TECHNOLOGY

Nanolab gets the rubber stamp

Forget cell sorters, minipreps, electrophoretic gels and beakers full of reagents; researchers have now found a way of carrying out the whole procedure — from single cell to purified DNA or mRNA — on a microchip that contains only nanolitre amounts of fluid.

The secret of creating this diminutive laboratory lies in an ingenious 'microfluidic chip' — this is a clear, rubbery square the size of a postage stamp on which an intricate number of channels are cast, each only the width of a human hair (see figure). The clever use of valves, which are operated hydraulically, allows fluids from different chambers to be mixed and reactions to take place in a versatile and controlled way. For example, a DNA-purification experiment might start by mixing the contents of three channels that are loaded with dilution buffer, cells and lysis buffer; the lysed cells can then be directed to a DNA-affinity column and purified, and the eluted DNA is recovered at the end. Cross-contamination simply does not occur, so different reactions can be processed in parallel — an innovative feature that was illustrated by simultaneously purifying genomic DNA from three bacterial populations.

Other than allowing you to say that you are carrying your benchtop in your lab-coat pocket, what practical purpose might this technology have? The ability to isolate nucleic acid from a single cell is an original aspect of the technique, and means that cells that are impossible to culture, or that would be modified by such a procedure, can be analysed. This feature can also be exploited to create cDNA libraries from a single cell. But the design of the chip itself has uses that go beyond the molecular genetics laboratory. Fiddle with the channel plumbing system and the nanolab is transformed into a computer or a protein-crystallography chamber.

Tanita Casci

References and links

ORIGINAL RESEARCH PAPER Hong, J. W. & Studer, V. *et al.* A nanoliter-scale nucleic acid processor with parallel architecture. *Nature Biotechnol.* 14 Mar 2004 (doi:10.1038/nbt951)

WEB SITE

Stephen Quake's laboratory: http://thebigone.caltech.edu/quake

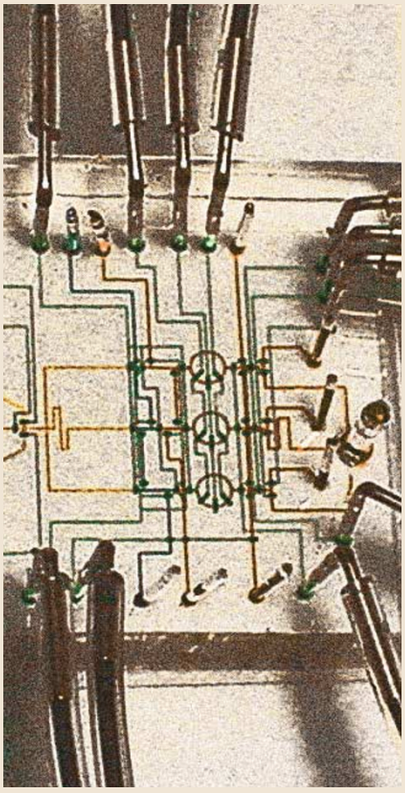

Image courtesy of J. W. Hong.

MOUSE GENETICS

Holding all the cards

The construction of a panel of uniquely useful mouse strains means that geneticists who want to dissect complex traits now have a full deck of cards to play with.

Chromosome-substitution strains (CSSs), in which a single chromosome comes from one inbred strain (the donor; A) and the rest come from another (the host; B), are not a new idea. However, Jonathan Singer and colleagues are the first to construct a complete panel of strains for a vertebrate species — one for each autosome, sex chromosome and for the mitochondria.

The principle behind the use of CSSs to dissect complex traits is elegantly simple: if a CSS differs from the host strain in any given phenotype, then at least one quantitative trait locus (QTL) that influences that phenotype is present on the substituted chromosome. So, with a full panel, QTLs for the trait of interest can be quickly localized to chromosomes.

Creating the panel in the first place was not quite so easy. Singer *et al.* needed more than 17,000 mice and 7 years of work to create their mouse-CSS panel from inbred donor (A/J) and host (C57B/6J) strains that differ in many complex traits. Although it is time-consuming and requires a complete genetic map, the construction strategy is conceptually straightforward: progeny with non-recombinant copies of the desired chromosome are successively backcrossed to the host strain, to produce progeny that are heterosomic for that chromosome (A/B); these are subsequently intercrossed to obtain homosomic progeny (A/A).

However, the end result is worth the effort: the authors chromosomally localized 150 QTLs — one or more for nearly all the 53 complex traits that are related to sterol levels, diet-induced obesity, anxiety and amino-acid levels that they attempted to dissect with the complete panel. They also showed that traits can be mapped to specific locations on the chromosomes through follow-up crosses to the host strain.

The mouse-CSS panel is now available to all through the Jackson Laboratory. However, the lessons that have been learned during the construction process might be more important than this specific panel: in a matter of years, equivalent panels could be derived for any given host and donor strains — for example, from mouse or rat strains that vary in different traits.

Nick Campbell

References and links

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FURTHER READING Demant, P. Cancer susceptibility in the mouse: genetics, biology and implications for human cancer. *Nature Rev. Genet.* **4**, 721–734 (2003)

WEB SITES

The Broad Institute: http://www.broad.mit.edu

Jackson Laboratory: http://www.jax.org

Joseph Nadeau's laboratory: http://genomics.case.edu/people_joseph.html