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Diet and lifestyle -- In the cancer fight, eating well is the best revenge

LOS ANGELES -- We all know that eating fruits, vegetables and soy products provides essential nutrition for a healthy lifestyle, while obesity leads to the opposite. Yet proving the effect of nutrition, or obesity, on cancer is an experimental challenge and a focus for scientists. According to emerging evidence being presented at the 2007 Annual Meeting of the American Association for Cancer Research, eating well might still be one of the more pleasurable ways to prevent cancer and promote good health.

A novel mechanism for the chemoprotection by 3,3-diindolylmethane (DIM) and genistein for breast and ovarian cancer: Abstract 4217

Eating such foods as broccoli and soy are believed to offer some protection against cancer, but how this occurs is not well-understood. Now, in laboratory experiments, researchers at the University of California, Los Angeles, have discovered a biological mechanism whereby two compounds in these foods might lower the invasive and metastatic potential of breast and ovarian cancer cells.

They found that diindolylmethane (DIM), a compound resulting from digestion of cruciferous vegetables, and genistein, a major isoflavone in soy, reduce production of two proteins whose chemotactic attraction to each other is necessary for the spread of breast and ovarian cancers.

When applying purified versions of DIM and genistein to motile cancer cells, the researchers could literally watch these cells come to a near halt. When either compound was applied, migration and invasion were substantially reduced.

"We think these compounds might slow or prevent the metastasis of breast and ovarian cancer, which would greatly increase the effectiveness of current treatments," said Erin Hsu, a graduate

student in molecular toxicology. "But we need to test that notion in animals before we can be more definitive."

Both DIM and genistein are already being developed for use as a preventive and a chemotherapy treatment for breast cancer, although more extensive toxicological studies are necessary, the researchers say.

The researchers looked at the potential of DIM and genistein to interfere with the "CXCR4/CXCL12 axis," which is known to play a central role in the metastasis of breast cancer and is also thought to play a role in the development of ovarian cancer. Primary cancer cells express very high levels of the CXCR4 chemokine receptor on the surface of their cells, and the organs to which these cancers metastasize secrete high levels of the CXCL12 chemokine ligand. This attraction stimulates the invasive properties of cancer cells and acts like a homing device, drawing the cancer cells to the organs they metastasize to.

When breast and ovarian cancer cell lines are exposed to purified DIM or genistein, levels of CXCR4 and CXCL12 messenger RNAs and proteins decrease in a dose-dependent manner, compared to untreated cells, according to Hsu.

To assess whether the compounds had any effect on the metastatic potential of the cells, the researchers placed the cells in one end of a compartment and watched how they moved toward CXCL12 at the other end. "The cells degrade the extracellular matrix in the upper compartment in order to move toward CXCL12 in the lower compartment, a system that represents a cell culture model for invasiveness," she said.

But if the cells are treated with either DIM or genistein, movement toward CXCL12 is reduced by at least 80 percent compared to untreated cells, the researchers say.

Hsu says that this same chemotactic attraction is thought to play a role in the development of more than 23 different types of cancer, and, so far, they have found that messenger RNA expression of CXCR4 and CXCL12 is substantially reduced when melanoma and prostate cancer cells are treated with the two compounds.

"We have also tested other phytochemicals and seen similar effects, indicating that this mechanism may mediate protective effects of other vegetable products as well," Hsu said.

The amount of DIM and genistein used in this study is probably comparable to use of a high dose of supplements, and is likely not achievable through consumption of food alone, the researchers say.

Flavonols and pancreatic cancer risk: The Multiethnic Cohort Study: Abstract 856

A study of food consumption in 183,518 residents of California and Hawaii has found that a diet high in flavonols might help reduce pancreatic cancer risk, especially in smokers. These compounds are generally ubiquitous in plant-based foods, but are found in highest concentrations in onions, apples, berries, kale and broccoli.

People who ate the largest amounts of flavonols had a 23 percent reduced risk of developing pancreatic cancer compared to those who ate the least, according to a research team led by Laurence Kolonel, M.D., Ph.D., at the Cancer Research Center of Hawaii.

