cell). The SGF will bind to the receptors at neutral pH and elute from them in weak acid with the biological activity (induction of anchorage-independent growth, stimulation of cell division, specific binding to EGF receptors) retained. Cells lacking EGF receptors are unable to respond to either EGF or SGF. The two growth factors differ from one another in several ways. Antiserum to EGF does not immunoprecipitate SGF, and antiserum to SGF does not immunoprecipitate mouse EGF. By isoelectric focusing EGF has a pI of 4.4, while SGF has a pI of 6.8. They also migrate differently from one another on polyacrylamide gradient gels. Most importantly, SGF acts in many ways as a "transforming" protein while EGF does not.

Certain human tumour cells have been found to produce a peptide growth stimulat-

ing factor that is similar in many respects to SGF. A factor produced by a human rhabdomyosarcoma cell line, A673, has been partially purified. It has an apparent mol. wt. of 21,000 and competes with EGF for EGF-specific membrane receptors. Like mouse SGF, it induces normal cells, of either rodent or primate origin, to proliferate in soft agar, and it also brings about a rapid morphological transformation of cells in monolayers. Binding to and eluting from the EGF receptor-rich human carcinoma cells, A431, results in substantial purification of this growth factor. The exact relationships between human SGF and mouse SGF remain to be determined. The possibility is considered that SGF is a more "virulent" form of a normal growth-regulatory protein.

ECTOPIC HORMONES—AN EPIGENETIC CHANGE EXPRESSED IN NEOPLASIA?

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THE PRODUCTION of a peptide hormone by a tumour arising in a tissue or organ not normally associated with that hormone is now a well established phenomenon in the biology of human tumours, particularly those of bronchial origin (Rees & Ratcliffe, 1974). This apparent phenotypic change accompanying the emergence of a neoplasm presents an attractive model in which to examine the relationship between the expression of cell differentiation and the new acquisition of specifically neoplastic characteristics.

First it is necessary to establish that a true heritable change in differentiation has taken place, not that there is simply a neoplastic emergence of a small hitherto cryptic population of hormone-producing cells. The normal lung contains populations of cells sharing ultrastructural (McDowell *et al.*, 1978) and histochemical (Taylor, 1977) characteristics with known peptide endocrine cells of the APUD series, but current evidence has failed to demonstrate the normal existence of any of the more commonly tumour-associated peptide hormones (*e.g.*, ACTH, calcitonin or vasopressin) in these cells. On the contrary, tissue-extraction studies have shown a rise in

one of these peptides, ACTH, in extracts from the lungs of a dog subjected to a potentially carcinogenic stimulus and from a range of human pathological lung tissues (Yalow, 1979). This suggests that a phenotypic change can occur in pathological conditions, though it is not clear which cells of the several types within the lung are involved.

Evidence on the nature of the hormones produced by the lung tumours suggests that they have essentially the same chemical identity as normal hormones or their precursors or fragments (*e.g.*, ACTH and related peptides in a small-cell Ca lung (Bertagna *et al.*, 1978), although the enzymes responsible for processing the hormones for release in their "normal" form may be absent or inappropriate (Lowry *et al.*, 1976). This suggests that the change which has brought about the hormone production is an epigenetic one in which the "normal" gene for the hormone is being expressed in an abnormal or inappropriate way.

The direct relationship between the phenotypic change and the neoplastic initiation is not yet clear. Evidence from other systems suggests that carcinogens can effect pheno-

typic changes (e.g., "intestinal" cell types appearing in rat liver after 3'-methyl-4-dimethylaminoazabenzene carcinogenesis (Yoshida *et al.*, 1978) and muscle cells, adipocytes and chondrocytes appearing from fibroblasts (10T $\frac{1}{2}$ cell line) after 5-azacytidine treatment (Taylor & Jones, 1979)). Further study on the influence of carcinogens on the lung, particularly with respect to local changes in hormone production, will be necessary to determine whether ectopic hormones are produced as a part of the carcinogenic change or are a consequence of altered cell relationships within the lung.

TERATOMA MODELS

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THERE HAS LONG been a suspicion that neoplasia might be in part a disease of differentiation. The juxtaposition of these two aspects of cellular behaviour is nowhere else seen so dramatically as in teratocarcinomas, which are malignant tumours, the stem cells of which not only proliferate rapidly but also differentiate into a wide variety of types of differentiated cell which are themselves essentially non-malignant. The biology of these tumours in mice has been elucidated largely by Stevens (1967). Pierce (1967) and his collaborators laid the foundations of the exploration of the cell biology involved. In subsequent years it has been shown that the stem cells (embryonal carcinoma cells) may be established as clonal tissue-culture cell lines. They will differentiate fully as well *in vitro* as *in vivo* (Martin & Evans, 1975) and some lines have been shown capable of integration with an early mouse embryo and to give rise to substantial parts of the subsequent normal mouse (Papaioannou *et al.*, 1978).

The growth and differentiation of teratocarcinoma cells *in vitro* is thus established as a tractable system (Martin, 1975) and exploration of its cell biology and molecular biology has proceeded on a number of fronts. Here the relationship between embryonal carcinoma cells and their putative normal counterparts in the embryo is considered. As teratocarcinomas may be induced experimentally

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by the ectopic implantation of early embryos (up to 7 $\frac{1}{2}$ days old or of germinal ridges containing undifferentiated germ cells) pluripotential early embryonic cells or primordial germ cells would seem to be likely candidates for the origin of teratocarcinomas. The expression of cell-surface antigens recognised by monoclonal antisera, and the major patterns of protein synthesis seen by two-dimensional electrophoresis, have been compared for embryonal carcinoma cells and various embryonic cell types.

These results suggest that choices are made in cell determination in which only one daughter line emerges at a time. The stem line continues in the same state until it subsequently changes in itself (Evans *et al.*, 1979). The most likely homologues of embryonal carcinoma cells are the cells of the inner cell mass of the early 5-day embryo.

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