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Chemical Biology

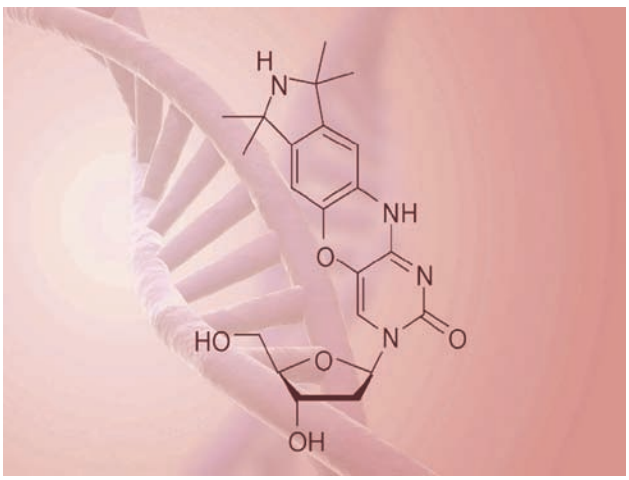
Discriminating probe presents possibility for disease detection

Matching nucleosides

A fluorescent probe can spot the difference between the four DNA bases: adenine, thymine, cytosine and guanine.

Snorri Sigurdsson and Pavol Cekan from the University of Iceland, Reykjavik, have synthesised a highly fluorescent nucleoside (a base bound to a sugar) which can report the identity of its base-pair when placed in a DNA duplex. The fluorescence emitted by the duplex differs depending on which DNA base is paired with the probe.

According to Sigurdsson and Cekan, the probe could find use in detecting single DNA base changes – single nucleotide polymorphisms (SNP) – at sites where variation can indicate disease. Changes within the gene apolipoprotein E, for example, are considered to be an indicator of predisposition to Alzheimer's. The researchers explain that detecting SNPs with their probe could make it possible to identify genetic diseases or recognise people who might be susceptible to them. Also, the probe would not only detect a SNP but could indicate which DNA base replaced the correct one.



The fluorescent nucleoside can report the identity of its base pair in duplex DNA

David French from LGC, in Teddington, UK, who has recently studied SNP in the gene encoding sheep prion protein agrees that 'technology that can reliably discriminate between the four naturally occurring bases of DNA to analyse SNPs will be a useful tool for diagnostic tests.'

Sigurdsson plans to investigate the nucleoside's fluorescence under many different conditions. 'Better understanding of the nucleoside's properties will lay the groundwork to develop further compounds that may be better suited for routine-based fluorescence assays,' he says. 'One of the challenges is to find base-discriminating fluorescent nucleosides that emit light at the higher wavelengths detected by instruments currently used in laboratories around the world.'

Rachel Cooper

Reference
P Cekan and S Th Sigurdsson, *Chem. Commun.*, 2008, 3393 (DOI: 10.1039/b801833b)

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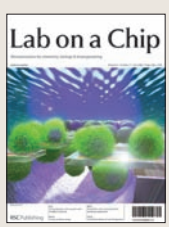

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Research highlights

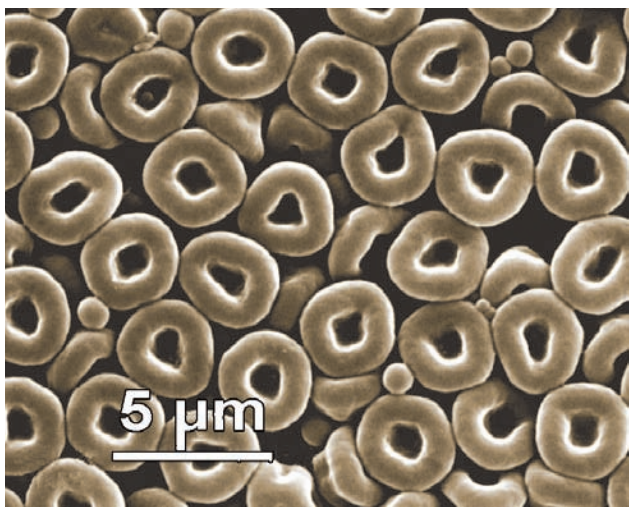
Miniature polymer rings show affinity for specific cell types

Dunking doughnuts into cells

Doughnut-shaped particles could help to reduce side effects from cancer treatments, says a team of scientists from the UK.

