

CHEMISTRY WORLD

Blue fluorescent DNA

BY MICHAEL GROSS | 9 MAY 2005

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Fluorescently labelled DNA building blocks are the unsung heroes of the genome era. This new, automated approach to DNA sequencing, which has all but replaced methods relying on radioactive labels, made gene sequencing fast and decoding entire genomes possible. Now, researchers have introduced a new variant of a DNA nucleotide, whose fluorescence can be switched on by an antibody.

A few years ago, groups led by Richard Lerner and Kim Janda at the Scripps Research Institute in La Jolla, California, US, developed antibodies against stilbene (Ph-CH=CH-Ph), which change the electronic properties of the molecule so it fluoresces bright blue upon binding.

Now, the researchers have constructed a variant of the DNA building block adenosine, in which stilbene is tethered to the adenine base via a deaza-polyethylene glycol linker. This is designed to ensure the stilbene remains accessible to antibody binding even when the nucleotide is incorporated in a double helix.

To obtain large quantities of stilbene-labelled DNA, the researchers had to find a thermophilic DNA polymerase that accepts the modified nucleotide during the polymerase chain reaction. All four polymerases tested achieved significant levels of label incorporation, with the exonuclease deficient version of the Vent polymerase performing best.

The incorporation works best when less than 10 per cent of the dATP offered carries

the stilbene label. For a gene with 801 base pairs, including 372 As, the fluorescence spectra suggest that around 10 stilbene labels per DNA double strand are accessible to the antibody; a few more may be present but not accessible.

The authors anticipate that further 'profluorescent' nucleotides will be developed and find applications 'in a variety of experimental settings such as investigations of protein-DNA interactions, gene arrays (DNA chips), detection of single nucleotide polymorphisms (SNPs), and *in situ* fluorescence hybridisation.'

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References G F Kaufmann *et al*, *Angew. Chem. Int. Ed.*, 2005, **44**, 2144

References

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