Body chemical enlisted to fight cancer

A number of chemical cues control the growth of normal cells. Cancer cells – characterized by rapid, unregulated growth – either ignore these cues or don't recognize them. Scientists have long thought that if cancer cells could somehow be taught to respond properly to the body's growth-controlling agents, they might change back into communities of normal cells. Now, a New York (City) University dermatologist says he may have found a naturally occurring chemical with the ability to elicit such a transformation. In the test tube, this substance has reversibly changed cancer cells into what appear to be normal cells. And in preliminary animal tests, injections of the apparently nontoxic chemical have not only slowed the growth of lethal tumors, but in some cases eliminated them.

Contact-inhibitory factor (CIF) was first isolated by George Lipkin and his colleagues from revertant hamster melanoma cells, which had lost some malignant characteristics. Over the past 15 years, these researchers have shown in tissue culture that CIF can help restore cancer cells' sensitivity to the body's growth-control agents.

At least in the test tube or tissue-culture flask, several characteristics differentiate normal cells from cancers:

- Contact inhibition of growth causes normal cells to spread out and grow in flat monolayers. Cancer cells, in contrast, pile up in disoriented, multilayered growths.
- Because healthy cells require "growth factors" carried in the blood, their growth medium must contain about 10 percent blood serum. Cancer cells do not share this serum dependence; they tend to produce their own growth factors. Malignant cells often survive in 1 percent serum or less.
- Finally, while cancer cells can grow in suspension, normal cells cannot. They must anchor to a flat surface and spread out before they divide.

Lipkin, Martin Rosenberg and their co-workers have shown CIF can restore contact inhibition, serum dependence and anchorage dependence to malignant cells. These studies – involving 15 cancer-cell lines of varying types – suggest CIF transformation "is a general response that extends beyond species or tissue specificity," Lipkin says.

While the way CIF works remains unknown, Lipkin's data do show that it will alter chemicals and structures on the surface of incubated cancer cells. Earlier this month, at the American Oil Chemists' Society annual meeting in Phoenix, Ariz., Lipkin described new animal data offering provocative hints of what CIF can do.

Lipkin

Disoriented, rapidly dividing, multilayer hamster melanoma cells (left) look typically cancerous. After CIF treatment (right), cells grow into flattened normal-appearing monolayer.

Four groups of six hamsters each were injected with melanoma cells. The same day, animals began 30 days of "treatment." One group received saline injections three times a week, another injections with saline and 150 microliters of a CIF suspension. The two other groups were injected twice weekly with liposomes – microscopic, lipid-based, controlled-release drug carriers (SN: 4/4/87, p.215). Six of these animals received empty liposomes, while the rest got liposomes with 150 microliters of the CIF suspension. In each treatment, the dose was divided into three shots and injected into healthy tissue around the cancer cells.

Within nine weeks, all the hamsters in the saline and the blank-liposome groups had died of cancer, though cancer growth had initially been slowed in the CIF/saline-treated animals. But tumors in the animals administered CIF via liposomes were small and shrinking by the end of the treatment. Moreover, those tumors continued to disappear in all the animals in this group once treatment stopped, allowing the animals to live out a normal lifespan. In a smaller experiment, CIF also eliminated lung tumors in two of four treated mice.

What these very preliminary experiments seem to suggest, Lipkin says, is that endogenous chemicals like CIF "may provide a powerful new approach in the treatment of recalcitrant tumors."

Lance Liotta of the National Cancer Institute in Bethesda, Md., says the concept of inhibitor factors that suppress the aggressiveness of tumors "is a good avenue of research." He says work in his lab (SN: 1/16/88, p.37) and studies of families having a high propensity for cancer indicate "there is a lowered expression of certain genes in the tumors. Loss of a gene means loss of the proteins that it codes for." CIF might represent one of those lost proteins that normally suppress a cancer's unregulated growth, Liotta says. However, he adds, Lipkin's research "suffers from not having used a purified material."

Lipkin agrees, noting that purifying and precisely identifying the chemical structure of CIF are currently his top research priorities. *– J. Raloff*

Breast cancer's link to alcohol assailed

Ties between alcohol consumption and breast cancer tightened last year when two studies found that even two to three drinks per week significantly increase the risk of the disease among women (SN: 5/9/87, p.292). But those apparent statistical bonds may be unraveling, according to recent scientific reports. Researchers now say the link between breast cancer and drinking alcohol is weak, if present at all.

In a study by the American Health Foundation in New York City, Randall E. Harris and Ernst L. Wynder used personal interviews to assess alcohol consumption and other risk factors among 1,467 women with breast cancer and 10,178 age-matched female hospital patients used as controls. Study participants, who came from 20 hospitals throughout the United States, were part of a larger, ongoing study designed to assess tobacco-related diseases.

After adjusting for confounding variables – including those known to be associated with breast cancer risk, such as a woman's age at first pregnancy – the scientists say they found no solid evidence that any amount of alcohol increases breast cancer risk.

Harris and Wynder concede in the May 20 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION that their results "do not entirely rule out a weak association . . . in certain subgroups [such as leaner women]," but add that their results fail to provide "compelling evidence that alcohol has a role in the genesis of [breast cancer]." They explain that it is difficult to separate socioeconomic factors' effects on drinking habits from their effects on reproductive histories and other potential cancer risks.

Those conclusions are echoed by data from the Centers for Disease Control (CDC) in Atlanta, where Susan Y. Chu and her co-workers interviewed roughly 3,000 women with breast cancer, plus an equal number of controls. Earlier this year at an American Cancer Society seminar in Daytona Beach, Fla., Chu reported that "overall, the CDC study found no relationship between drinking alcohol in the last five years [prior to the study] and breast cancer risk."

Like Harris and Wynder, Chu acknowledges such studies have inherent problems and rely on subjects' recall of drinking habits from years past. Rather than the usual approach of estimating the amount of alcohol per day or week, it may be better to consider total years of drinking, Chu says. She says studies that find an alcohol/cancer link should not be ignored, but emphasizes that "positive findings are different from *conclusive* results." *– D.D. Edwards*