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Catalytic promiscuity of a proline-based tautomerase

Rahimi, Mehran

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PROPOSITIONS

Belonging to the thesis

Catalytic Promiscuity of a Proline-Based Tautomerase

Aldolase Activities and Enzyme Redesign

by Mehran Rahimi

1. Catalytically promiscuous enzymes provide a highly promising starting point for laboratory evolution of new biocatalysts. (this thesis)
2. Enzyme promiscuity has great promise as a source of synthetically useful carbonyl transformation activities, which could be exploited to create new enzymes for challenging aldolizations. (this thesis)
3. Systematic mutagenesis of the entire enzyme is a powerful strategy to identify ‘hotspots’ at any place in the amino acid sequence of an enzyme. These ‘hotspots’ can be used as targets for combinatorial mutagenesis to yield novel enzymes with improved solubility, stability and/or catalytic properties. (this thesis)
4. For new catalytic activities in a promiscuous enzyme, mutations closer to the active site improve the enzyme more effectively than distant ones. (this thesis)
5. Promiscuous enzyme activities are physiologically irrelevant to the organism. However, under new selective pressures they may confer a fitness benefit (to the organism), thereby prompting the evolution of the promiscuous activity to become the new primary activity. (Annu. Rev. Biochem. 2010, 79:471-505)
6. Computational prediction of the functional effects of single amino acid substitutions can be a good alternative for experimental identification of functional ‘hotspot’ positions. Such an alternative method may enormously reduce the experimental screening efforts. (my view)
7. Imagination is the basis of creativity that leads to scientific discoveries. Imagine more, discover more. (my view)
8. Social intelligence is more important than scientific intelligence. A combination of both is needed to become a true scientist. (my view)
9. No peace will be reached in the world, until we reach peace inside ourselves. (my view)