Novel Chip Produces DNA Faster, Less Expensively

Duke University

DURHAM, N.C. -- Duke University bioengineers have designed a 1-by-3 inch chip that can produce custom-made segments of DNA in two days that currently would require many large pieces of equipment, significant human labor and two weeks to produce.

Creating and copying novel pieces of DNA quickly and inexpensively could have broad implications in the production and screening of new drugs, as well as replacing current technologies for genetic cloning, the researchers said.

DNA is the genetic material -- or software -- in all living things that acts as a blueprint for the production of proteins, the building blocks of life. An improved ability to create and test these protein-producing molecules could be a boon to the new field of synthetic biology, where scientists design new genes to produce novel proteins, which can be used in such fields as medicine and environmental monitoring.

“Using current technology, it takes between about 50 cents to a dollar to create each base pair of DNA; using the new chip reduces costs to less than half of 1 cent per base pair,” said Jingdong Tian, assistant professor of biomedical engineering at Duke’s Pratt School of Engineering.

The results of the Duke experiments were published in the journal Nature Biotechnology.

“In addition, current methods create many mistakes that must be accounted for,” Tian continued. “The chip-based method is self-correcting, so that whenever an error in copying is detected, it is automatically fixed.”

As an example of how time-consuming and expensive current technology is, Tian cited the recent cloning of the entire genome of a single bacterium which took more than four years to complete, with a price tag of more than $40 million. The new chip system would have reduced that to a small fraction of the time and expense, Tian said.

Gene synthesis involves a number of steps, including synthesis, purification and assembly of oligonucleotides or oligos, short snippets of DNA, usually less than 50 base pairs. Each of these steps currently takes one to two days to complete. The new chip performs all three of these activities.

The chip itself has row upon row of tiny indentations, or wells. The biochemical equivalent of an inkjet printer shoots the desired DNA bases into each well. The

bases assemble within the well and since it is a enzymatic reaction, harsh chemicals are not needed to release the DNA strand, as it done now, from the walls of the well.

“The chip basically combines the three steps into one, which can be completed in less than two days, and without all the labor currently needed,” Tian said. “Also, since the wells are so small, significantly smaller amounts of expensive chemicals are needed to run the reactions.”

The final step involves checking the product for any errors, which are usually missing or altered base pairs. This can be a time-consuming process, sometimes taking up to a week to complete.

“Using the chip-based system, we add an enzyme that can recognize when a base pair is not where it should be, cut the defect out, and reassemble the strand,” Tian said. The researchers tested the chip on genes from E. coli and found that the error rate was much lower using the chip compared to traditional methods.

Because researchers can produce so many oligos so quickly, they can screen many versions with subtle differences to see which particular version produces the most of a desired protein, Tian said.

Tian’s research was supported by the Beckman Foundation, the Hartwell Foundation, and the Duke-Coulter Translational Partnership.

Other members of the team were, from Duke, Jiayuan Quan, Ishtiaq Saaem, Nicholas Tang, and Hui Gong. Nicolas Negre and Kevin White, from the University of Chicago, were also members of the team.

SOURCE [1]

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[1] http://prattpress.pratt.duke.edu/duke_den_june_2011_dnachip