CHEMICAL PHYSICS

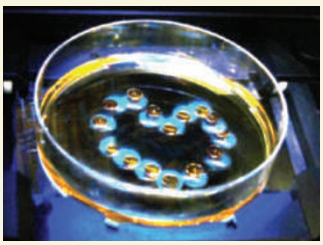
Guiding light

With microfluidic devices gaining prominence for many applications in chemistry and biology, the hunt is on to find ways of accurately controlling the motion of liquid droplets. In *Angewandte Chemie*, Antoine Diguet *et al*. describe a method for using light to trap and move oil droplets floating on an aqueous solution (A. Diguet *et al*. *Angew. Chem. Int. Edn* doi:10.1002/anie.200904868; 2009).

This isn't the first time that light has been used to push droplets around. But Diguet and colleagues take a new approach based on the chromocapillary effect, in which light generates a tension gradient at a liquid–liquid interface. This gradient can induce an interfacial flow between droplets and bulk liquids, which propels the droplet in the opposite direction to the gradient.

The authors' technique depends on the compound dissolved in the bulk liquid. Diguet *et al*. used a surfactant that isomerizes in response to different wavelengths of light — it adopts a polar isomeric form when illuminated with ultraviolet light, and a less polar form when lit with visible light. The light-induced changes in polarity modulate the surface tension between the surfactant solution and oil droplets floating on its surface. So, when the authors partially illuminated such a droplet with ultraviolet light, the tension gradient caused the droplet to move away from the lit area. If they then partially irradiated the droplet with visible light, the droplet moved towards the lit area.

By combining ultraviolet and visible light, Diguet *et al*. made a chromocapillary trap that captured oil droplets cast onto the surface of the surfactant solution. The authors could then drag the droplets across the surface of the solution, at speeds of about 300 micrometres per second, simply by moving the trap around. The image above is a montage of superimposed frames from a movie, and shows a droplet (gold colour) being directed by a trap (cyan halo) along a heart-shaped path; the Petri dish is 5.1 centimetres in diameter.



Chromocapillary traps should work for various combinations of immiscible liquids, and could thus be useful for controlling droplets in micro- or millifluidic devices. The authors' system could also be used to safely handle dangerous liquids, or in light-responsive materials.

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differences. Many genomic regions vary in the density of methylation of cytosines that lie immediately 5′ to a guanosine (known as CpG methylation), with the differentiated cells having large, prevalent, partially methylated tracts of DNA, which are associated with the reduced activity of genes that lie 5′ to these tracts. In fibroblasts, 99.98% of all methylation occurs at CpG dinucleotides (Fig. 1). This is not unexpected given that these dinucleotides are believed to be the exclusive target of DNA methylation in vertebrates.

Surprisingly, however, in the stem cells studied, around 25% of the methylation sites do not occur in the context of CpGs, but rather are found on cytosines that neighbour other bases, in particular adenosine (Fig. 1). Non-CpG methylation had been observed before[5] in mouse stem cells, but its prevalence in the genome was not widely appreciated and its genomic location was unclear. Lister *et al*.[1] show that its frequency varies between individual cells and is relatively low — only a small percentage of non-CpG cytosines in stem cells is methylated. Yet their genome-wide analysis also reveals that non-CpG cytosine methylation is enriched at active genes, specifically on the DNA strand that serves as a template for transcription. The authors speculate that this differential targeting is linked to the process of active transcription, reminiscent of the targeting of non-CpG methylation to expressed genes in the plant *Arabidopsis thaliana*[6,7]. Although the function and enzyme (or enzymes) responsible for non-CpG methylation are yet to be identified, this mark remains a curiously exclusive feature of stem cells. If terminally differentiated cells that lack non-CpG methylation are engineered to become induced pluripotent stem cells, they regain this unusual modification at the few loci tested by Lister and colleagues. Only further functional studies will reveal the specific role this mark has in stem-cell biology.

The work by Lister *et al*.[1] provides a milestone in the quantitative description of mammalian DNA cytosine methylation and highlights the dynamic nature of this mark during cell differentiation. The maps they have generated reveal that our understanding of the establishment and function of DNA methylation patterns is far from complete. Most notably, the question remains as to what extent the observed differences are consequences of differential gene activity or are actively involved in transcriptional regulation.

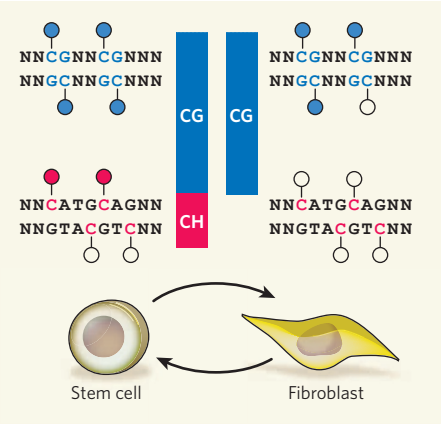

Figure 1 | DNA methylation patterns differ between stem cells and differentiated cells[1]. In stem cells, regions of DNA with CpG methylation (blue) are mostly uniformly methylated, whereas this modification is more heterogeneous in fibroblasts. Non-CpG methylation (red), which occurs primarily at CA nucleotides, is detected only in stem cells, yet is asymmetric and more scarce and patchy than CpG methylation. If fibroblasts are converted to induced pluripotent stem cells they regain non-CpG methylation. Filled circles, methylated cytosines; unfilled circles, unmethylated cytosines. H stands for A, C or T; N stands for any nucleotide.

The fact that DNA cytosine methylation patterns are cell-type specific and variable has led to the proposal that cytosine methylation may function as a memory module of cell identity and developmental state[8]. The feasibility of measuring complete DNA methylomes at the base-pair level provides the technical starting point to address this hypothesis in a quantitative and unbiased manner. Given the current cost of sequencing, these are still expensive experiments. Nevertheless, owing to the dynamic nature of DNA methylation, it is clear that we will appreciate the complexity of the distribution of this mark only after generating additional methylome maps from many distinct cell types from different individuals. Furthermore, unravelling the functional basis of DNA methylation will require combining such descriptive sequencing efforts with mechanistic studies. Global initiatives in defining genetic variations in humans provide a framework for how these endeavours can be achieved. Such coordination has already been initiated in the United States by the National Institutes of Health's Roadmap Epigenomics Program. And efforts are under way to coordinate an international initiative[9] to ultimately decode the function of this still-enigmatic base modification. ■

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