an epitope-tagged CDC6 protein bound to $RD^{INK4/ARF}$ in several human cell lines, but not to neighbouring regions of the DNA. The fusion protein was also shown to bind the well-characterized lamin-B2 DNA replication origin. Other replication-origin proteins were also bound to $RD^{INK4/ARF}$, indicating that a full pre-replication complex can form at this site.

High expression levels of CDC6 repressed the expression of all three tumour-suppressor proteins that are encoded by the *CDKN2B–CDKN2A* locus, but did not have an effect on other genes, such as *MYC* and *DNMT1* that also reside close to origins of replication. Moreover, mouse-embryo fibroblasts (MEFs) expressing high levels of CDC6 were able to form colonies in culture, unlike wild-type MEFs, but did not show increased levels of proliferation, indicating that CDC6 overexpression is not oncogenic *per se*. But, CDC6-expressing MEFs were transformed by the expression of a Ras oncogene, indicating that the repression of the INK4 and ARF tumour-suppressor pathways by CDC6 increases the likelihood of oncogenic transformation.

Does the expression of CDC6 in human tumours correlate with a loss of INK4a expression? The authors examined this in 162 non-small-cell lung carcinomas. Tumours with no expression of INK4a were not included, as loss of INK4a could be caused by mechanisms other than CDC6 overexpression. However, tumours that expressed low levels of INK4a were found to express high levels of CDC6, indicating that this mechanism of INK4 and ARF repression might be relevant to human cancer.

Nicola McCarthy

ORIGINAL RESEARCH PAPER Gonzalez, S. *et al.* Oncogenic activity of Cdc6 through repression of the INK4/ARF locus. *Nature* **440**, 702–706 (2006)

IN BRIEF

TUMOUR SUPPRESSORS

The regulation of exosome secretion: a novel function of the p53 protein

Yu, X. *et al. Cancer Res.* **66**, 4795–4801 (2006)

p53 is a transcription factor that is activated in response to cellular stress. Yu *et al.* have used a proteomics approach to identify proteins that are secreted by cells in a p53-dependent manner after DNA damage. p53 activation was found to increase the secretion of a set of proteins that are encoded by genes that are not transcriptional targets of p53. These proteins are secreted through small vesicles called exosomes. Furthermore, exosome production by cells is regulated by activation of the p53 pathway, so this pathway has a newly discovered function in the communication between cells.

MICRORNA

Pre-B cell proliferation and lymphoblastic leukaemia/high-grade lymphoma in Eμ-miR155 transgenic mice

Costinean, S. *et al. Proc. Natl Acad. Sci. USA* **103**, 7024–7029 (2006)

MicroRNAs (miRNAs) are small, non-coding RNAs that are involved in post-transcriptional regulation of gene expression. The miRNA miR155 has previously been shown to be highly expressed in human B-cell lymphomas. Now, Crostinean *et al.* show that transgenic mice that carry an miR155 transgene, the expression of which is targeted to B cells (Eμ-miR155), show preleukaemic pre-B-cell proliferation, and later develop a B-cell malignancy. miR155 might be a new target for the treatment of B-cell cancers.

ONCOGENES

Reversible kinetic analysis of Myc targets *in vivo* provides novel insights into Myc-mediated tumorigenesis

Lawlor, E. R. *et al. Cancer Res.* **66**, 4591–4601 (2006)

The transcription factor MYC is frequently deregulated in human cancers. Lawlor *et al.* used a reversible-switch transgenic model of MYC-mediated β-cell tumorigenesis, in combination with oligonucleotide microarrays, to identify MYC-regulated genes that are responsible for maintaining MYC-dependent tumours. In addition to genes that are involved in cell proliferation and tumour progression, a proportion of the MYC-regulated genes were found to be β-cell specific, which indicates that MYC action is, in part, cell-type specific.

TUMOUR IMMUNOLOGY

IL-23 promotes tumour incidence and growth

Langowski, J. L. *et al. Nature*, 10 May 2006 (doi:10.1038/nature04808)

Langowski *et al.* show the first molecular connection between tumour-associated inflammation and the failure of the adaptive immune response to target tumours. They show that expression of the cytokine IL-23 is increased in human tumours, and that this both promotes the inflammatory response and reduces cytotoxic T-cell infiltration. Inhibition of IL-23 increased tumour infiltration by cytotoxic T-cells, and the growth of transplanted tumours was reduced in mice that were depleted of IL-23. So, anti-IL-23 therapy might prove to be an effective treatment for solid tumours.