Article for consideration

Site-specific positioning of dendritic alkyl chains on DNA cages enables their geometry-dependent self-assembly. *Edwardson, T. G. W., Carneiro, K. M. M., McLaughlin, C. K., Serpell, C. J. & Sleiman, H.* Nature Chemistry 5, 868-875, doi:10.1038/nchem.1745

Intro

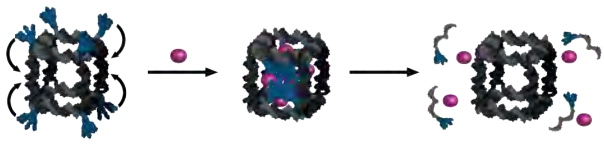
DNA carries the genetic information of all living organisms from one generation to the next. The base-pairing code used in biological systems can be also used as a tool for building DNA materials on the nanometer scale. Our research group works in the area of DNA nanotechnology, and we focus on creating three-dimensional DNA structures for biological and materials applications.

WHAT'S NEW IN THIS PAPER?

In this paper we show that DNA cages can be loaded with small molecule drugs and release them in the presence of a specific DNA sequence. To carry out this function, we first created DNA cubes using short component DNA strands. We then decorated them with lipid-like molecules. When organised on the three-dimensional DNA scaffold, these lipids can act like sticky patches, that come together in a well-defined way. Depending on their geometry, they can engage in a 'handshake' on the inside or outside of the DNA cube.

When these sticky patches are assembled within the cube cavity they create a core which can hold cargo, such as drug molecules. Due to the programmability of DNA, we can design a specific sequence which will be recognised by the cargo-containing DNA cube and cause it to release the guest molecules.

Our group has shown the loading and release of gold nanoparticles in DNA nanotubes before, but this is the first time that small molecules have been manipulated in such a way using a DNA nanostructure.



WHY IS IT IMPORTANT?

What is great about DNA nanostructures is that they can be built with a great deal of precision, and they are biodegradable and many of them do not cause adverse immune reactions. DNA nanostructures thus have great potential in the area of drug delivery as their size, shape and properties can be tuned easily by design, and they are stimuli responsive.

A limiting factor for many medicinal drugs is instability, toxicity to healthy cells and transport to the

desired place in the body. To overcome this challenge, drug delivery vehicles can be employed to carry and protect the drugs. These delivery vehicles are often synthetic materials and may not be compatible with the body, and often these synthetic materials cannot be precisely controlled in terms of their structure.

One way around this is to use biological materials such as DNA. Our discovery of this novel DNA structure is a step towards the application of such nanomaterials for biomedical applications.

In a future application, one can imagine a DNA cube that carries drug cargo being administered to an organism (a patient). Many diseased cells, such as cancer cells overexpress certain genes. When this cube is in the diseased cell environment, this will trigger the release of the drug. This drug release is conditional and will only occur in response to a specific nucleic acid sequence.

Our group is currently carrying out cell and animal studies to assess the viability of this method, in collaboration with the group of Prof. Lawrence Panasci at the Lady Davis Institute, and with support from CIHR/NSERC (Collaborative Health Research grant) and Prostate Cancer Canada (Movember grant).

Additionally we found that when the sticky patches on our DNA cages were oriented on the outside face of the cube they could assemble two-cubes together. This new mode of assembly is analogous to the way that proteins fold into their functional structures. It opens up a range of new possibilities for designing DNA based nanomaterials.

HOW DID WE DISCOVER IT?

The field of DNA nanotechnology continues to produce increasingly complex materials and nanodevices. Our lab has developed simple methods to create DNA cages using chemical concepts. One benefit of our methods is that they produce 3D scaffolds made of DNA which can then be decorated with other molecules.

We were interested in decorating a simple DNA cube with lipid-like molecules and studying the behaviour of these decorated cages, as a novel type of nanomaterial. These lipid molecules have a high affinity for each other, and we found that this persisted when they are assembled on our DNA scaffolds.

