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► COVER: 'Child's play' by Claudia Bentley, inspired by the review on p193.



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Since it became possible to examine the genetic basis of cancer, much of the basic cancer research has focused on the function of oncogenes and tumour-suppressor genes. However, tumour cells do not exist in isolation, and their many interactions with surrounding non-tumour cells and the extracellular matrix are known to have a crucial effect on tumour initiation and development.

A publication by Beatrice Mintz and colleagues in 1975 showed that malignant teratocarcinoma cells could produce viable adult chimeric mice, indicating that these cells, when placed in a regulated environment, could function normally. This inspired Mina Bissell to investigate how an environment other than the Petri dish influenced the growth of transformed cells. In 1982, she and her colleagues published a highly cited paper on the extracellular matrix and its function in directing gene expression, and the world of the tumour microenvironment was brought sharply into focus.

This is now a key area of cancer research and although many of the ideas, such as angiogenesis and inflammation, have been examined individually for many years, uniting them under one umbrella — the tumour microenvironment — has increased our understanding of how tumour growth is regulated. Indeed, recent publications indicate that blocking signals from the surrounding stromal cells could be therapeutically viable.

In recognition of this, we are running a series of articles in 2006 that highlight different aspects of current tumour-microenvironment research. We start with an Opinion article by Christopher Overall and Oded Kleinfeld in this issue (page 227) that discusses whether the matrix metalloproteinases (MMPs) will be useful anticancer targets. MMP inhibitors have proved disappointing in clinical trials, perhaps reflecting the pro- and anti-tumour functions of MMPs *in vivo*.

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