New technique permits development of enzyme tool kit

May 10 2010

An Arizona State University graduate student, Jinglin Fu, in collaboration with Biodesign Institute researchers Neal Woodbury and Stephen Albert Johnston, has pioneered a technique that improves on scientists' ability to harness and modulate enzyme activity.

The new approach, reported in the Journal of the American Chemical Society (published recently online), could have wide applicability for designing a range of industrial catalysts, health care diagnostics and therapies centered on understanding the control of enzymatic activity.

Enzymes, key catalysts that speed up the reactions inside every cell, are critical for life. As Neal Woodbury, chief scientist the Biodesign Institute at Arizona State University notes, "all the processes that happen inside of your body, essentially without exception, are run by enzymes." Enzymes are also a prized tool in biomedical research, aiding the development of diagnostic tests and therapeutics for a range of human diseases.

But studying the role of enzymes can be tricky. One approach has been to use a specialized platform known as a microarray—where glass slides are deposited with 10,000 protein fragments, called peptides, that are screened for their ability to react with specific enzymes and alter their activity. "On the microarray, you can screen thousands of molecules at the same time," Fu says, allowing the simultaneous monitoring of the peptide-enzyme binding and the change in enzyme activity at each spot on the array.

But there is a problem with this approach, that has so far hampered enzyme research. "When you try to monitor the chemical reaction that the enzyme catalyzes in the microarray, the molecule generated by the enzyme reaction quickly diffuses away, causing serious cross-contamination between spots on the array," Fu explains. To solve this problem, Fu applied polyvinyl alcohol (PVA)—a thick, viscous and clear polymer— to the microarray slide to limit the diffusion of molecules and hold the reactions in place, preventing contamination.

In the current study, Fu's team was able to observe the effects that peptides had on the activity of three broad classes of enzymes. In some cases, peptides blocked the activity of an enzyme but in others, peptides acted to alter the whole structure of the enzyme—often in unanticipated ways—allowing it to function differently.

"What Jinglin has invented," Woodbury stresses, "is a way of finding a peptide that will allow us to both put an enzyme in a particular place and modulate its activity. It allows us to begin to group different enzymes according to function." In addition to possible biomedical applications, the enzyme tool kit made possible through the group's research could be applied to modulating enzymes for a variety of industrial purposes, for new detergents or pharmaceuticals. Further, the strategy is not limited to peptides. It can theoretically be applied to virtually any small molecule suitable for an array, making the technique extremely versatile.

Provided by Arizona State University