We then noticed a dependence on the number and geometry of these lipid-like molecules, finding that certain patterns can act like glue to stick DNA cages together. We discovered that high numbers of the lipid-like molecules organised on the cage had a preference to fold inside the cavity creating an environment capable of encapsulating molecules, such as drugs, as cargo.

Article Metrics

The article was ranked number 8 in *Nature Chemistry's Altmetric top 10 for 2013*, with an altmetric score of 69 and 5,561 page views. (http://blogs.nature.com/thescepticalchymist/2013/12/nature-chemistrys-altmetric-top-10-for-2013.html)

Press Coverage

Upon publication, the article in question received international media coverage. A list of articles is given below:

- Wired Magazine (UK), 'Highly programmable' DNA cubes could be used for drug delivery, Kadhim Shubber, Sept. 2, 2013
- ACCN (Canadian Chemical News), Hydrophobic groups enable DNA nanocages to hold drugs, Tyler Irving, Dec. 2013
- The Scientist (Canada), Some Assembly Required, Tracy Vence, Sept. 3, 2013
- McGill University News (Canada), DNA 'cages' may aid drug delivery, Chris Chipello, Sept. 3, 2013
- Scicasts (UK), Researchers Find Nanostructures Made of DNA Strands Can Encapsulate, Release Small-Molecule Drugs, Sept. 2, 2013
- Science Daily (USA), DNA ‘Cages’ May Aid Drug Delivery, Sept. 1, 2013
- ecancer news (UK), DNA ‘cages’ may aid drug delivery, Sept. 7, 2013
- Phys.org (UK), Nanostructures made of DNA strands can encapsulate, release small-molecule drugs, Sept. 1, 2013
- Las Vegas Guardian Express (USA), Cancer Drugs Delivered by DNA Nanoscale Cages, Douglas Cobb, Sept. 2, 2013
- French Tribune (France), DNA Nanoscale Cages Deliver Cancer Drugs by Raoul Girard, Sept. 3, 2013
- National Monitor (USA), Nanoscale ‘cages’ of DNA strands may aid drug delivery, researchers say, Lance Tillson Sept. 2, 2013
- Headlines & Global News (USA), Nanostructure 'Cages' Could Capture Cancer-Fighting Drugs and Deliver Them To Diseased Cells,Rebekah Marcarelli, Sept. 2, 2013
- Jersey Evening Post (USA), DNA ‘cages’ hope for drug delivery, Sept. 1, 2013
- La Stampa (Italy), “Gabbie” di Dna per portare farmaci alle cellule malate, Sept. 2, 2013
- Design & Trend (USA), New DNA 'Cage' Encapsulates Drugs Aiding In Biological Delivery Processes, Sep 3, 2013
- Portal de Oncologia Portugues (Portugal), "Gaiolas" feitas de fitas de ADN melhoram entrega de medicamentos, Sept. 4, 2013
- Fierce Drug Delivery (USA), Nanosized DNA cages could deliver drugs with triggered release, Michael Gibney, Sept. 4, 2013
- Azonano.com (UK), Cage-Like DNA Nanostructures Used For Small-Molecule Drug Delivery, Gary Thomas, Sept. 3, 2013
- Gentside (France), Des nanocubes d'ADN pour délivrer des medicaments, Lionel Huot, Sept. 3 2013
- Ntvmsnbc (Turkey), Kansere nano-ilaçla müdahale, Sept. 3, 2013
- T24 (Turkey), Kansere nano-ilaçla müdahale edilecek, Sept. 3, 2013
- Haber3 (Turkey), Sadece hastalıklı hücrelere ilaç iletiminde devrim, Sept. 3, 2013
- Futurity (USA), SEND DNA ‘CAGES’ FILLED WITH DRUGS TO SICK CELLS, Sept. 5, 2013
- Nanotechnology Now (International), DNA 'cages' may aid drug delivery: Researchers find nanostructures made of DNA strands can encapsulate, release small-molecule drugs, Sept. 2, 2013
- Softpedia (Romania), Nanoscale DNA “Cages” Promise to Make Drug Delivery Easier, More Effective, by Laura Sinpetru, Sept. 2, 2013