URLs for web team

***Genome Research* Special Issue:** http://www.genome.org/content/vol15/issue11/?etoc

International HapMap Project: http://www.hapmap.org

IN BRIEF

HUMAN DISEASE

Sequence variants in *SLITRK1* are associated with Tourette's syndrome.

Abelson, J. F. *et al*. *Science* **310**, 317–320 (2005)

Tourette syndrome (TS) has been associated in linkage studies with regions on several human chromosomes, but this paper is the first to study a specific candidate gene. SLIT and NTRK-like 1 (*SLITRK1*) was identified because of its proximity to a chromosomal inversion in a child with TS. In other patients, a frameshift mutation and a microRNA-binding site mutation in *SLITRK1* were found. Expression patterns in the brain of *SLITRK1* and the microRNA, and the ability of wild-type SLITRK1 to promote dendritic growth, further support a role for *SLITRK1* in TS.

MOUSE MODELS

The homeodomain transcription factor Irx5 establishes the mouse cardiac ventricular repolarization gradient.

Costantini, D. L. *et al*. *Cell* **123**, 347–358 (2005)

The rhythmic beating of the heart depends on waves of depolarization and repolarization, with defects in the latter leading to arrhythmia. This study demonstrates that mice that lack the Irx5 transcription factor are susceptible to fatal arrhythmias because they overexpress the K_v4,2 potassium channel. Irx5 negatively regulates K_v4,2 and is expressed in an opposing gradient. Together these two proteins establish the potassium gradients that ensure repolarization.

RNA WORLD

DICER-LIKE 4 is required for RNAi and produces the 21nt siRNA component of the plant cell-to-cell silencing signal.

Dunoyer, P., Himber, C. & Voinnet, O. *Nature Genet.* 6 November 2005 (doi:10.1038/ng1675)

In plants, the production of 21-nt small interfering RNAs (siRNAs) leads to the degradation of homologous RNAs, and this silencing signal can also move between cells. This paper reports the long-awaited identification of the Dicer protein that is involved in the silencing process. By analysing *Arabidopsis thaliana* mutants that are deficient in cell-to-cell silencing, the authors showed that DICER-LIKE 4 is required to produce the 21-nt siRNAs that mediate this form of RNA interference.

COMPUTATIONAL BIOLOGY

Genomic variability within an organism exposes its cell lineage tree.

Frumkin, D. & Wasserstrom, A. *et al*. *PLoS Comp. Biol*. **1**, e50 (2005)

Reconstructing the cell-lineage tree of *Caenorhabditis elegans* was a tremendous feat, and was made possible by the transparency of the organism and its relatively few cells. The paper shows that it is feasible to accurately determine the cell-lineage trees of complex organisms by analysing the pattern of microsatellite mutations that accumulate during somatic cell divisions. Although the approach is currently only applicable to small cell populations, it might one day be powerful enough to reconstruct the cell-lineage tree of an entire human.

IN BRIEF

HUMAN GENETICS

Special Issue: Human Genome Variation

Genome Research **15**, 1463–1600 (2005)

To coincide with the publication of the HapMap paper in *Nature* (see the Highlight on p874) *Genome Research* have devoted their November issue to describing how the data emerging from the project have been applied to understanding human biology, genome structure and disease. As well as research updates on diseases such as prostate cancer, and technical papers on the gene-mapping methods themselves, the issue includes useful resources, such as a guide to using the analysis tools on the International HapMap Project web site.

CANCER GENETICS

The tumour suppressor HIC1 directly regulates SIRT1 to modulate p53-dependent DNA-damage response.

Chen, W. Y. *et al*. *Cell* **123**, 437–448 (2005)

HIC1 — hypermethylated in cancer 1 — suppresses age-dependent tumorigenesis in mice by functionally cooperating with p53. The authors show that a HIC1–SIRT1 (sirtuin 1) complex represses transcription of the stress-responsive SIRT1 deacetylase. Cells that lack HIC1 do not apoptose in response to DNA damage because SIRT1 deacetylates and inactivates p53. The authors point out that in ageing cells, in which *HIC1* is more likely to be epigenetically silenced, SIRT1 overexpression promotes cell longevity while increasing cancer risk.

CHROMOSOME BIOLOGY

Telomere-binding protein Taz1 establishes Swi6 heterochromatin independently of RNAi at telomeres.

Kanoh, J. *et al*. *Curr. Biol.* **15**, 1808–1819 (2005)

Despite much attention, the mechanism of heterochromatin formation at telomeres is far from clear. Working in fission yeast, these authors show that telomeric repeats are required to establish HP1 heterochromatin, and that this process is mediated by Taz1, a telomere binding protein that, as shown here, also mediates subtelomeric heterochromatin formation. Establishment of telomeric heterochromatin also requires a *cis* element that lies in the subtelomeric region and is regulated by RNAi–RITS, which in fission yeast initiates heterochromatin formation at the centromere and the silent *mat* locus.

RNA WORLD

Silencing of microRNAs *in vivo* with 'antagomirs'.

Krützfeldt, J. *et al*. *Nature* 30 October 2005 (doi:10.1038/nature04303)

This paper reports important progress in our ability to investigate the *in vivo* functions of microRNAs (miRNAs) and to manipulate their levels therapeutically. The authors generated synthetic RNA analogues — antagomirs — that are complementary to miRNAs, chemically modified for stability, and conjugated to cholesterol to enable *in vivo* delivery. As a test, antagomirs that target endogenous miRNAs were administered to mice intravenously. This resulted in the specific downregulation of the miRNAs and allowed the identification of several miRNA target genes through their increased expression.