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► **COVER:** 'Guardian' by Lara Crow, inspired by the Review on p714.


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When it was discovered in 1979 p53 was thought to be another oncogene, but it was later shown to be a tumour suppressor. This finding, along with the identification of the recessive gene involved in retinoblastoma, helped to kick-start a new research field in cancer biology.

Although the function of p53 has been the subject of intensive research since 1979, and we have some understanding of its function in maintaining genomic stability and modulating apoptosis, its multifaceted qualities have meant that new findings have not declined with age. For example, in the past 15 years p53 has been shown to be part of a family — reflecting the evolution of p53 in multicellular organisms. How p53 activates target genes has also become a complex issue, and roles for p53 independent of its activities as a transcription factor have also been described. Indeed, as the diversity of p53-dependent activities widens to include key roles in metabolism (both endogenously and in response to stress), fecundity and development, old debates continue about how p53 suppresses tumour development. For example, how important is its role in maintaining genomic stability to tumour suppression? What is the significance of its crosstalk with other pathways, such as the E2f–Rb pathway? How is one p53-dependent response selected from many possible options? One thing is clear: p53 is therapeutically important. Numerous approaches are being taken to reconstitute the expression of p53 in tumours and to use the function of the p53 pathway as an indicator of prognosis and response to therapy.

This issue of *Nature Reviews Cancer* contains specially commissioned articles that reflect the history of p53 and the emerging directions that will be important to the future of p53 and cancer research. Full content is available online at www.nature.com/nrc/focus/p53.com.

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