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A MODEL FOR THE STUDY OF HUMAN CHROMOSOMES ASSOCIATED WITH MALIGNANCY

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Abstract

Nonrandom chromosomal abnormalities have been described in several cancerous or precancerous conditions but, with a single exception (the translocation of the long arm of chromosome 22 to chromosome 9 has been related to chronic myelogenous leukemia), the association between a specific chromosomal abnormality and a specific malignancy remains uncertain. With human cells that have been transformed by the oncogenic virus SV40, however, such an association can be made. When maintained in culture, these cells displayed the permanent hereditary changes characteristic of cancer cells. SV40-transformed cells fused with normal mouse fibroblasts resulted in the formation of hybrid cells in which the human chromosomes were partially and preferentially lost, whereas, the complement mouse chromosomes was retained. Both the presence of SV40-T (tumor) antigen and the rescue of SV40 were associated with human chromosome 7 in the hybrid cell clones.

When nondividing mouse cells such as macrophages were hybridized with human cells transformed by SV40, all hybrid cells able to replicate in culture contained human chromosome 7 with the SV40 genome. Some of the hybrid cells contained only human chromosome 7 and produced hemangiosarcomas when they were injected into athymic "nude" mice. Cells from these tumors grown in culture again showed human chromosome 7 with the SV40 genome. Molecular hybridization studies of these cells indicated that SV40 DNA was integrated into the cellular DNA, and that the number of copies of viral genome per cell equalled the number of human chromosomes 7 per cell. Hybridization of SV40-transformed cells with normal human fibroblasts resulted in the production of clones, of cells that retained the transforming phenotype with a near tetraploid number of chromosomes.

These studies show that in human cells one specific chromosome is responsible both for expressing the function of an oncogenic virus genome and for maintaining the malignant phenotype. They also show that tumorigenicity is inherited as a dominant trait in human cells transformed by DNA virus.

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