Proteins that Halt Cancer Cells

One of the big problems with anticancer drugs is that they tend to kill healthy cells as well as cancer cells. Consequently, such drugs can give patients almost as many problems as the cancer itself. Researchers would like to find some substance that selectively homes in on villainous cancer cells and that spares normal cells.

Such a substance may now have been found in the form of tiny proteins naturally present in human urine. Stanislaw R. Burzynski of Baylor College of Medicine and his team reported this last week at the annual meeting of the Federation of American Societies for Experimental Biology in Anaheim, Calif. The proteins Burzynski and his co-workers have isolated have the ability to interfere with the division of cancer cells without interfering with the division of normal cells. If cancer cell division is thwarted, cancer is arrested. Once the chemical composition of these proteins has been determined and once the proteins are synthesized, then the synthetic proteins can be tried as therapy in cancer patients.

It all started when Burzynski and his associates wondered why people sometimes undergo spontaneous cancer remission. There must be something, they reasoned, that allows the body to fight cancer on its own—some chemical that diverts potential cancer cells, in the process of division, back onto the normal path. Since proteins are a major class of chemicals produced by cells and are considered excellent carriers of biological information between cells, the team suspected that they might have enough information to reprogram potential cancer cells. They screened human blood for such esoteric proteins. Sure enough, they found a group of small proteins—10 to 15 amino acids in length—that were effective in stopping the division of cancer cells but which did not stop the division of healthy cells.

Harvesting proteins from blood is difficult though. So Burzynski and his colleagues looked for the same proteins in urine, which was easier. Working with 105 gallons of urine from healthy persons, the researchers isolated four different proteins that could inhibit the division of three types of cancer cells with 96 to 97 percent efficiency. One protein inhibited growth of all three types. The other three were more specific, inhibiting the growth of a specific type of cancer. The researchers dubbed the proteins "antineoplastons," since "neoplasm" means tumor.

If National Institutes of Health research funds shine upon them, Burzynski and his team should be able to determine the amino acid sequence of the proteins within a year and to synthesize the proteins in six months after that. The synthesized proteins could then be injected into cancer patients to see whether they could arrest cancer. It would now cost $100,000 to $200,000 to isolate enough of the natural proteins from urine to give one cancer patient one treatment. □

Heart disease: A link with cancer?

In spite of a widespread public belief that dietary fats and cholesterol trigger heart disease, the cause remains as elusive as ever. True, atherosclerosis, the major form of arteriosclerosis (hardening of the arteries), has been strongly linked to the presence of cholesterol and lipoproteins in the blood and aorta. But atherosclerosis has also been tied to high blood pressure, heavy cigarette smoking and other factors. So what actually makes atherosclerotic lesions (fatty plaques) form in the aorta in the first place?

Since 1970, a radical new explanation for atherosclerosis has been quietly but persistently building from several laboratories. It was reported last week during a major symposium at the FASEB meeting in Anaheim.

The new explanation, based on experimental evidence, is that atherosclerotic plaques consist of a unique population of cells and that this population arose from one cell gone haywire. Such proliferation may be triggered by environmental chemicals, viruses or other stressors. If the hypothesis indeed turns out to be correct, the implications are profound: The origins of heart disease would share certain similarities with the origin of cancer, because a number of tumors have been found to be of one-cell origin and to be sparked by chemicals, viruses and other stressors.

The first evidence supporting the new explanation for atherosclerosis was reported in 1970 by Earl P. Benditt, chairman of pathology at the University of Washington School of Medicine, and his co-workers. Atherosclerotic plaques formed spontaneously in chickens and closely resembled those in people. What's more, the chicken plaques appeared to consist of a small population of cells and cells differing from those comprising healthy chicken aortas.

"This finding," Benditt recalls, "strongly suggested that atherosclerosis is a cellular proliferation." In brief, it challenged an article of faith accepted by a number of heart researchers that atherosclerotic arteries are simply cholesterol-clogged drainpipes, rather than living tissue that might be injured and start acting in weird ways.

Subsequently, Benditt and his coworkers examined cells in human plaques and also in healthy human arteries. Once again they found differences in the types of cells comprising both, again suggesting that atherosclerotic plaques constitute a unique population of cells. How does this unusual cellular population arise?

Benditt and his team then found, in 1973, that the unique population derives from one cell. In healthy aortas and other tissues of women, two forms of a particular enzyme—glucose-6-phosphate dehydrogenase—may be present. In contrast, they found that atherosclerotic plaques contain one or the other form of the enzyme, not both. This result suggested that each of the cell masses comprising a plaque had a common genetic origin—that it starts from one cell and that this cell somehow gains a proliferative advantage.

"This was an exciting development from Professor Benditt's lab," Elspeth B. Smith, a University of Aberdeen pathologist, declared at the FASEB meeting. The matter was put even more strongly by Robert H. Heptinstall, chairman of pathology at Johns Hopkins University School of Medicine:

"This finding opened a whole new field of research. It is one of the most significant observations that has been made in the field of arteriosclerosis in the past 20 years." Heptinstall and his colleagues have recently confirmed what Benditt and colleagues first found in 1973—that either form of G6PD, but not both, is found in women's atherosclerotic plaques.

So if atherosclerotic plaques consist of a unique cell population derived from one cell, why does that one cell start multiplying? Benditt and Heptinstall both believe that the original cell starts multiplying because it has been injured by a chemical, virus or other environmental stressor, just as similar factors may turn healthy human cells into cancer cells. In fact, Benditt and his colleagues have found that high blood pressure, which has been linked with atherosclerosis, promotes the multiplication of cells in human arteries. They have also found that lipoproteins in blood carry chemical mutagens, and these lipoproteins are known to be taken up by human arteries.

How might cholesterol fit in with this new explanation for heart disease? A preexisting proliferation of cells in arteries might trap cholesterol, Smith suggests. Benditt, on the other hand, proposes that "cholesterol, while not itself injurious, might possibly be the source of some injurious agent. There is already evidence that there is such a substance, cholesterol-A-oxide. It is a known inducer of tumors." □