

Nicholas Katsanis at Duke University in Durham, North Carolina, and his colleagues have developed a model system using zebrafish (*Danio rerio*) to tease out such contributions to a rare genetic disorder known as Bardet–Biedl syndrome (BBS). Fourteen human genes have been linked to BBS, which has a range of symptoms, from retinal degeneration to mental retardation.

The researchers systematically replaced the fish versions of BBS genes with some of the 125 known human variants of the genes and observed developing fish embryos. Their technique revealed surprising quirks in the disease's inheritance, including interactions between genes that affect disease severity. The approach could be used to study the genetics of other diseases. **B.M.**

ORGANIC CHEMISTRY

Trifluoro triumph

Science **328**, 1679–1681 (2010)

Chemists would like to attach trifluoromethyl groups to organic molecules to improve their pharmacological properties, such as fat solubility or metabolic stability, but have struggled to find a simple way to add them to compounds containing aromatic rings.

Now Stephen Buchwald at the Massachusetts Institute of Technology in Cambridge and his colleagues have used a palladium catalyst to attach these groups to benzene-based aryl chloride molecules, under mild conditions.

Their method avoids the harsh conditions needed in previous methods and should allow the addition of trifluoromethyl groups to drugs at late stages in synthesis. **D.P.C.**

CANCER GENOMICS

Probing prostate cancer

Cancer Cell doi:10.1016/j.ccr.2010.05.026 (2010)

An in-depth genetic analysis has identified several gene alterations associated with prostate cancer.

Charles Sawyers and his colleagues at the Memorial Sloan-Kettering Cancer Center in New York analysed protein expression and the number of copies of genes in 218 prostate-cancer samples, including some that had metastasized to other parts of the body. They also analysed 12 prostate-cancer cell lines and sequenced 157 genes of particular interest from a subset of the samples.

The researchers identified three genes as potential tumour suppressors in some prostate cancers and found that differences in copy number of certain genes indicated clear subgroups of patients with high or low risk of tumour progression. **A.K.**

NEUROSCIENCE

Snakes on the brain

Neuron **66**, 949–962 (2010)

A hair-raising study has revealed a brain signal for acts of courage performed in the face of fear.

Yadin Dudai at the Weizmann Institute of Science in Rehovot, Israel, and his team used functional magnetic resonance imaging to scan the brains of volunteers as they decided whether to slide a live snake towards their heads.

In people fearful of snakes, a region called the subgenual anterior cingulate cortex (sgACC) was activated (pictured) if they mustered up the courage to move the snake closer. Skin conductance — an indication of bodily arousal — dropped as activity in the sgACC rose, even though the volunteers said that they still felt frightened.

The researchers propose that sgACC activation promotes courageous action and that manipulating its activity could help in treating fear disorders. **A.A.**



EVOLUTIONARY BIOLOGY

Meat-eating tadpoles

Proc. R. Soc. B doi:10.1098/rspb.2010.0877 (2010)

Exposure of ancient tadpoles to novel foodstuffs may have awoken genetic variation previously hidden from natural selection, leading to the evolution of new eating habits.

Cris Ledón-Rettig of the University of North Carolina at Chapel Hill and her team studied Couch's spadefoot tadpoles (*Scaphiopus couchii*), which eat algae and other organic material. The authors fed the tadpoles a shrimp diet resembling that eaten by tadpoles of the spadefoot toads (genus *Spea*), which probably evolved from ancestors similar to *S. couchii*. After feeding on the shrimps, the *S. couchii* tadpoles showed greater variation in growth and development speed than controls.

Similar results were seen in tadpoles treated with a hormone that is produced in response to dietary changes, suggesting that hormones may have mediated the *Spea* tadpoles' transition to carnivory. **J.F.**

JOURNAL CLUB

Marcelo A. Nobrega
University of Chicago, Illinois

A human geneticist explores the ways that genes are regulated.

Gene expression is the cellular process that decodes the genetic information in DNA and converts it into proteins. It is regulated at many levels: when messenger RNA is transcribed from DNA; when mRNA is translated into proteins; and at the epigenetic level, when the structure of chromatin, coils of DNA wound around histone proteins, is altered. Although most discussion of gene expression focuses on the regulation of transcription, the other components of the process are also crucial. Yet little is known about how they are integrated.

Work by Tom Misteli at the National Cancer Institute in Bethesda, Maryland, and his team provides a striking example of the integration of seemingly disparate components in gene-expression regulation (R. F. Luco *et al. Science* **327**, 996–1000; 2010). They describe how patterns of alternative splicing of newly made RNA, a key regulatory mechanism, can themselves be regulated by specific chemical modifications in the chromatin. They also found that a given set of modifications to histones predicts patterns of RNA splicing. The authors conservatively estimate that this mechanism occurs in dozens to hundreds of genes in the human genome.

This remarkable study makes a connection between a quintessential transcription-regulation mechanism, histone modification, and a post-transcriptional process, alternative splicing. It shows that chromatin can regulate not only how much of a protein, but also which protein, is made in a cell.

We have seen a surge of intriguing studies suggesting that molecules that were thought to regulate transcription also direct epigenetic modifications, modify alternative-splicing patterns and participate in the intracellular transport of RNA. These findings and the work of Misteli and colleagues provide insight into how the components of gene regulation are integrated.

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