S27-3 Holoabzyme: A Single Antibody Catalyzes Multiple Chemical Transformations upon Replacement of Artificial Cofactors

◯Ikuo FUJII[1]

[1]Osaka Prefecture Univ., Grad. Sch. of Biol. Sci.

In designed biocatalysts such as catalytic antibodies (abzymes), stereoelectronic complementarity between the antibody and hapten has been used to elicit catalytic amino acid residues in the antigen-combining site. These amino acids are involved in a variety of catalytic mechanisms. The introduction of small molecule cofactors acting as “chemical teeth” into antibodies would broaden their catalytic versatility. Here, we demonstrate a single antibody catalysing multiple chemical transformations by the generation of antigen-combining site that function as an apoprotein for binding functionalized small non-protein components. We immunized mice with a hapten designed to induce both a substrate- and cofactor-binding site, and isolated two antibodies which catalyse an acyl-transfer reaction by using an alcohol cofactor. Replacement of this cofactor with acidic and amino cofactors enabled the antibodies to catalyse β-elimination, decarboxylation and aldol reactions with large rate accelerations. These results demonstrate a new strategy for generating catalytic antibodies, namely, by controlling the reactivity and mechanism of the antibody using designed artificial cofactors. This approach promises to both broaden the scope of catalytic antibodies and push back the boundaries of protein-based catalysis.