Biochip allows genes to express themselves

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Biochip platforms that work as artificial cells are attractive for medical diagnostics, interrogation of biological processes, and for the production of important biomolecules. However, to match the complexity of nature, the biochips need to be designed such that proteins, DNA, and other important biological components can be located in specific, spatially well-defined regions on the chips.

This allows these devices to mimic the complex, sequential, and often cascaded events involved in biological processes. Now, in a major breakthrough, a group of researchers at the Weizmann Institute of Science in Israel, led by Roy Bar-Ziv, in collaboration with Margherita Morpurgo from the University of Padova in Italy, have designed a molecule affectionately called the “daisy” that is able to bind genes onto chips in miniature patterned arrays.

Bar-Ziv and co-workers have been able to use the daisy to pattern tiny regions of double-stranded DNA onto silicon dioxide surfaces. Indeed, these immobilized genes are able to conduct their business on patterned silicon substrates without the need for living cells. These biochips can act as protein microtraps, selectively trapping specific proteins from crude cell extracts with high spatial resolution. Moreover, the gene sequences immobilized on the biochips can be used for the on-chip production of proteins by transcription/translation processes such as those occurring within cells.

Bar-Ziv and his colleagues have also demonstrated the integration of these systems with microfluidics. Integration with flow systems is of

interest for the fabrication of miniature assembly lines on chips, wherein proteins can be synthesized on the chips and transported to their final destinations through microfluidic channels.

In a remarkable demonstration of the utility of the daisy approach, the researchers have patterned two different genes as alternating stripes on a biochip. The protein synthesized on one stripe diffuses to the second stripe where it regulates the synthesis of a second protein. More complex artificial gene circuits can be envisioned by extending this protocol, and thus the biochips may be able to carry out complex cascaded information-processing functions, mimicking those in living organisms.

“This approach is a first step towards functional cell-free biochemical factories for synthesizing biomolecules and decision-making modules”, said Bar-Ziv. Amnon Buxboim, a Ph.D. student in Bar-Ziv's group and one of the primary researchers involved in this work, added that placing genes close to one another on a surface provides opportunities not available in bulk solution by allowing communication between individual gene sequences in these artificial cells.

Citation: Roy Bar-Ziv, A Single-Step Photolithographic Interface for Cell-Free Gene Expression and Active Biochips, *Small* 2006, 2, No. 3, doi: 10.1002/smll.200600489

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