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Research published in the May 15th issue of *American Journal of Epidemiology* confirms that men with diabetes mellitus have a reduced risk of prostate cancer. After controlling for potential confounders, the investigators found that diabetes was associated with a 36% reduction in the risk of prostate cancer.

The researchers examined data for men from the Cancer Prevention Study II Nutrition Cohort who completed a mailed questionnaire on diabetes in 1992, and again in 1997 and 1999. The study group also included 1110 case and control subjects who were followed from 1982 to 1995. A total of 5318 cases of prostate cancer were reported in 72,670 participants.

In addition to the general association of diabetes with prostate cancer risk, further examination showed that the relationship was significantly affected by the timing of diabetes diagnosis.

Analysis confirmed that diabetes had a protective effect against the development of prostate cancer, with a rate ratio (RR) of 0.67 for men with diabetes compared with those without the condition.

Specifically, the risk of prostate cancer was elevated during the first 3 years after the patient received a diagnosis of diabetes (RR: 1.23), but fell in men who were diagnosed 4 years or more before (RR: 0.63).

"In theory, because low insulin levels are linked to low levels of testosterone, diabetes should protect against prostate cancer, a malignancy stimulated by high androgen levels", explain Kangmin Zhu and colleagues from the US Military Cancer Institute in Washington, DC, USA.

"The results contribute to the understanding of factors that may delay prostate cancer progression and are helpful for developing therapeutic and preventive interventions," said the investigators. "Large studies with similar results will help to solidify the present findings."

POKEMON: new cellular oncogene essential for cancer development

Researchers from the Memorial Sloan-Kettering Cancer Center (MSKCC) in NY, USA, in collaboration with teams from Japan and the UK, have announced that the newly identified gene, POKEMON, plays a key role in initiating malignancy. As a result, scientists now believe they have stumbled upon an important new target for anticancer therapy. These findings have been published in the January 20th issue of *Nature.*

The investigators have named the gene POKEMON, for POK Erythroid Myeloid ONtogenic factor.

POKEMON occurs naturally in human cells and is beneficial when working properly. However, when it malfunctions, like the electronic game figures – tiny monsters with bad tempers – the cancer-triggering gene apparently instigates the misbehavior of other cancer-causing genes, leading to tumorigenesis.

Unlike the oncogenes identified so far, POKEMON plays a governing role in the network of events that control cell transformation. "This is the master switch that interacts with other genes," said Carlos Cardon-Cardo, a molecular pathologist at the cancer center and coauthor of the research. "It acts differently to other oncogenes. Others regulate cell growth, but POKEMON impacts on critical properties of cancer cells."

Among its key properties, POKEMON enhances a cancer cell's ability to resist aging and death. This immortalizing factor essentially endows cancer cells with a quality that renders them robust indefinitely, the very trait that makes tumors difficult to treat.

POKEMON's cancer-causing role was confirmed by inserting it into mice. POKEMON repressed the function of other proteins, including the tumor suppressor ARF, and the mice developed aggressive, fatal forms of lymphoma. The researchers also found that when they knocked out POKEMON, transformation was blocked and the cells did not become cancerous.

"The unique property of POKEMON is that it is doing this when it's overexpressed," MSKCC cancer geneticist and senior author of the study Pier Paolo Pandolfi explained. "But when you take it out, remove its activity from the cell, then none of the other oncogenes in the cell are able to transform, to behave as oncogenes. In other words, POKEMON is essential for the activity of these other oncogenes."

In further work using tissue microarrays, it was confirmed that POKEMON is present in very high levels in certain types of B- and T-cell lymphomas. The investigators also found that tumors with high levels of POKEMON protein were much more likely to be aggressive. "We know already that, as an oncogene, POKEMON is involved in other tumors," said Pandolfi, "and is likely active in a wide range of cancers, including breast, lung, prostate and bladder malignancies."

The aim now would be to develop a diagnostic tool to determine the status of the gene in human cancers and a drug to block its function, just as the drug imatinib (Gleevec®) is used to treat a variety of distinct cancers that share one molecular flaw.

"This is going back to a unifying theme to understand how cancer works," Pandolfi said. "What is emerging is this idea that genes work in networks. Targeting

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specific sites will be important in drug development." Surgery or conventional chemotherapy, no matter how targeted, "are clearly very toxic because there's no way you can avoid damaging the surrounding region," Pandolfi explained. "But with gene therapy, we are correcting the misbehavior of a specific cell type, going against the underlying molecular reason as to why the cells are proliferating. It's becoming apparent that this type of targeted intervention is much less toxic."

