Lab-on-a-Chip Performs 1,000 Chemical Reactions At Once

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Flasks, beakers, and hot plates may soon be a thing of the past in medicinal chemistry labs. Instead of handling a few experiments on a benchtop, scientists may simply pop a microchip into a computer and instantly run thousands of chemical reactions, with results -- literally shrinking the lab down to the size of a thumbnail.

Toward that end, a team of investigators at the University of California, Los Angeles (UCLA), have developed technology to perform more than a thousand chemical reactions at once on a stamp-size, PC-controlled microchip, which could accelerate the identification of potential drug candidates for treating diseases such as cancer. The results of their study appear in the journal Lab on a Chip.

Heading the multidisciplinary were Hsian-Rong Tseng, Ph.D., a member of the Nanosystems Biology Cancer Center, one of eight Centers of Cancer Nanotechnology Excellence created by the National Cancer Institute. Their miniaturized laboratory uses microfluidics to automatically handle and channel tiny amounts of liquids and chemicals. The chemical reactions were performed using in situ click chemistry, a technique often used to identify potential drug molecules that bind tightly to protein enzymes to either activate or inhibit an effect in a cell, and were analyzed using mass spectrometry.

Traditionally, only a few chemical reactions could be produced on a chip, but the research team pioneered a way to instigate multiple reactions, thus offering a new method to quickly screen which drug

molecules may work most effectively with a targeted protein enzyme. In this study, scientists produced a chip capable of conducting 1,024 reactions simultaneously, which, in a test system, ably identified potent inhibitors to the enzyme bovine carbonic anhydrase.

A thousand cycles of complex processes, including controlled sampling and mixing of a library of reagents and sequential microchannel rinsing, all took place on the microchip device and were completed in just a few hours. At the moment, the UCLA team is restricted to analyzing the reaction results offline, but in the future, they intend to automate this aspect of the work as well.

“The precious enzyme molecules required for a single in situ click reaction in a traditional lab now can be split into hundreds of duplicates for performing hundreds of reactions in parallel, thus revolutionizing the laboratory process, reducing reagent consumption, and accelerating the process for identifying potential drug candidates,” said Dr. Tseng. Next steps for the team include exploring the use of this microchip technology for other screening reactions in which chemicals and material samples are in limited supply—for example, with a class of protein enzymes called kinases, which play critical roles in the malignant transformation of cancer.

This work, which is detailed in the paper “An integrated microfluidic device for large-scale in situclick chemistry screening,” was supported by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. Investigators from Siemens Medical Solutions and China’s Wuhan University also participated in this study. An abstract is available at the journal’s Web site.

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