Has the Carcinoembryonic Antigen Been a Valuable Discovery?

A.	Munro	Neville
----	-------	---------

Zürich

The ever increasing recognition that human tumors possess diverse functional properties has, and continues to have, numerous important ramifications in their diagnosis as well as providing valuable basic biological data. The discovery in 1965 by Gold and Freedman of the Carcinoembryonic Antigen (CEA) was, by no manner of means, the first human tumor functional property to be recognized. Nonetheless, its initially reported fetal colonic and adult colorectal cancer specificity sparked off a major flurry of research activity in many centers throughout the world, most aimed at examining its clinical utility.

Unrealistic scientific disillusion followed when the originally reported specificity was not confirmed, albeit using different immunological reagents. Still today, valuable studies of the occurrence of CEA in diverse normal human tissues continue to be the main theme of some communications (see this issue, p. 145). The fact that the level of CEA or immunologically-related materials was elevated in the sera in non-gastrointestinal lesions and that, even in colorectal cancer, major increments in the blood were most associated with metastatic disease caused one discouraged researcher in a talk to the

Royal Society of Medicine in London in 1972 to paraphrase Shakespeare and state 'I come, not to praise, but to bury CEA'.

Now, blood CEA assays have an established role in the postoperative surveillance of several forms of cancer. The research exercises conducted by so many workers to enable the affirmation of this clinical role have in retrospect been extremely important. These CEA studies served to establish critical, yet constructive, approaches to determining the clinical role of many other tumor index substances reported more recently and especially following the 'monoclonal explosion'. Perhaps the time is ripe for further gains in our understanding about CEA and its related family of molecules to be reached through research using some newer laboratory tools. Indeed, molecular cloning of CEA and its crossreacting antigens has already shown that of the order of 10 genes on chromosome 19 are involved (see pp. 63-83). The use of suitable vectors and the expression of these genes in other systems, such as in transgenic mice, may give the first real hints as to its biological function. Cell-cell recognition and/or adhesion and antimicrobial functions have been suggested. Perhaps,

62

Editorial

it will have none of these. Moreover, gene cloning from normal human as opposed to cancer cells may, if feasible, be highly rewarding in unearthing previously alluded to differences as yet awaiting proof.

The ready ability to demonstrate the functional and structural properties of tumor cells at the light and electron microscopic level using immunocytochemical techniques on conventionally prepared material has proved to be a most valuable technical advance. Again, CEA had a part to play, although some peptide hormones and enzymes had been demonstrated in this way for at least the prior decade. The availability of monoclonal antibodies to a wide range of tumor cell-associated moieties has obviously given further impetus to such research.

In clinical terms, such immune probes may have not only radioimmunodiagnostic and immunotherapeutic roles but also assist through immunocytochemistry in the readier morphological detection of small foci and/or minimal numbers of cancer cells. This latter approach using diverse probes has been shown to have value in the detection of micrometastases in lymph nodes and the bone marrow. On p. 101 of this issue, a study of tumor-associated pleural effusions showed the increased value of antibody staining which resulted in a significantly improved detection rate in effusions where no malignant cells were seen by conventional morphology.

This editorial posed a question. The present commentator believes that the answer is most certainly in the affirmative.