Peptide provides target for a cancer killer

Ovarian and breast cancer cells, like other malignant cells, may have an Achilles' heel after all. Researchers now report that part of the immune system will kill malignant cells that display a telltale protein fragment (peptide) on their surface. This finding may lead to the development of a therapy that magnifies the body's own attack on such cancers.

Previously, researchers had identified several warning peptides on the surface of cancerous pigment-producing skin cells. Yet malignant melanoma, the deadliest form of skin cancer, accounts for just 1 percent of all cancer deaths. George E. Peoples and Timothy J. Eberlein of Brigham and Women's Hospital in Boston and their colleagues wondered if they could nab a peptide that would target the much more common breast and ovarian cancers.

In the Jan. 17 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, the researchers report synthesizing a nine-amino-acid peptide they call GP2. This peptide, when held in place by another molecule on the cell surface, presents an inviting target for the immune system. In this case, a type of T lymphocyte (a white cell) destroys cells carrying the GP2 target, the researchers say.

The instructions for building this peptide come from a gene called HER2/neu. Some researchers believe this gene codes for a protein that enables breast, ovarian, and other body cells to divide. In the fetus, HER2/neu cranks out its protein product, making fast-paced growth possible. In most adult cells, however, this gene remains relatively inactive. Scientists believe these cancers result when the gene goes into high gear in an adult cell.

In their experiment, Eberlein's team ground up fresh tumor samples taken from women with ovarian or breast cancer. Next, they isolated the cytotoxic T lymphocytes, killer white cells that destroy tumors. The researchers found that such T cells taken from breast tumors destroy malignant ovarian cells displaying the GP2 peptide. Likewise, they showed that such cells taken from ovarian tumors decimate cancerous breast cells bearing the same target. The team suspects that T cells trained to recognize GP2 in the test tube will become more efficient at killing tumors in the body.

Indeed, the researchers believe that killer T cells will home in on any malignant cell displaying the GP2 peptide. Although healthy cells occasionally display GP2, the immune system goes on red alert only when it notices cells showing lots of this peptide. If the researchers can translate these findings into therapy, it may benefit not only people with breast and ovarian cancer, but those with gastric cancer and one type of lung cancer as well, Eberlein says.

The researchers are beginning to fashion a treatment based on the immune system's reaction to GP2. They plan to remove killer T cells from tumors of patients and culture those cells with GP2 in order to spur recognition of this target. Then the researchers would inject the primed T cells back into the patient. Alternatively, doctors could give cancer patients GP2 directly, in an effort to rev up the T cells in the body.

To create an effective therapy, researchers would have to give patients a cocktail of different peptide targets, says Olivera Finn, an immunologist at the University of Pittsburgh School of Medicine. Those peptides would spur killer T cells to recognize not just one, but several targets on the malignant cancer cell, she adds. Researchers believe some cancer cells evade detection by producing an altered peptide. "If that tumor can be targeted three or more ways . . . it's not likely to escape," Finn says.

In the future, such research may lead to an actual vaccine for cancer. Eberlein and others believe that a mix of peptides given to an individual at high risk of cancer may provide the edge the immune system needs to rout a malignant growth before it gets a foothold in the body.

— K.A. Fackelmann

Obesity, diet linked to deadly cancers

Esophageal cancer usually kills its victims within 6 months of diagnosis. Since the early 1970s, the incidence of one form of this malignancy has tripled among white men, the group at highest risk in the United States. A new study now suggests that obesity may foster this form of the cancer, while diets high in fiber and fresh produce seem to offer comparable protection against it.

Another study finds that produce and olive oil may help protect against breast cancer, the second leading cause of cancer deaths in U.S. women.

Linda Morris Brown of the National Cancer Institute in Bethesda, Md., led a four-state team of researchers who used questionnaires on diet and medical history to hunt for esophageal cancer risks in men.

Two malignancies predominate in the esophagus — the digestive tract between the pharynx and the entrance to the stomach. Squamous cell carcinoma, which preferentially strikes blacks, develops high in the esophagus. In contrast, Brown's team found, adenocarcinoma — which usually develops lower in the esophagus — tends to claim heavy victims.

To the researchers' surprise, the new study turned up 184 cases of adenocarcinoma — 174 of them in white men. The researchers compared their data on these white men with information on 750 cancerfree white men matched by age. In the Jan. 18 JOURNAL OF THE NATIONAL CANCER INSTITUTE (JNCI), Brown's team reports that the heaviest 25 percent of the men in the study had more than three times the cancer risk of the thinnest quarter.

How heavy was the top quartile? Based on a weight-to-size ratio, a 6-foot man needed to weigh about 215 pounds to qualify. Upon further investigation, Brown and her coworkers found that the most obese men in that quartile faced almost four times the cancer risk of men in the thinnest quartile.

Calorie and fat consumption didn't appear to correlate with adenocarcinoma risk. But men who ate the most fiber and the most vitamin C from vegetables displayed just half the risk of those eating the least. And those in the highest quartile for consuming cruciferous vegetables, raw vegetables, or raw fruits had just 30 to 40 percent of the lowest quartile's cancer risk.

Going into this study, "we had no idea what diet would show," Brown says. "Weight also proved a total surprise. I would have thought that, as with those having squamous [cancer], these men would appear malnourished."

"Vegetables also seem protective against breast cancer," notes Dimitrios Trichopoulos of the Harvard School of Public Health in Boston.

He and his colleagues compared the diets of 820 Greek women with breast cancer and 1,548 others admitted to the same Athens-area hospitals for reasons other than cancer. In the Jan. 18 JNCI, they report a 12 percent decrease in breast cancer risk between each successively higher quintile (20 percent of women) of vegetable consumption. An 8 percent decrease in risk occurred with each quintile increase in fruit consumption.

Though many studies have reported similar trends, Trichopoulos notes, the benefits never appeared quite as high and strong as those seen here.

What's more provocative, his team found that women who eat olive oil only once a day face a 25 percent higher risk of breast cancer than women who consume it twice or more daily. *— J. Raloff*