Mystery compound in beer wards off cancer

Mice given beer while exposed to cancer-causing chemicals had 85% less damage to their liver, lungs and kidneys than those given water, report Sakae Arimoto-Kobayashi's team at Okayama University in Japan.

Some cancers are caused by heterocyclic amines, DNA-damaging chemicals found in cooked meat and fish. When the investigators fed these chemicals to mice, the DNA damage was significantly reduced if the mice drank nonalcoholic beer. Arimoto-Kobayashi believes that as-yet unidentified compounds in lager and stout may prevent the amines (the carcinogenic agents) binding to and damaging DNA. If these compounds can be identified, brewers might be able to produce beers particularly rich in them, or they could be added to foods.

Heavy alcohol consumption is blamed for around 6% of all cancers in Western countries, although moderate consumption of both beer and red wine, which contain numerous natural polyphenols, is associated with many health benefits, including reduced risk of heart disease, as well as anticancer, antiviral and antiallergic properties.

However, Arimoto-Kobayashi said that since the mice drank nonalcoholic beer, the findings do not show whether moderate consumption of normal beer has any anticancer benefits, and would not encourage increased intake. "The total benefits and risks of beer with alcohol are still under consideration," says Arimoto-Kobayashi.

Helen Shovelton, Chief Executive of the British Lung Foundation, warned "We would not encourage anyone to drink more beer with the aim of preventing cancer as alcohol has been proven to have some detrimental health effects."

ACS Statistics for 2005

More Americans are surviving cancer and rates are generally falling, mostly because fewer people are smoking, but in 2005, according to the American Cancer Society (ACS), more people under the age of 85 years are expected to die of cancer than of heart disease.

The ACS predicts that 1.372 million Americans will be diagnosed with cancer in 2005 and 570,280 will die of the disease.

"This compares with 1.368 million cases in 2004 and 563,700 deaths. Overall numbers will be higher in 2005 because the population is growing in size and growing older", the group report.

"The death rate from all cancers combined has decreased by 1.5% per year since 1993 among men and by 0.8% per year since 1992 among women," the report states.

"Overall, the major reason for the decline in mortality rates is progress in tobacco control," explained Elizabeth Ward, Director of Surveillance Research for the group. She said that smoking causes about a third of all cancer cases, and poor diet and a lack of exercise cause another third.

"Death rates for all cancers at all three major sites in men have been decreasing," Ward said, referring to lung, prostate and colon cancer. "But rates of death among men from liver and esophageal cancer have been rising, probably due to obesity".

Better detection and treatment have lowered breast cancer mortality, but more cases are being diagnosed.

More cases of colon and cervical cancer are also being detected, but screening can prevent these cancers or catch them at early, more curable stages.

The 5-year survival rate for all cancers is 64%, up from 50% for those first diagnosed in 1976.

In 2005, the American Cancer Society predicts there will be:

- 232,090 cases of prostate cancer with 30,350 deaths
- 212,930 cases of breast cancer with 40,870 deaths
- 172,570 cases of lung cancer with 163,510 deaths
- 104,950 cases of colon cancer with 56,290 deaths
- 59,580 cases of melanoma with 7770 deaths
- 56,390 cases of non-Hodgkin's lymphoma with 19,200 deaths.

Red wine consumption may reduce prostate cancer risk

Evidence is accumulating to support the role of red wine consumption in reducing the risk of prostate cancer in middle-aged men. Recent results published in the January 1st issue of *International Journal of Cancer* indicate a statistically significant 6% decrease in relative risk of prostate cancer with each additional glass of red wine consumed per week.

Janet L Stanford and colleagues from Fred Hutchinson Cancer Research Center, WA, USA, used logistic regression analysis to estimate odds ratios and evaluate significance in a population-based, case-control study to assess the association between alcohol consumption and prostate cancer. A total of 753 newly diagnosed prostate cancer patients between the ages of 40 and 64 years and 703 frequency-matched controls were selected.

Although no clear associations were observed between the risk of prostate cancer and overall alcohol consumption, a significant linear trend of declining prostate cancer risk with increasing categories of red wine consumption was found.

"Alcohol consumption is a modifiable lifestyle factor that may affect prostate cancer risk," explained Stanford's group. "Alcohol alters the hormonal milieu and contains chemical substances such as flavonoids (red wine), which may alter tumor cell growth."

There is clearly a need for further research on the biologic effects of polyphenol-rich foods and beverages in preventing or at least reducing the risks of certain cancers.