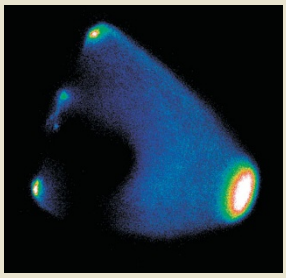
Transcript tracking



Scientists have imaged the migration of mRNA in live cells using nuclease-resistant molecular beacons. Until now, mRNA has been visualized using fluorescently labeled nucleic acid probes or green fluorescent protein fused to a phage RNA coat protein. The first approach works only on fixed cells, however, and the second approach, although suitable for live cells, requires that the mRNA of interest be modified to contain coat-protein binding sites. Molecular beacons are hairpin-shaped oligonucleotide probes bearing a fluorophore and a quencher molecule in close proximity; they fluoresce only when a binding event opens the stem-loop structure. Early attempts to adapt molecular beacons for mRNA detection were limited by endonuclease degradation of the probes and probe-mRNA duplexes. In the new work, Tyagi and coworkers employ molecular beacons with a 2′-*O*-methyl modification, which are more resistant to nucleases. Using probes specific to *oskar* mRNA from *Drosophila*, the researchers followed the mRNA's movement in real time from its origin in fly nurse cells through the oocyte's cytoplasm to its posterior end. (*Proc. Natl. Acad. Sci. USA* **100**, 13308–13313, 2003) *KA*

Communication models

Understanding and predicting the flow of information among cells is an important goal for biologists. But an accurate determination of signaling pathway dynamics has been hindered by a lack of sufficient quantitative data on the molecular interactions among the different components of signaling networks. In an effort to reverse this, Kirschner and colleagues have developed a mathematical model for understanding quantitative interactions among Wnt signaling proteins and used it to predict the behavior of their communication network. The authors first recreated the Wnt network in frog (*Xenopus laevis*) eggs and obtained a set of high time-resolution interaction data to define a kinetic model. They then used the model to predict the dynamics of the Wnt pathway and tested the accuracy of the model by simulating the corresponding communication states in the *Xenopus* model. This paper demonstrates the potential of modeling for uncovering unexpected kinetic properties of signal pathways. (*PLoS*, published online 13 October 2003; doi:10.1371/journal.pbio.0000010) *GTO*

Smoking gun in retroviral gene therapy

Earlier this year, the field of gene therapy was rocked when two patients with severe combined immunodeficiency disease, ostensibly cured by retrovirus-mediated gene transfer, developed T-cell leukemia. Now Fisher and colleagues have tracked down the likely cause of these leukemias. In both patients, who appeared normal for almost three years after treatment, they found T-cell populations with a single retrovirus insertion site close to the gene encoding a hematopoietic transcription factor (*LOM-2*) that is required for normal hematopoiesis. In tests earlier after treatment, upwards of 50 different insertion sites were found. These patients also had aberrant levels in their T cells of both LOM-2 mRNA and protein, which are elevated and implicated in childhood T-cell leukemias. These data indicate that the inserted retrovirus acts as a transcription enhancer of the *LOM-2* locus, providing a growth advantage for the cells with that insertion. However, as the affected patients were the youngest to be treated, the authors consider that the hyperproliferative activity of hematopoietic cells in the very young may provide an environment that fosters this type of event. (*Science* **302**, 415–419, 2003) *LD*

Virus kills tumors

Researchers have identified variants of vesicular stomatitis virus (VSV) that potently kill tumor cells while sparing normal counterparts. A significant limitation to the use of viruses as cancer therapeutics is the potential for uncontrolled virus growth in normal tissues. A variety of viruses have been selected or engineered to be therapeutics that exploit defects in tumor cells. One type of defect common to tumor cells is reduced sensitivity to the cytokine interferon (IFN), which regulates cell growth and death. IFN also controls a cell's antiviral response, so this diminished sensitivity makes tumor cells vulnerable to virus attack. In previous work, Bell and coworkers showed that wild-type VSV could kill tumors, but because VSV can interfere with IFN signaling, the researchers had to provide the animals with the cytokine to keep them from succumbing to viral infection. Now, they have isolated VSV variants that do not block interferon production. The VSV variants are able to kill 80% of the human tumor cell lines tested. When delivered intravenously, they destroy tumors in a mouse model of metastatic colon cancer. (*Cancer Cell* **4**, 263–275, 2003) *MS*

Arabidopsis in the frame

Now that many genome sequences are available, better methods for identifying genes are needed. Theologis, Ecker and colleagues describe a system that has enabled them to identify 30% of the complete ORFeome—the compilation of all open reading frames—of the plant model system *Arabidopsis thaliana*. Combining full-length cDNA discovery with hybridization of RNA populations to high-density tiling oligonucleotide arrays, they found almost 6,000 new transcription units to join the previously described 25,500. This is the first application to a eukaryote of tiling arrays, which, unlike conventional expression arrays, display the entire genome, including promoters, introns and intergenic 'dark matter.' Although the five *Arabidopsis* chromosomes were equally transcriptionally active in various conditions and developmental stages, the pattern of activity was distinct for each chromosome. These studies also revealed that 30% of the annotated genes showed significant tissue-specific antisense expression, and that 20% of pseudogenes are transcribed, suggesting a possible role for them in gene regulation. The authors point out that whole-genome arrays, which make no presumptions on the importance of particular DNA sequences, will find uses in other types of global analyses, such as mapping of DNA binding sites, DNA methylation sites and single nucleotide polymorphisms. (*Science* 302, 842–846, 2003) *LD*

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