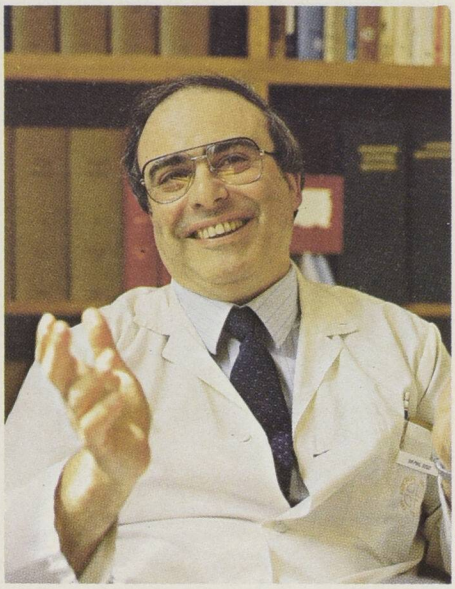
Genes turned off at birth turn on again in tumors

bodies are modified blood proteins that pour forth, each tailored like miniature strait jackets, to fit to antigens and thus set the invaders up for destruction by other elements of the defence system.

Cancer immunology is concerned with ways of utilizing the immune sytem to distinguish between malignant and normal cells, and with encouraging the body's natural defences to reject malignant cells. Only recently, in the 1950s and 1960s, were the concept and experimental techniques developed that enable researchers to probe deeply into the mysteries of cancer. The key question that many hoped to answer was: "Is the transformation of a normal cell into a cancer cell a transformation from self to nonself?" For, if the immune system were to see cancer cells as foreign cells, then the body's



Dan Getz

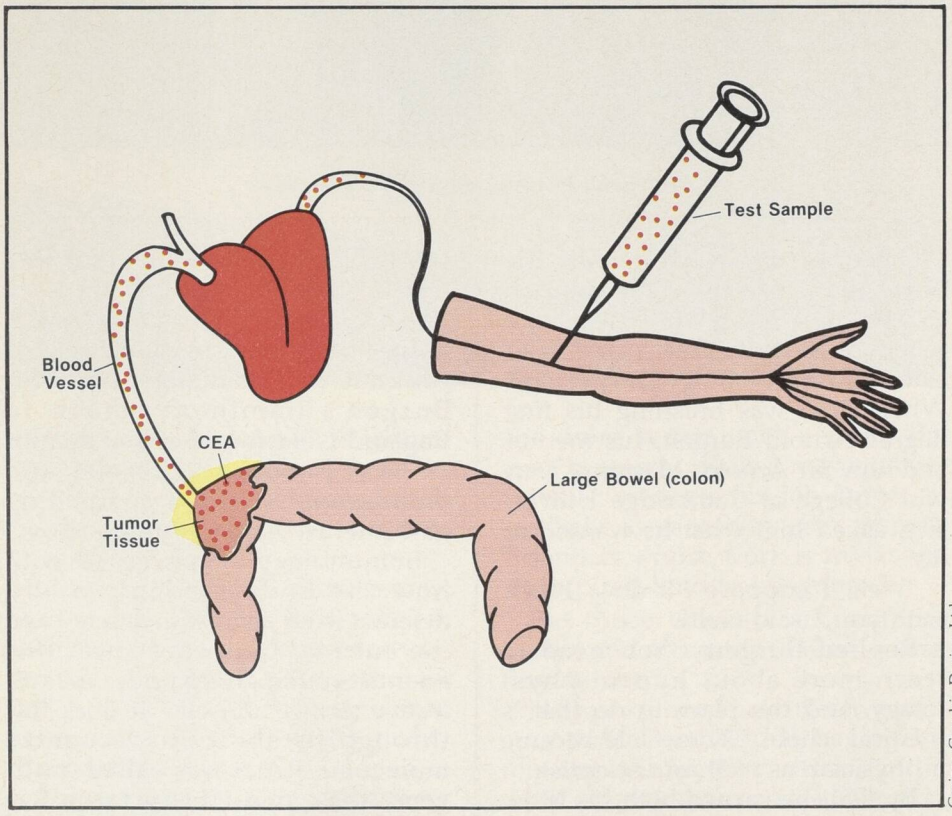
natural defences might be enlisted to fight cancer. Moreover, examination of the differences would provide greater insights into the biological changes that occur in cancer.

Cancer immunology, then, was in a state of creative ferment when Gold chose it as his research field, and began the series of experiments that made his name in science.

In essence, what he did in these experiments was use immunological techniques to probe for differences between a malignant cell and its normal counterpart.

He injected extracts from human colons into rabbits. Rabbits injected with normal colon cells produced antibodies tailored to these normal cells. Rabbits injected with malignant colon cells, Gold reasoned, might produce antibodies to normal cells and antibodies to the malignant cells. By subtracting the first kind of antibodies from the second (by a number of sophisticated techniques), Gold ended up with antibodies *specific* to cells from human colon tumors. He had, in other words, isolated antibodies directed against antigens present on the surface of the colon tumor cells, and absent from the normal colon cells. He had found a tumor marker.

The antigens he had found seemed to be specific to malignancies; they did not show up, for instance, in benign (non-cancerous) tumors of the colon. He found them on every one of the 40 samples of colon primaries that he tested (a 'primary' tumor of the colon originates in that tissue), but not on samples of colon secondaries — not on malignancies, that is, that had spread to the colon from other sites. And, most suggestively, the tissues in which the antigens were found — those of the lower digestive tract — had all developed from the one small ball of cells in the embryo. Following this, Gold then probed *normal* cells of the digestive organs in human embryos — and here again he found his antigen. He named what he had found carcinoembryonic antigen (cancer + embryo antigen) — or CEA.



Carisse Graphic Design Ltd.

How the CEA test works. Bowel tumor cells produce a cancer-specific molecule, the CEA antigen, some of which sloughs off into the bloodstream. By taking a blood sample and exposing it to antibodies for CEA molecules, technicians can detect the disease with few false positives or false negatives.