Cover illustration
Adapted from a network graph of protein–protein interactions in J.-F. Rual *et al. Nature* **437,** 1173–1178 (2005).

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SIGNALLING IN CANCER

The past 30 years have led from the discovery of the first cancer-causing gene, or 'oncogene', to the emergence of a new generation of cancer therapies — those targeted at specific signalling molecules.

The signalling pathways controlling cell growth and differentiation are almost invariably altered in cancer. These interconnected pathways are being deciphered, but understanding the alterations that lead to cancer and correcting them is a substantial challenge. The reviews in this Insight discuss the molecular circuitry regulating several key cellular processes, and illustrate how defining the signalling mechanisms is aiding the development of therapies.

Among the key pathways are those controlling cell proliferation, which coordinate a response to the cellular environment, with the mTOR kinase as a critical node. Tumour development is influenced by infections and inflammation, and the complex role of the nuclear factor-κB transcription factors is being unravelled. Expansion of tumour cells depends on nutrient supply and vascularization, which is orchestrated by the transcription factor known as HIF. And the metastatic spread of primary tumours to other organs is facilitated by many signalling pathways; exploring their functional contributions has just begun.

Evaluating signalling molecules as drug targets is important for prioritizing research, even though we cannot predict the success of drugs in the clinic. Still, with several inhibitors of signalling molecules now approved for clinical use, and more in the pipeline, there is reason to celebrate 30 years of oncogene research. We hope these reviews provide a glimpse of recent excitements. Thanks are due to the authors for their contributions and to reviewers for their input.

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REVIEWS

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