising research area. Many studies have been reported to identify mutations of different hydrolases that can improve PET degradation. Recently, the mutation of glycine and phenyl alanine with alanine in cutinase was found to improve the activity of PET degradation 6-fold.[1,2] Yet, a deep insight into the overall structural basis as well as the explicit role played by the amino acid residues for PET degradation is still elusive, which is nevertheless important for comparative analyses, structure–function relations and rational optimization of the degradation process.

Our molecular dynamics simulations coupled with quantum mechanical study demonstrate that mutations of anchor residue phenyl alanine to alanine at the PET binding cleft of cutinase unveiled a distal yet novel binding subsite, which alters the nature of dispersive interaction for PET recognition and binding. The phenyl alanine engages in π– π interaction with the phenyl ring of PET (-8.5 kcal/mol), which on one side helps in PET recognition, but on the other side restricts PET to attain fully extended conformations over the entire binding cleft. The loss of π – π interaction due to mutation of phenyl alanine to alanine is not only compensated by the favourable cation– π and hydrophobic interactions from the arginine residues (-17.1 kcal/mol) found in the newly discovered subsite, but also favours the fully extended PET conformation.[3] This subsequently impacts the overall increased catalytic activity of mutated cutinase.

References

1. J. Then, R. Wei, T. Oeser, A. Gerdts, J. Schmidt, M. Barth and W. Zimmermann, FEBS Open Bio, **2016**, *6*, 425–432.
2. V. Tournier, C. M. Topham, A. Gilles, B. David, C. Folgoas, E. Moya-Leclair, E. Kamionka, M.-L. Desrousseaux, H. Texier, S. Gavalda, M. Cot, E. Guémard, M. Dalibey, J. Nomme, G. Cioci, S. Barbe, M. Chateau, I. André, S. Duquesne and A. Marty, Nature, **2020**, *580*, 216–219.
3. A. James and S. De, RSC Adv., **2022**, *12*, 20563–20577.