in either of the secondary mice — indicating that these are short-term clones of reduced self-renewal capacity. Other clones that persisted in the primary mice then only occurred transiently in secondary mice, indicating that short-term clones can be generated from long-term clones. Fewer clones were seen after tertiary transplants, indicating that only a restricted population of SL-ICs have extensive long-term self-renewal potential. In addition, a few clones were detected in secondary mice that were not seen in primary mice. The authors hypothesize that these cells might be largely quiescent in the primary mice, but then differentiate into a rapidly expanding clone, or that although the cell-cycling speed remains slow, the proliferating pool becomes detectable with subsequent divisions.

The similar complexity of the LSC and HSC compartments indicates that initiating leukaemogenic events of AML probably occur in HSCs, with subsequent alterations in either stem cells or downstream progenitors altering the self-renewal potential and resulting in LSCs. Standard therapies for AML target proliferating cells; the presence of quiescent cells that can later proliferate illustrates the shortcomings of this approach. These data highlight the need for therapies targetting the long-term repopulating LSCs, which are responsible for aggressively driving the growth of AML.

Ezzie Hutchinson

References and links

ORIGINAL RESEARCH PAPER Hope, K. J., Jin, L. & Dick, J. E. Acute myeloid leukemia originates from a hierarchy of leukaemic stem cell classes that differ in self-renewal capacity. *Nature Immunol.* **30** May 2004 (doi:10.1038/ni1080)

negative form of PML. The authors suggest that loss of PML function or disruption of nuclear bodies by this fusion protein could, among other things, compromise the stability and activity of p73 in APL blasts. Retinoic acid, which is used to treat patients with APL, has been shown to cause the degradation of PML–RAR-α fusion protein and reorganization of the nuclear bodies, so further experiments are required to determine if the drug also stabilizes p73.

Kristine Novak

References and links

ORIGINAL RESEARCH PAPER Bernassola, F. *et al.* Ubiquitin-dependent degradation of p73 is inhibited by PML. *J. Exp. Med.* **199**, 1545–1557 (2004)

FURTHER READING Melino, G. *et al.* p73: friend or foe in tumorigenesis. *Nature Rev. Cancer* **2**, 605–615 (2002)

WEB SITE

Pier Paolo Pandolfi's lab: http://www.mskcc.org/prg/mrg/bios/221.cfm

IN BRIEF

CARCINOGENESIS

Evaluation of carcinogen exposure in people who used 'reduced exposure' tobacco products.

Hatsukami, D. K. *et al. J. Natl Cancer Inst.* **96**, 844–852 (2004)

Some tobacco products are being marketed as containing lower levels of carcinogens than conventional products. Stephen Hecht and colleagues found that carcinogen levels were reduced in users of snuff or cigarettes who quit and used medicinal nicotine patches, and in those who switched to 'reduced-exposure' products. However, the reduction was more pronounced when medicinal nicotine was used, showing that this is a safer alternative.

GENE EXPRESSION

Large-scale meta-analysis of cancer microarray data identifies common transcriptional profiles of neoplastic transformation and progression.

Rhodes, D. R. *et al. Proc. Natl Acad. Sci. USA* 7 June 2004 (doi:10.1073/pnas.0401994101)

Meta-analysis of microarray data from more than 3,700 samples from a range of cancer types was used to identify a set of genes that are consistently differentially expressed in tumour versus normal cells. A common transcriptional profile was also obtained for undifferentiated versus differentiated tumours, and these profiles were validated using independent data sets.

LYMPHANGIOGENESIS

Preexisting lymphatic endothelium but not endothelial progenitor cells are essential for tumor lymphangiogenesis and lymphatic metastasis.

He, Y. *et al. Cancer Res.* **64**, 3737–3740 (2004)

In tumour angiogenesis, bone-marrow-derived endothelial progenitors contribute to the formation of blood vessels. By transplanting tumour cells into mice with genetically labelled bone marrow, He *et al.* showed that this does not apply to tumour lymphangiogenesis. Instead, the pre-existing lymphatic network was found to be required for this process and for metastasis to lymph nodes.

BREAST CANCER

Contralateral breast cancer in *BRCA1* and *BRCA2* mutation carriers.

Metcalfe, K. *et al. J. Clin. Oncol.* **22**, 2328–2335 (2004)

Women who carry inherited mutations in either *BRCA1* or *BRCA2* face a life-long high risk of developing breast cancer. For those women diagnosed with unilateral breast cancer, the risk of developing cancer in the unaffected breast is unclear. Here the authors show that these women have a 40% risk of developing contralateral breast cancer within 10 years, which is reduced if patients opt for oophorectomy or are treated with tamoxifen.