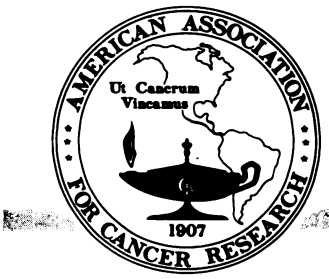
April 1, 1989



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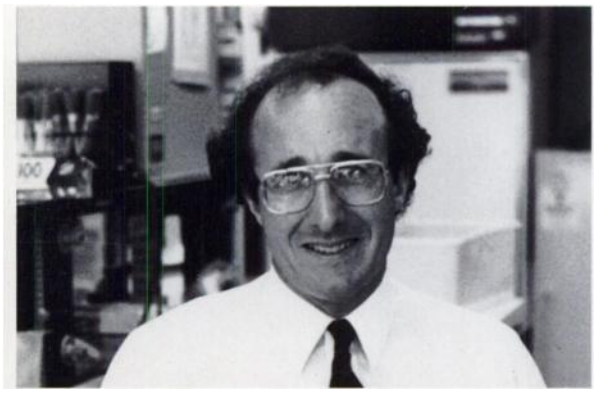
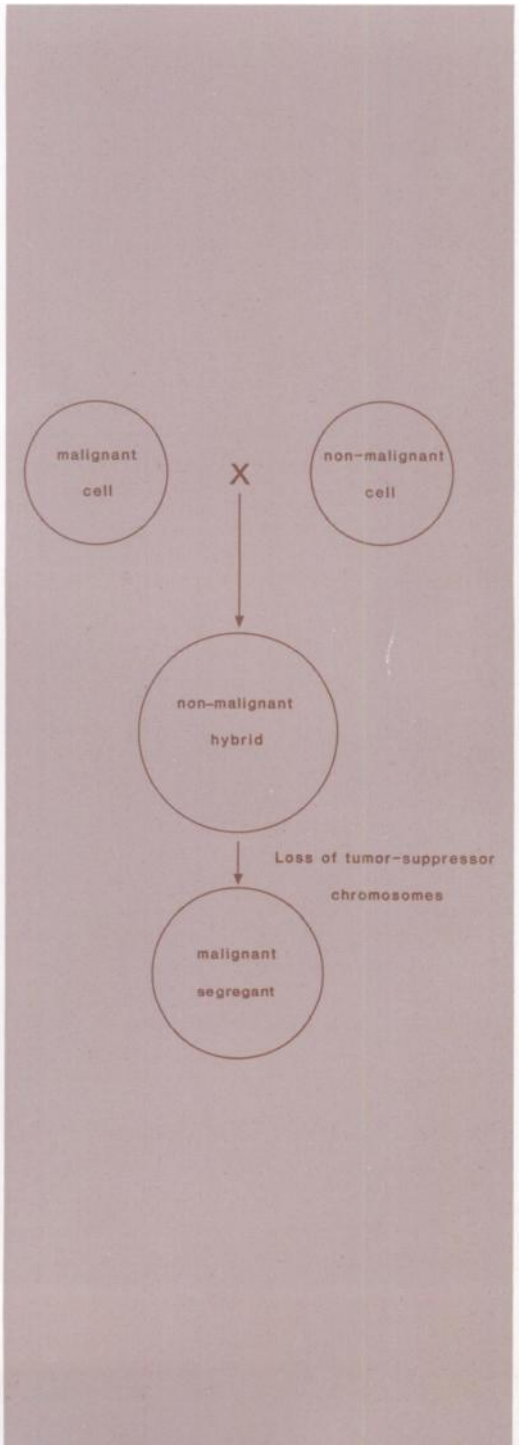
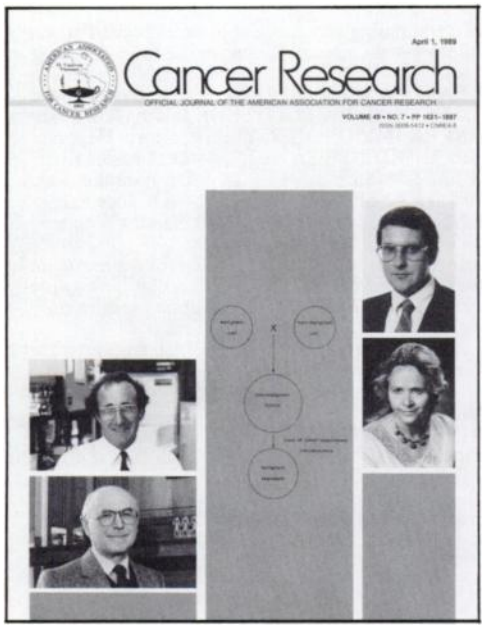




