The development of better biotech enzymes

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Enzymes are proteins that speed up chemical reactions, such as laundry detergent digesting protein stains, which are otherwise very difficult to remove. A research team led by Professor Kam-bo Wong of the Centre for Protein Science and Crystallography, School of Life Sciences at The Chinese University of Hong Kong demonstrated a fundamental principle in changing the activity of enzymes by means of protein engineering. The findings provide potential insights into the future design of biotechnologically important enzymes, and will be published in next week's issue of the online, open access journal *PLoS Biology*.

Proteins from thermophiles, organisms that live in high temperatures, are more resistant to heat denaturation than those from mesophiles, organisms that live in moderate temperatures. In nature, enzymes from microbes that thrive in extremely hot habitats like hydrothermal vents can remain stable even at 100 C. These thermophilic enzymes are useful for the biotech industry because of their superior stability.

One intriguing problem is that thermophilic enzymes are less active than their mesophilic homologs despite having similar structures. "It is like two cars having similar engines but one runs 10 times faster than the other. If thermophilic enzymes can be made more active without compromising their stability, it will be of great commercial value to the biotech industry," explained Professor Wong.

Wong's research team used protein engineering methods to investigate why thermophilic enzymes are less active. They discovered that the thermophilic enzyme acylphosphatase has a unique property in that its

active site is rigidified by a salt-bridge. Thermophilic enzymes tend to have more stabilizing interactions like salt-bridges. By removing this salt-bridge, his team converted thermophilic properties of acylphosphatase to mesophilic-like properties. Likewise, a mesophilic acylphosphatase from human was engineered to become thermophilic-like by introducing the salt-bridge. Professor Wong's team concluded that the rigidifying salt-bridge increases the activity of enzymes at high temperatures, but at the same time reduces the activity at low temperatures. The principles learned from Professor Wong's study will hopefully guide the improvement of enzymes in the biotech industry.

More information: Lam SY, Yeung RCY, Yu T-H, Sze K-H, Wong K-B (2011) A Rigidifying Salt-Bridge Favors the Activity of Thermophilic Enzyme at High Temperatures at the Expense of Low-Temperature Activity. PLoS Biol 9(3): e1001027. doi:10.1371/journal.pbio.1001027