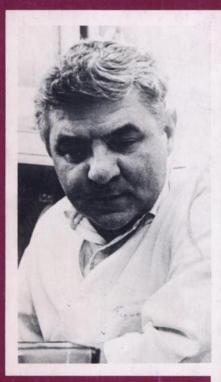


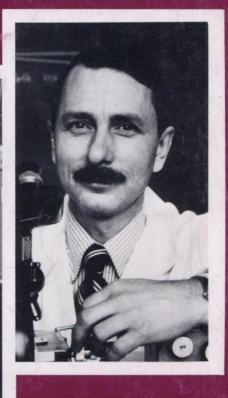
Cancer Research

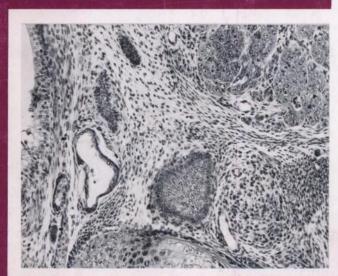
VOLUME 42 • NO. 9 CNREA 8 • PP 3471-3909

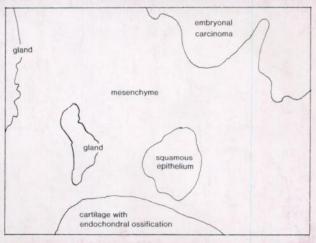
September 1982











SIXTH ANNUAL BRISTOL-MYERS AWARD FOR DISTINGUISHED ACHIEVEMENT IN CANCER RESEARCH



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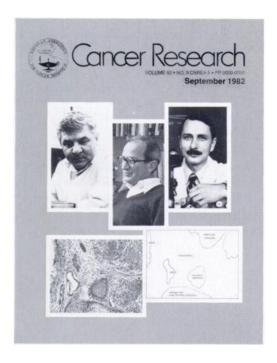
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COVER LEGEND



This month *Cancer Research* directs attention to developmental approaches to neoplasia, in particular research on teratocarcinomas. It was upon these tumors that differentiation of malignant stem cells into benign cells was first demonstrated in 1959 by G. B. Pierce and F. J. Dixon.

The research was made possible after L. C. Stevens and C. C. Little in 1954 established transplantable lines of teratocarcinomas in strain 129 mice. Stevens continued studies on the genetics of the tumors, their development, and experimental production. He discovered that spontaneous teratocarcinomas developed from primordial germ cells in the male and by parthenogenesis in the female. Tumors could be induced by transplanting eggs and embryos into the testis, arising from disorganized embryonic epithelium.

Pierce and his associates demonstrated the multipotent stem cell nature of embryonal carcinoma and the benign nature of the differentiated tissues derived from embryonal carcinoma, developed methods of mass producing embryoid bodies, and studied their development in vivo and in vitro.

The developmental implications of differentiation in neoplasms took a great leap forward in 1974, when R. L. Brinster, using techniques first developed by Richard Gardner, injected single embryonal carcinoma cells into the blastocytes of homologous mice and transferred the injected blastocytes into the uteri of pseudopregnant mice. Chimeric mice occurred in the resultant litters, as evidenced by coat color mosaicism. Cancer cells were thus regulated to behave like normal embryonic cells, which took part in the normal development of the skin. These results were confirmed and extended in two laboratories: B. Mintz et al., using isoenzyme markers demonstrated the proportion of cells in various organs that were derived from the cancer cell; and V. E. Papaioannou and her associates showed that there was a limit to the number of cancer cells that the blastocyte could control. It was then shown that there may be specificity to the reaction, in that the blastocyte could control only closely related malignant cell types.

If one embryonic environment can control its closely related carcinoma, there may be a controlling embryonic environment for each carcinoma. Study of these controls may lead to noncytotoxic therapy of cancer through directing the differentiation of malignant to benign cells.

The research field of the role of differentiation in neoplasia has been summarized by G. B. Pierce, R. Shikes, and L. M. Finck (eds.), in *Cancer: A Problem of Developmental Biology*. New Jersey: Prentice Hall, 1978.

Pictured are L. C. Stevens, of The Jackson Laboratory, Bar Harbor, Maine (*left*); G. Barry Pierce, of the Department of Pathology, University of Colorado, Denver (*center*); and Ralph L. Brinster, University of Pennsylvania, School of Veterinary Medicine (*right*). The section is of a teratocarcinoma of strain 129 mice, indicating some of its malignant and benign elements.

We are indebted to Dr. Pierce for the information and illustrations.

M.B.S.