Of mice and conditional chromosomal translocations

Cancer is often caused by chromosomal translocations leading to gene fusion. Mouse models for such fusions have proven difficult to make, as many chimeric proteins are toxic. Rabbitts and colleagues overcame this problem by creating a conditional gene fusion model. They inserted an inverted \textit{loxP}-flanked gene segment into the intron of the target gene without causing a phenotype in these 'inverter mice.' Only in mice that also express Cre recombinase is the gene segment flipped and the fusion protein expressed. This inverter knock-in model allows the study of tissue-specific chromosomal translocations.

Brief Communication p27

Simplifying mutation detection

Finding new single nucleotide polymorphisms (SNPs) and other small mutations involved in human disease is an arduous endeavor beset with uncertainty. Even when a disease-linked gene is known, the mutations involved often lie outside the coding region. To characterize them, researchers must therefore sequence hundreds of kilobases from each individual in a disease population. Lovett and colleagues present a detailed protocol to simplify this task that results in a 10,000-fold enrichment of the target region. This enables simple shotgun sequencing to find new mutations in the region of interest.

Protocol p63

Counting tadpoles

Years after the PCR revolution, today's molecular biology students seem to acquire the capacity to measure minute amounts of nucleic acids shortly after they learn how to hold a pipette. The difficulties inherent to the detection and quantification of other scarce molecules, however, continue to frustrate even seasoned scientists. Burbulis, Brent and their colleagues unveil in this issue their contribution to ease this fundamental vexation: tadpoles. Stop, don't rush to the nearest pond yet! All you need is some basic chemistry skills and the good old PCR machine.

Article p31, News and Views p11

Inspired by the SAGE

Iyer and colleagues have combined the power of ChIP and SAGE—that is, chromatin immunoprecipitation and serial analysis of gene expression—to allow for genome-wide identification of transcription factor binding sites. After cross-linking of DNA to proteins in cells, the transcription factor of interest is specifically immunoprecipitated, pulling along the associated DNA, which is then processed, by digestion and amplification, into 21-base-pair sequence tags. As in SAGE, the tags are concatemerized for sequencing and analysis. Once the trick worked in yeast, Iyer's group introduced additional stratagems to make this technique combination work in mammalian cells. Optimization, control procedures and an algorithm for the careful analysis of sequence data were the keys to success. This technique promises to become a useful basic component of the ENCODE project toolbox, where it will complement the already famous ChIP on chip.

Article p47

Fluorescent lipids

Whenever fluorescent tags are used to label molecules in living cells, there is a concern that the tag will have undesirable effects. This is particularly true of smaller molecules such as lipids, in which the size of the tag is a large fraction of the size of the native molecule. Biologists have spent years using fluorescent tags to examine lipid biochemistry and visualize their localization in living cells. During this time chemists have tried to develop better ways of tagging lipids. Now, Thiele and colleagues show how the use of some clever chemistry enables incorporation of a polyene fluorescent tag that is less disruptive to the native lipid structure than any previous fluorescent tag and promises new avenues into the illumination of lipid function.

Article p39, News and Views p14