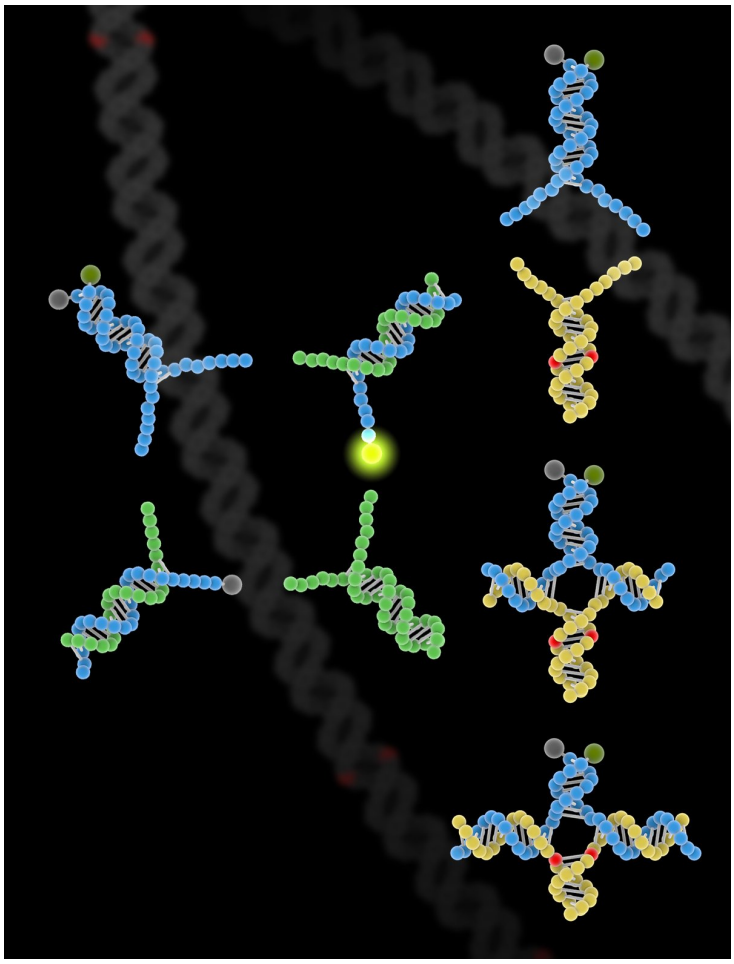
BioSpectrum
the business of Bio & Health Sciences
ASIA EDITION

Scientists find new way to detect SNPs

July 30, 2013 | News | By BioSpectrum Bureau



Singapore: Scientists at Rice University and the University of Washington (UW) unveiled a groundbreaking new method for detecting minute changes known as single nucleotide polymorphisms (SNPs) in the human genome. The human genome has more than six billion base pairs, and one of the revelations of modern genomics is that even the slightest change in the sequence - a single-nucleotide difference - can have profound effects.

The new SNP genotyping technique, dubbed "double-stranded toehold exchange," is described in a new paper in *Nature Chemistry*. The patent-pending method is markedly different - in both form and performance - than any of the dozen-plus methods already used to detect SNPs.

"There are two axes of performance in SNP detection - read length and specificity," said study co-author David Zhang, who joined Rice's Department of Bioengineering recently. "We're at least an order of magnitude better on each axis. In fact, in terms of specificity, our theoretical work suggests that we can do quadratically better, meaning that whatever the best level of

specificity is with a single-stranded method, our best will be that number squared," he said.

Scientists have sequenced the genomes of dozens of species, but those species-level genomes only tell part of the genetic story for a given individual. In people, for example, slight differences in just a few nucleotides can mean the difference between having green or brown eyes. This type of genetic variation within a species is called polymorphism, and SNPs are the smallest unit of polymorphic variation.

SNPs are the most frequently occurring genetic variation in the human genome; more than 30 million have been confirmed. But they also occur in other species, even in single-celled organisms. In the bacteria that cause tuberculosis (TB), for example, an SNP in the right location can allow the disease to fight off antibiotics like rifampicin, one of the most commonly prescribed anti-TB drugs. Though small on a molecular scale, that single-nucleotide difference has serious implications for TB patients. Rather than going through a six-month course of antibiotics costing about $20, patients with drug-resistant TB often face more than two years of treatment with drugs that sometimes have permanent side effects and can cost more than $2,500.

Existing SNP detection methods have a relatively short read length; this means that scientists might have to run a half-dozen or more of the tests to look for an SNP in a 200-base-pair region of a genome. The Rice-UW method uses a novel approach to allow for much longer read lengths. "In these tests, our read length was 198 base pairs because that was the length of the region we needed to scan for SNPs related to rifampicin resistance," said Georg Seelig, assistant professor of computer science and engineering and of electrical engineering at UW. "We could have designed a longer probe if we'd needed one. There is no inherent limitation to the length of the probe we can make. Reaction time - not read length - is likely to be the limiter with this method," Seelig said.