IN BRIEF

TECHNOLOGY

Scanning of guanine–guanine mismatches in DNA by synthetic ligands using surface plasmon resonance.

Nakatani, K. *et al*. *Nature Biotechnol*. **19**, 51–55 (2001)

Scanning methods that will detect DNA sequence variations are in high demand and this paper presents a highly specific and sensitive way of detecting G•G mismatches without using labour-intensive gel-based techniques. A synthetic ligand that is specific for G•G mismatches is bound to a sensor chip. The DNA molecules that are captured by the chip change the reflective index of polarized light, thus revealing the presence of a G•G mismatch in a DNA sample.

GENOMICS

Functional annotation of a full-length mouse cDNA collection.

The RIKEN Genome Exploration Research Group Phase II Team and the FANTOM Consortium. *Nature* **409**, 685–690 (2001)

The aim of the Mouse Gene Encyclopaedia Project is to identify and sequence every transcript encoded in the mouse genome by sequencing and annotating full-length cDNA clones, and mapping them onto the genome. They now report the characterization of the first 21,076 clones of the collection. The clones, which correspond to ~13,000 unique genes, were functionally annotated according to their degree of relationship to known mouse or human genes, their metabolic function and the presence of protein motifs.

DISEASE MODEL

A mouse model of multiple endocrine neoplasia, type 1, develops multiple endocrine tumors.

Crabtree, J. S. *et al*. *Proc. Natl Acad. Sci. USA* **98**, 1118–1123 (2001)

Multiple endocrine neoplasia type I (MEN1) is characterized mainly by tumours of the parathyroid, pancreas and anterior pituitary. The responsible gene, *MEN1*, is inherited as an autosomal dominant and behaves as a tumour-suppressor gene in humans. Somatic loss of the wild-type copy of *MEN1* is seen in affected patients. A mouse knockout model of *MEN1* was made using homologous recombination. Whereas homozygous *Men1* mice die *in utero*, heterozygous mice recapitulate most features of the human disease, and support a tumour-suppressor role of *Men1*.

GENE EXPRESSION

Mammalian SWI/SNF complexes promote MyoD-mediated muscle differentiation.

De la Serna, I. L. *et al*. *Nature Genet*. **27**, 187–190 (2001)

The transcriptional regulator MyoD can induce fibroblasts to differentiate as muscle cells in culture. The process involves the activation of MyoD target genes, but what other molecules are required to switch on the right genes? These authors used an inducible dominant-negative version of a chromatin remodelling protein to show that the SWI/SNF chromatin remodelling complex is necessary for the induction of MyoD targets, and therefore for the initiation of a cellular differentiation programme.

TECHNOLOGY

Monkeying about with transgenics

The problem with transgenic mouse models of human disease is just that — they are mouse models. And although they can be very useful, the many differences between us and mice have proved problematic for the fine-tuning of some therapies. So a goal of the past few years has been to produce transgenic (non-human) primates, but a major obstacle to this has been getting conventional gene-transfer methods to work. Now, a team of Oregon scientists have overcome this problem to produce the first live-born and (so far) healthy transgenic monkey.

Chan *et al.* overcame the technical barrier to transgenic success in primates by adapting a vector that they had previously used to good effect in cattle. The key to this protocol is that the transgene-carrying retroviral vector is introduced into oocytes and not into embryos. Often retroviral vectors give rise to transgenic mosaics because they only integrate into dividing cells — cells in which the nuclear envelope is degraded during mitosis, so allowing the retroviral pre-integration complex access to the host cell DNA. Chan *et al.* therefore reasoned that, rather than targeting embryos, they would introduce their vector into metaphase II oocytes, which have no nuclear envelope. This timing should allow vector complexes to access the DNA. Additionally, as the genes are inserted before fertilization, the resulting offspring should not be mosaic.

So how successful was this strategy when transferred to rhesus monkeys? The authors injected their green fluorescent protein-encoding retroviral vector — either under the control of the cytomegalovirus early promoter or the human elongation factor-1 alpha promoter — into 224 mature rhesus oocytes. Six hours later, they fertilized them. Of these 224 fertilized oocytes, 126 developed to 4-cell stage embryos, 40 of which were selected by their morphology for transfer, in pairs, to 20 surrogate mothers. Five pregnancies resulted, three of which produced healthy males. One pregnancy miscarried fraternal twins mid-gestation, possibly because rhesus monkeys rarely sustain twin pregnancies.

Courtesy of Gerald Schatten, Oregon Health Sciences University, USA.

Transgene integration, transcription and expression analyses revealed that the miscarried twins and one of the liveborn males were transgenic and that this male does not express the transgene. The authors named him ANDi (for inserted DNA in a reverse-transcribed direction, see picture), but they will have a four-year wait until ANDi hits puberty before they can test for germline transmission. The other two males also require further testing to see whether they are transgenic mosaics.

Although successful gene-targeting in primates has many more barriers to overcome, this method of producing transgenic monkeys could be combined with other approaches to hasten progress in this field. But the questions that remain are not all of a technical nature — the advanced cognitive awareness of our primate relatives requires careful thought as to what is and what is not ethically appropriate when it comes to genetically modifying them.

Jane Alfred

References and links

ORIGINAL RESEARCH PAPER Chan, A. W. S. *et al*. Transgenic monkeys produced by retroviral gene transfer into mature oocytes. *Science* **291**, 309–312 (2001)

FURTHER READING Chan, A. W. *et al*. Transgenic cattle produced by reverse-transcribed gene transfer in oocytes. *Proc. Natl Acad. Sci. USA* **95**, 14028–14033 (1998)

WEB SITE Link to video of ANDi