ARTIFICIAL GENETIC CIRCUITS FOR HIGH THROUGHPUT DIRECTED EVOLUTION OF WIDE VARITY ENZYME ACTIVITIES

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Synthetic biology inspires new engineering principles of biological systems, yielding advanced DNA-encoded-devices and new biological applications. For the last decade, we have focused on the development of genetically-encoded biosensors to monitor single cell enzymes, metabolites, and protein-protein interactions.

The biosensors were used as the critical tool to develop a variety of high throughput screening methods for enzyme functions. First, transcription factors were constructed to have a specific response against small xenobiotic chemicals such as phenolics. The transcription signal was regarded to indicate the presence of single cell enzyme activity because the xenobiotic chemicals could only be present only by the cellular activity acting on the supplied substrates. The approaches were confirmed to be very useful to find new enzymes working on lactams, isoprene, and others.

Flow cytometry and cell-imaging techniques were established to analyze the circuit behaviors, later to isolate the better hits from tremendous amounts of genetic diversities. Currently, we are applying the sense circuits for practical uses like the rapid profiling of million diversity of microbes or enzymes based on their catalytic functions.

We also tried to connect the sensors signal to the precise metabolic controls based on CRISPR interferences to regulate target metabolisms, which is expected to provide a synergistic effect with the biosensor circuits for the guided balancing of designed metabolisms.