Developed by a team fronted by Mark Bradley at the University of Edinburgh, the uniquely-shaped polystyrene particles can penetrate specific cell types in the body, and have a particular affinity for the liver. 'This opens up the possibility of using these particles to deliver therapeutics solely to the liver in cases of disease and could limit side effects associated with the treatment,' says Bradley. Side effects, such as hair loss in cancer treatment, can arise because drugs aimed at cancer cells may also affect similar cell types in other parts of the body.

Bradley explains that the team stumbled on the micro-doughnuts accidentally during their investigations. Whilst using a simple technique called dispersion polymerisation to grow small particles in a polymer mixture, they found that adding a small amount of dioxane to the usual ethanol solvent gave their surprise result. 'The particles' unique and highly uniform structure was immediately interesting to us and we considered the possible applications they might have,' says Bradley.



Bradley's microscopic polystyrene loops were discovered by accident

Andy Sutherland, an expert in polymer chemistry, at Aston University in Birmingham, UK, says the particles' selective cellular uptake is striking. 'By understanding the basis of this cellular choice it may, in the future, be possible to design polymer constructs that both target specific cell types and allow molecular cargoes to be imported into these cells for therapeutic, diagnostic and imaging applications.'

The team suggests it is the particles' shape that is responsible for their cell specificity. And their unusual shape and uniform, tiny size – thirty times smaller than a human hair – mean they could also be suitable in filtration and purification devices, for example, says Bradley. The next challenge will be to understand how the doughnuts form, he adds. *Katherine Davies*

Reference
L Alexander *et al*, *Chem. Commun.*, 2008, DOI: 10.1039/b805323e

Lab-on-a-chip confines bacteria in droplets for fast antibiotic screening

Faster superbug detection

Chip technology could cut the wait for test results on clinical samples, say US scientists. A team at the University of Chicago has developed a method to detect bacteria in blood plasma samples and simultaneously screen their response to antibiotics.

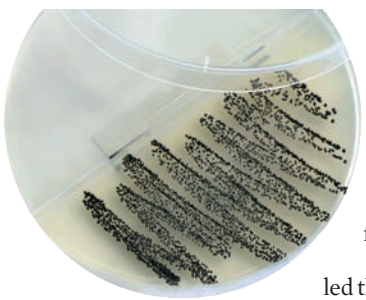
The group's technique works by mixing a sample with a dye that fluoresces in the presence of bacteria; the mixture is then converted into droplets inside a microfluidic chip. If the sample contains bacteria some of the droplets will contain a single bacterium and fluoresce. Because of the very small droplet size, the occupied droplets will have a high bacterial density, removing the need to incubate samples to increase their concentration before detection.

The team was able to use the method to detect the MRSA (methicillin-resistant *Staphylococcus aureus*) 'superbug', so-called because of its resistance to several antibiotics. They were also able to find potential treatments for MRSA infections by treating an array of the droplets with different antibiotics and looking at the change in fluorescence.

Rustem Ismagilov, who led the team, explains that his motivation was rooted in improving medical diagnostic tests. Traditional methods of diagnosing bacterial infections rely on time-consuming sample incubations or amplifying the bacterial DNA which, while faster, cannot be used to look at antibiotic response. 'Our technique can potentially provide access to new types of diagnostic tests for bacterial infections and simultaneously identify a treatment regime to provide same-day test results,' says Ismagilov.

But not only that, 'it could also provide a simple and inexpensive solution to testing for bacteria in other fields where contamination by bacteria is a concern, including the food industry and water management,' Ismagilov adds.

Samuel Sia, an expert in lab-on-a-chip diagnostic devices at Columbia University, New York, US, is enthusiastic about the research. 'The finding that confining a single bacterium to a small volume can decrease detection time is a striking demonstration of the advantages of microfluidics,' he says. Whilst he explains that considerable development and clinical testing will be needed before such an assay could be used for real-world diagnostics, he adds that 'the experimental design is very clever, and the results convincing.' *Kathleen Too*



ISTOCKPHOTOS

Chip technology removes the need for time-consuming sample incubations

Reference
J Q Boedicker *et al*, *Lab Chip*, 2008, DOI: 10.1039/b804911d