Smokers gained the most benefit. Those who ate the most flavonols reduced their risk of developing pancreatic cancer by 59 percent, compared to those who ate the least, says the study 痴 lead author, Ute N hlings, DrPH, who conducted the study as a postdoctoral fellow in Hawaii and is now a researcher at the German Institute of Human Nutrition Potsdam-Rehbruecke.

禅he effect was largest in smokers, presumably because they are at increased pancreatic cancer risk already," said N hlings. Smoking is the only established risk factor for pancreatic cancer, and "short of stopping tobacco use, it has been difficult to consistently show lifestyle factors that might help protect against this deadly cancer," she says.

As part of a larger research project known as The Multiethnic Cohort Study, Kolonel and N hlings followed the participants for an average of eight years after they filled out a comprehensive food questionnaire.

Although N hlings says the study has a large statistical power because of the large number of pancreatic cancer cases (529) that occurred in the study population, she says that this one study cannot firmly answer the question of whether flavonols can prevent development of pancreatic cancer. "Further epidemiological studies in other populations and geographic regions are needed to confirm our findings," she said.

The study also is the first to examine prospectively specific classes of flavonols and pancreatic cancer risk.

The researchers looked at consumption of three flavonols: quercetin, which is most abundant in onions and apples; kaempferol, found in spinach and some cabbages; and myricetin, found mostly in red onions and berries.

Of the three individual flavonols, kaempferol was associated with the largest risk reduction (22 percent) across all participants. When the researchers divided intake into quartiles, and then compared highest intake to lowest, all the three classes of flavonols were associated with a significant trend toward reduced pancreatic cancer risk in current smokers, but not in never or former smokers. The interaction with smoking status was statistically significant for total flavonols, quercetin and kaempferol.

The researchers say their study did not examine the biological mechanisms by which these flavonols could exert a protective effect against pancreatic cancer. "But anti-carcinogenic effects of flavonoids in general have been attributed to the ability of these constituents to inhibit cell cycle, cell proliferation and oxidative stress, and to induce detoxification enzymes and apoptosis," N hlings said.

Polyp characteristics, diet, lifestyle factors and high-risk colorectal adenoma recurrence in the polyp prevention trial: Abstract 861

Experts agree that people who have had three or more potentially precancerous adenomatous polyps removed during a colonoscopy should be "rescoped" in three years to make sure the polyps do not recur. But now researchers at the National Cancer Institute (NCI) have identified other factors that independently raise the risk of recurrence.

Two of these risk factors - being over 65 years old, and male - cannot be modified, but the third ‧obesity ‧can, say the researchers.

The results can further help physicians stratify patients at greatest need for follow-up colonoscopies, they say, and can also inform patients about their own risk.

"In a situation where there are not enough physicians, or where doctors have long waiting lists for those who are not first-timers to a colon cancer check-up, then this risk stratification may help physicians prioritize which patients should be seen first," said Adeyinka Laiyemo, M.D., a cancer prevention fellow at NCI.

For patients, Dr. Laiyemo says that "it is important to follow your doctor痴 recommendation based on the nature of polyp removed during colonoscopy, and maintain a healthy weight.

However, men should also recognize that they may be at a higher risk for developing worrisome polyps, and so should women who are over 65 years of age."

The researchers say the findings support the 2006 consensus guidelines, developed jointly by the U.S. Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. These guidelines recommend that people with an advanced adenoma or three or more adenomatous polyps should undergo repeat colonoscopy in three years. The issue, according to the group, is that many patients were being rescoped earlier than recommended, and that these repeat colonoscopies constituted a significant portion of endoscopic practices, draining resources away from patients in need of first time screenings. Previous studies have found that a three-year interval was just as safe for people with three or more adenomatous polyps, high-grade dysplasia, or an adenoma one centimeter or larger in diameter.

This study was designed to see if these guidelines adequately identified patients who later developed dangerous polyps, and also sought to discover other factors associated with increased risk. The research team used data from participants in the Polyp Prevention Trial (PPT), which assessed the impact of a low-fat, high-fiber, high fruits and vegetables diet on polyp recurrence. They examined the diet, lifestyle, and polyp characteristics in 1,905 participants at baseline, after they had a colonoscopy in which at least one polyp was removed and before they altered their eating habits to conform to PPT rules.

