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CANCER GENETICS

History rings true for the dividing cell

A century-old model that links problems in cell division to genome instability and so to the development of cancer has now been validated.

The German biologist Theodor Boveri proposed that the chromosome imbalances that are typical of cancer cells arise because the failure of a cell to divide during mitosis would lead to tetraploid cells; these in turn would be vulnerable to complications during cell division and therefore produce daughter cells that have an abnormal number of chromosomes. Two studies have experimentally shown this to be the case and have provided some mechanistic details.

David Pellman and colleagues chemically blocked cell division in mouse mammary epithelial cells that lacked the tumour suppressor gene *p53*, and showed that the resulting tetraploid cells were more likely to generate cancers in mice and to have unstable genomes.

In the second study, Qinghua Shi and Randall King followed the behaviour of chromosomes in the dividing cells of various human cells lines either by fluorescently tagging histone 2B or by fluorescence *in situ* hybridization. Surprisingly, they found that the spontaneous occurrence of chromosome non-disjunction that occurs at some cell divisions does not necessarily lead to aneuploid cells, as was always assumed. Instead, in cells that undergo non-disjunction, mitosis is halted and the cleavage furrow regresses, giving rise to tetraploid cells. Such tetraploids can then produce further tetraploid daughter cells (if the mitosis is bipolar), but they can also lead to aneuploid progeny (if multiple spindles are formed).

This work explains why the chromosome anomalies that are observed in tumours rarely consist of the occasional missing or extra chromosome but instead seem to have arisen by genome doubling followed by chromosome loss. The results also indicate that changes in ploidy number seen in cancer cells might not be the result of mutational events; genetic changes might in fact occur after the ploidy changes, to promote the formation of multipolar spindles and/or the proliferation of the aneuploid progeny.

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References and links

ORIGINAL RESEARCH PAPERS Shi, Q. & King, R. W. Chromosome nondisjunction yields tetraploid rather than aneuploid cells in human cell lines. *Nature* **437**, 1038–1042 (2005) | Fujiwara, T. *et al*. Cytokinesis failure generating tetraploids promotes tumorigenesis in *p53*-null cells. *Nature* **437**, 1043–1047 (2005)