The figure illustrates the result, which, at this point, confirms the earlier evidence[3] for a large-scale field reversal in the vicinity of the Sagittarius Arm. However, their 'map' of our Galaxy's magnetic field now provides much better detail in the 'plan view' of the galactic field geometry in the first quadrant of the galactic plane.

The confirmation of a field reversal provides an important constraint on dynamo theories, which attempt to describe how the large-scale galactic field evolved over cosmic time. Different versions of the dynamo theory produce either an axisymmetric field distribution (in which there are no large-scale systematic reversals), or bisymmetric galactic fields, which have large-scale reversals, or more complex global field patterns. Most of the 20-odd spiral galaxies in the 'nearby' Universe whose large-scale magnetic fields have been investigated seem to have axisymmetric fields. Rand and Lyne's results thus indicate that the Milky Way is among the 'bisymmetric field minority' among nearby galaxies.

However, the latest observational indications are that intermediate cases may well also occur, in which the magnetic field direction reverses only over limited regions, not globally within a galaxy's disk. Some theoretical calculations suggest that such subglobal reversals may be 'transient' features over a galaxy's 10^{10} year lifetime. If the latter idea is borne out by future RM observations and theory, then the current global field distribution in galaxies may not, after all, contain a memory of the primordial field orientation at the time the galaxy formed. This question is an example of several reasons why it is interesting to define the strength and geometry of the large-scale magnetic field structure in galaxies. Pulsars will enable us to do that in increasingly fine detail for our own Milky Way.

The measurement of actual magnetic field strengths along various pathlengths through the Galaxy is also of great interest — in particular in deciding the currently debated question of how, and at what epoch in the history of the Universe, galactic magnetic fields were amplified up to their current, relatively strong levels. Through a variety of measurement techniques, including pulsar RM/DM ratios, interstellar magnetic field strengths are known to be of the order of 2–5 μG at the Sun's radius (~9 kiloparsecs from the Galactic Centre). These results reveal that the magnetic energy density in the interstellar medium is comparable to that of the cosmic (extragalactic) microwave background density, the local cosmic-ray energy density, and also (coincidentally?) that of the general starlight in the Milky Way. However, the causes and effects that may have determined these similarities are very much unknown at present. Future pulsar RM/DM ratios towards the outer Galaxy will solve the very interesting question of if, and by how much, the galactic magnetic field strength decreases toward the periphery of our Galaxy. □

Philipp P. Kronberg is in the Department of Astronomy, University of Toronto, Toronto, Ontario M5S 1A1, Canada.

1. Rand, R. J. & Lyne, A. G. *Mon. Not. R. astr. Soc.* **268**, 497–505 (1994).
2. Davies, R. D. *Nature* **218**, 435–437 (1968).
3. Simard-Normandin, M. & Kronberg, P. P. *Astrophys. J.* **242**, 74–79 (1980).

TUMOUR-SUPPRESSOR GENES

Open questions on p16

Laura Bonetta

AT the beginning of last year, the very existence of the cyclin-dependent kinase (CDK) inhibitors was unsuspected. By the end of it, it had become clear that these proteins are critical regulators of the cell-cycle and act as 'brakes' at various points. Could removing the brakes throw the cell into unregulated proliferation? The discovery that the CDK inhibitor p16 is homozygously deleted in a striking proportion of human tumour cell lines[1,2] suggested that it could, and raised the possibility that p16 might be a major contributor to cancer development. It now seems that things are not so simple. On page 183 in the Scientific Correspondence section of this issue[3], Spruck *et al.* show that although p16 deletions are indeed frequent in tumour cell lines, they are much less common in primary tumours.

The gene for p16 lies on chromosome 9p21. This region is frequently rearranged or deleted in primary human tumours, and often shows loss of heterozygosity, strongly suggesting that it includes a tumour-suppressor gene analogous to the retinoblastoma or p53 genes. When the status of the gene encoding p16 (also known as *MTS1*, for multiple tumour suppressor 1) was examined, it was found to be deleted in about half of the cell lines analysed[1,2]. Several melanoma cell lines were also found to have missense and nonsense mutations wihtin the gene[2], indicating that p16 might be the critical tumour-suppressor gene in 9p21.

But these initial studies looked at cell lines, which are notoriously prone to genetic rearrangements as a result of culture conditions. Spruck *et al.* have now examined primary cells from bladder tumours for p16 alterations: only 6 out of 31 bladder tumours had homozygous deletions in the p16 gene, and only one had a point mutation, indicating that p16 defects are three times less common than in the cell lines.

These results raise two issues. First, despite the fact that only 19 per cent of primary bladder cancers have homozygous deletions in p16, 80 per cent of such tumours show loss of heterozygosity at 9p21. So there may be other tumour-suppressor genes in this region, which would also be affected by these deletions.

Second, the discrepancy between the mutation frequencies seen in primary tumours and in cell lines demands explanation. Although several hypotheses have been put forward, other work published this month shows that the frequency of mutations seems to vary with the tumour type. Cairns *et al.*[4] looked for p16 mutations in various primary tumours in which the 9p21 region had lost heterozygosity but the p16 gene was not deleted. Out of 75 tumours examined, none of which were melanomas, only two carried somatic mutations in p16. By contrast, Mori *et al.*[5] looked specifically at oesophageal squamous cell carcinomas and found somatic mutations of p16 in 14 out of 27 tumours.

But the discrepancy may also reflect the ease with which cell lines can be derived from the tumours in question (just as the N-*myc* gene is amplified in every neuroblastoma cell line examined so far). Spruck *et al.* show that in three cell lines for which normal and tumour DNAs were available, the p16 gene was already altered in the corresponding tumours. Of the 13 cell lines examined, 12 had alterations in either the p53 or the p16 gene (the remaining cell line had a mutation in Ha-*ras*), implying that lesions in either p53 or p16 confer a long-term growth advantage in culture.

What is the bottom line? p16 is obviously involved in controlling cell growth, and some primary tumours indeed have nonsense mutations and deletions within the p16 gene. Its contribution to tumorigenesis, however, may not be as significant or as general as initially anticipated. The final verdict awaits a comprehensive analysis of primary tumours with loss of heterozygosity in 9p21 from which cell lines have been derived, comparing point mutation and deletion frequencies. The answer may well be that p16 is important in some types of tumours but not others. □

Laura Bonetta is an assistant editor at Nature.

1. Kamb, A. *et al. Science* **264**, 436–440 (1994).
2. Nobori, T. *et al. Nature* **368**, 753–756 (1994).
3. Spruck, C. H. III *et al. Nature* **370**, 183–184 (1994).
4. Cairns, P. *et al. Science* **265**, 415–416 (1994).
5. Mori, T. *et al. Cancer Res.* **54**, 3396–3397 (1994).