COVER LEGEND



In 1969, a landmark paper by Henry Harris and coworkers [Nature (Lond.), *223:* 363–368, 1969] reported that malignancy was suppressed by fusion of cancer cells with noncancer cells. In the ensuing years, this observation has been repeated in other laboratories and in several species. In 1968 [Natl. Cancer Inst. Monogr., *31:* 365–397, 1968] and in 1978 [Science (Wash. DC), *200:* 1448–1459, 1978], Elizabeth Gateff, with Schneiderman, reported evidence for tumor suppressor genes in *Drosophila.* In the homozygous mutated state (both suppressor alleles lost or inactive), differentiation does not occur, but malignant growth ensues. These observations have been extended by Gateff's colleague, Bernard Mechler, to the cloning of a *Drosophila* tumor suppressor gene and to investigation of its mechanism. (EMBO J. *4:* 1551–1557, 1985).

By 1982, the suppressor problem was carried to the level of chromosome analysis in Henry Harris's laboratory (Evans *et al.*, J. Cell Sci., *56:* 113–130, 1982). Nonmalignant mouse cell hybrids had the full complement of chromosomes expected from both parental cells, whereas malignant segregants lacked a chromosome 4 derived from the nontumor parental cell.

Eric Stanbridge, who in 1976 made the same observation with human cell fusions as reported by Harris for mouse cells [Nature (Lond.), *260:* 17–20, 1976] reported in 1986 [Srivatson *et al.*, Cancer Res., *46:* 6174–6179, 1986; Saxon *et al.*, EMBO J., *5:* 3461–3466, 1986] that transfer of a normal human chromosome 11 could suppress tumorigenic expression of tumor cells. Cloning of a suppressor gene from the suppressor chromosome should prove to be very informative.

It is noteworthy that suppression of tumorigenicity occurs with continued expression of such activated oncogenes as Ha-*ras* shown in Stanbridge's laboratory (Geier *et al.*, Proc. Natl. Acad. Sci. USA, *83:* 5209–5213, 1986), in Ruth Sager's laboratory (Sager *et al.*, Proc. Natl. Acad. Sci. USA, *80:* 7601–7605, 1983), and in the laboratory of Carl Barrett (Oshimura *et al.*, Cancer Res., *48:* 1623–1632, 1988). Barrett's laboratory demonstrated in a Syrian hamster embryo model system the progressive appearance of (1) an immortalized but suppressed stage, (2) a pretumorigenic stage that has lost suppression, and (3) a tumorigenic anchorage-independent stage. Attaining the unsuppressed state involves nonrandom loss of hamster chromosome 15 when transformation by v-Ha-*ras* plus v-*myc* occurs [Oshimura *et al.*, Nature (Lond.), *316:* 636–639, 1985].

Pictured on the cover from *left* to *right* are Stanbridge, Harris, Barrett, and Gateff, together with a diagram of cell fusion between a nontumor and a tumor cell yielding a suppressed hybrid and the emergence of tumorigenic segregants following loss of a suppressor chromosome. Harris is Regius Professor of Medicine, University of Oxford, and Head of the Sir William Dunn School of Pathology, University of Oxford. Gateff is Professor of Genetics, Institute of Genetics, Johannes Gutenberg University, Mainz, Federal Republic of Germany. Stanbridge is Professor, Department of Microbiology and Molecular Genetics, University of California, Irvine, CA. Barrett is Chief, Laboratory of Molecular Carcinogenesis, National Institute of Environmental Health Sciences, Research Triangle Park, NC.

We are indebted to Harris, Gateff, Stanbridge, and Barrett for the photographs and to Harris for the diagram.

Nancy Colburn