IN BRIEF

CANCER GENETICS

HIF-1α induces genetic instability by transcriptionally downregulating MutSα expression.

Koshiji, M. *et al. Mol. Cell* **17**, 793–803 (2005)

HIF-1α, a transcription factor responsible for the cellular response to hypoxia, now seems to control the expression of proteins that are involved in DNA mismatch repair. The authors show that, during oxygen-starvation conditions, HIF-1α is a transcriptional repressor of MSH2 and MSH6 (*Escherichia coli* MutS homologues), which safeguard the integrity of the genome. Although HIF-1α overexpression is frequently observed in human cancers, whether hypoxia-associated genetic instability caused by HIF-1α contributes to tumour formation is unknown.

HUMAN GENETICS

Regulatory variation at glypican-3 underlies a major growth QTL in mice.

Oliver, F. *et al. PLoS Biol.* **3**, e135 (2005)

Of the ~2,000 QTLs that have been identified in rodents, few have been characterized at the molecular level. The authors extend their previous work on a single QTL that is associated with body-size variation in mice, and show that differences in the transcript levels of glypican-3 are responsible for this phenotype. Because mutations in glypican-3 cause Simpson–Golabi–Behmel syndrome in humans, these findings show that a gene linked to a Mendelian growth disorder in humans can contribute to quantitative variation in mice.

EVOLUTION

The transcriptional consequences of mutation and natural selection in *Caenorhabditis elegans.*

Denver, D. R. *et al. Nature Genet.* 24 April 2005 (doi:10.1038/ng1554)

Divergent species differ in their gene-transcription profiles, but what do these differences mean? Are they neutral, as some claim, or do they have an adaptive purpose? These authors used microarrays to examine the transcription-variation patterns of two types of *Caenorhabditis elegans* population — mutation-accumulation lines and natural isolates — and show that, for thousands of expressed sequences, transcription evolution is governed by stabilizing selection.

EPIGENETICS

Genomic characterization reveals a simple histone H4 acetylation code.

Dion, M. F. *et al. Proc. Natl Acad. Sci. USA* **102**, 5501–5506 (2005)

Histone modifications have been proposed to provide a complex combinatorial code that can cause variation in gene expression. Dion *et al.* made yeast strains that carry all possible combinations of mutations in the four histone H4 lysine residues that undergo acetylation, and examined the effects on genome-wide gene expression. Only one of the acetylation sites had specific effects on gene expression, whereas mutations in the other three had non-specific, cumulative effects. Acetylation on histone H4 therefore provides a relatively simple transcriptional code.