Within four years, 230 PPT participants developed high-risk polyps, and 524 had a low-risk adenoma recurrence. Dr. Laiyemo and his team found that, indeed, the presence of multiple adenomas was the largest risk factor associated with polyp recurrence, but that age, gender and obesity played important, if lesser, roles in stratifying risk. Of these factors, age was the most statistically significant, followed by gender and then obesity, he reports.

The only statistically significant factor they found that lowered risk was use of non-steroidal anti-inflammatory drugs (NSAIDs).

"We know from previous studies that NSAIDs can reduce polyp formation, but perhaps at a cost, due to some side effects that have been observed," Dr. Laiyemo said. "We think that people should follow the consensus guidelines, but these other variables should also be considered when judging an individual痴 risk and the need for follow-up colonoscopies at the appropriate time."

Fruit and vegetable intake and head and neck cancer in a large United States prospective cohort study: Abstract 849

A new study among AARP members shows that just one additional serving of fruit and vegetables per day may lower your risk of head and neck cancer, but the data suggest that you may not want to stop at just one, according to researchers from the National Cancer Institute.

A large prospective study of 500,000 men and women aged 50 and older has found that those who ate more fruit and vegetables had a reduced risk of head and neck cancer. Head and neck cancer is the sixth leading cause of cancer-related mortality worldwide, resulting in more than 350,000 deaths annually.

"Identifying protective factors for head and neck cancer is particularly important as it has a high mortality rate," said Neal Freedman, Ph.D., cancer prevention fellow at the National Cancer Institute.

At the beginning of the study, participants reported their typical dietary habits on a food frequency questionnaire. Freedman and his colleagues followed participants for five years and recorded all diagnoses of head and neck cancer cases during this time.

In their findings, the researchers report that participants who ate six servings of fruit and vegetables per day per 1000 calories had 29 percent less risk for head and neck cancer than did participants who consumed one and a half servings per 1000 calories per day. Typically, adults consume approximately 2000 calories per day. One serving equals approximately one medium sized fresh fruit, one half cup of cut fruit, six ounces fruit juice, one cup leafy vegetables, or one half cup of other vegetables.

"Increasing consumption by just one serving of fruit or vegetables per 1000 calories per day was associated with a six percent reduction in head and neck cancer risk," Freedman said.

According to Freedman, people who ate a lot of fruit also tended to eat a lot of vegetables, and vice versa. To measure these two types of foods independently, the researchers included both fruit and vegetable intake in the statistical models, a common statistical approach. This allowed them to compare participants with different levels of fruit consumption while holding constant the level of vegetable intake and vice versa. When examining fruit and vegetable intake simultaneously, the protective association with vegetables seemed to be stronger than the association with fruits.

"Although we cannot absolutely rule out a cancer preventive role for other lifestyle factors that go along with eating more fruits and vegetables, our results are consistent with those from previous studies," Freedman said. "Our study suggests that fruit and vegetable consumption

may protect against head and neck cancer and adds support to current dietary recommendations to increase fruit and vegetable consumption."

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The mission of the American Association for Cancer Research is to prevent and cure cancer. Founded in 1907, AACR is the world 痴 oldest and largest professional organization dedicated to advancing cancer research. The membership includes more than 25,000 basic, translational, and clinical researchers; health care professionals; and cancer survivors and advocates in the United States and more than 70 other countries. AACR marshals the full spectrum of expertise from the cancer community to accelerate progress in the prevention, diagnosis and treatment of cancer through high-quality scientific and educational programs. It funds innovative, meritorious research grants. The AACR Annual Meeting attracts over 17,000 participants who share the latest discoveries and developments in the field. Special Conferences throughout the year present novel data across a wide variety of topics in cancer research, diagnosis and treatment. AACR publishes five major peer-reviewed journals: Cancer Research; Clinical Cancer Research; Molecular Cancer Therapeutics; Molecular Cancer Research; and Cancer Epidemiology, Biomarkers & Prevention. Its most recent publication, CR, is a magazine for cancer survivors, patient advocates, their families, physicians, and scientists. It provides a forum for sharing essential, evidence-based information and perspectives on progress in cancer research, survivorship and advocacy.