

## Targeted control of neuronal activity

Recent years have seen the development of several methods to manipulate neuronal activity. These are powerful tools for dissecting the function of the intact nervous system. The major existing methods use photorelease of locally applied caged chemicals or photostimulation of heterologously expressed photoreceptors. Kramer and colleagues now describe the first method that turns endogenous neuronal receptors into light-regulated proteins, using a photoswitchable affinity label. Bathing neurons with this label results in covalent modification of potassium channels. Light can then be used to switch the neurons between normal and hyperexcitable states. Ehlers and colleagues present a new transgenic mouse expressing a heterologous ligand-activated channel for chemical activation of neurons in the intact animal. These tools provide new options for researchers investigating neuronal function.

**Article p331, Brief Communication p299, News and Views p293**

## Mapping mutations in the fly

Inducing mutations with interesting phenotypes in flies is easy; mapping these mutations to the genome is not. To facilitate a better connection between phenotype and genotype, Dickson and colleagues present a two-step strategy. First, using a high-density single-nucleotide polymorphism (SNP) map with a SNP every six genes and an optimized array-based technique to genotype the SNPs, the location of a mutation is narrowed down to 1–5 Mb. Then, a set of fly stocks with reference chromosomes carrying visible eye markers spaced every 0.5–2 Mb allows the fine mapping of the mutation to ~50 kb, a region that can be sequenced easily.

**Article p323, News and Views p295**

## On an xQuest to find cross-links

Protein cross-linking followed by identification of the cross-linked peptides by mass spectrometry can yield valuable information about protein structure and protein interactions. Owing to both experimental and computational challenges, however, such studies have been limited to single proteins or purified protein complexes. Aebersold and colleagues now address both issues with the use of isotopically coded cross-linkers in an optimized workflow and with the development of

a software search engine called xQuest. xQuest can be operated in an exhaustive search mode for up to 100 proteins, or a rapid 'ion-tag' mode for large databases. They show that xQuest can identify both intra- and inter-protein cross-links from complex proteomic samples, such as a total *Escherichia coli* lysate.

**Brief Communication p315**

## From SNPs to allele-specific transcription

The two copies of each gene present in somatic mammalian cells are not always expressed equally. In fact, some important genes—notably those involved in development, cell proliferation and immune response—are transcribed from only one of the two alleles. The mechanisms governing the establishment and maintenance of allele-specific expression are poorly understood in part because of the lack of analytical methods for high-throughput analysis. Ren and colleagues have now adapted the procedure of chromatin immunoprecipitation on DNA microarrays (ChIP-chip) to study the allele-specific binding of the transcription machinery throughout the genome. They use an RNA polymerase for ChIP and let a single-nucleotide polymorphism genotyping array, coupled with a stringent analytical process, lead them to the transcribed allele.

**Brief Communication p307**

## PhylCRM and Lever find regulatory motifs

Transcriptional regulation of genes is guided by sets of sequence motifs targeted by the transcription machinery. These motifs are often enriched in *cis*-regulatory modules (CRMs) and occur

in noncoding sequences flanking a gene. Bulyk and colleagues tackled the problem of how to identify CRMs spread across the genome with the algorithm named PhylCRM, which scans genomes for conserved regulatory motifs and then predicts combinations of CRMs. To map these to gene sets of interest, the researchers developed the algorithm Lever. Together, PhylCRM and Lever will help to unravel the intricacies of transcriptional networks.

**Article p347, News and Views p297**

