New method for mass-producing high-quality DNA molecules

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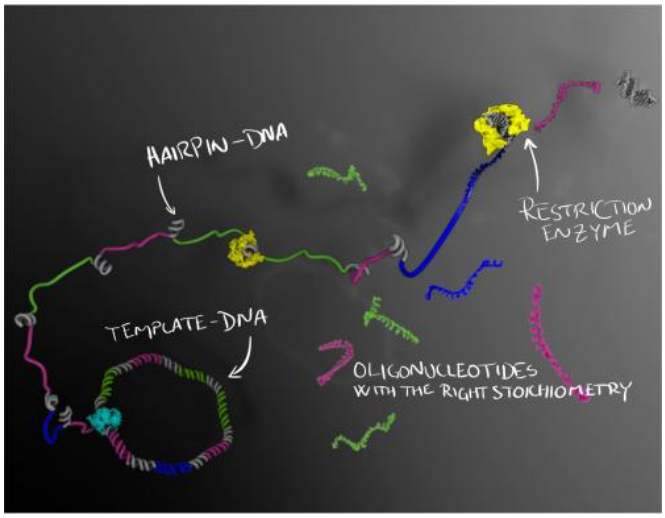

An illustration of the production of oligonucleotides. Credit: Björn Högberg

A new method of manufacturing short, single-stranded DNA molecules can solve many of the problems associated with current production methods. The new method, which is described in the scientific periodical *Nature Methods*, can be of value to both DNA nanotechnology and the development of drugs consisting of DNA fragments.

The novel technique for manufacturing short, single-stranded DNA molecules – or oligonucleotides – has been developed by researchers at Karolinska Institutet in Sweden and Harvard University. Such DNA fragments constitute a basic tool for researchers and play a key part in many fields of science. Many of the recent advances in genetic and molecular biological research and development, such as the ability to quickly scan an organism's genome, would not have been possible without oligonucleotides

The new method is versatile and able to solve problems that currently restrict the production of DNA fragments.

"We've used enzymatic production methods to create a system that not only improves the quality of the manufactured oligonucleotides but that also makes it possible to scale up production using bacteria in order to produce large amounts of DNA copies cheaply," says co-developer Björn Högberg at the Swedish Medical Nanoscience Center, part of the Department of Neuroscience at Karolinska Institutet.

The process of bioproduction, whereby bacteria are used to copy DNA sequences, enables the manufacture of large amounts of DNA copies at a low cost. Unlike current methods of synthesising oligonucleotides, where the number of errors increases with the length of the sequence, this new method according to the developers also works well for long oligonucleotides of several hundred nitrogenous bases.

The DNA molecules are first formed as a long string of single-stranded DNA in which the sequence of interest is repeated several times. The long strand forms tiny regions called hairpins, where the strand folds back on itself. These hairpins can then be cut up by enzymes, which serve as a molecular-biological pair of scissors that cuts the DNA at selected sites. Several different oligonucleotides can thus be produced at the same time in a perfectly balanced combination, which is important if they are to be crystallised or used therapeutically.

"Oligonucleotide-based drugs are already available, and it's very possible that our method could be used to produce purer and cheaper versions of these drugs," says Dr Björn Högberg.

More information: 'Enzymatic Production of Monoclonal Stoichiometric Single-Stranded DNA

Oligonucleotides', Cosimo Ducani, Corinna Kaul, Martin Moche, William M. Shih, and Björn Högberg, *Nature Methods*, online 2 June 2013.

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