MedicalXpress

High dietary phosphate intake may promote skin cancer formation

March 23 2010, by Quinn Eastman

A high dietary intake of phosphate promotes tumor formation in an animal model of skin cancer, researchers at Emory University School of Medicine have found. The results, published in the journal *Cancer Prevention Research*, suggest that a high intake of phosphates may promote tumor development and contribute to tumor growth in skin cancer, while restricting phosphate intake may help prevent cancer.

The researchers applied dimethylbenzanthracene, a carcinogen found in cigarette smoke, to the skins of mice, followed by another chemical that stimulates cell growth. Feeding these mice a high phosphate diet (1.2 percent by weight) increased skin papilloma number by 50 percent compared with a low phosphate diet (0.2 percent). Skin papillomas are the initial stage of skin cancer development, which may progress to full carcinoma.

"This is a very well established model for the initiation and progression of cancer, and the effects of many physiological conditions on cancer initiation have been measured this way," says senior author George Beck, PhD, assistant professor of medicine (endocrinology). Beck also is a member of the Winship Cancer Institute, Emory University.

Phosphate is an essential nutrient forming both the physical support for bones, when complexed with calcium, and the chemical backbone of DNA. Phosphate chemical bonds provide the energy currency in the cell, in the form of ATP (adenosine triphosphate). In addition, many oncogenes, the motors driving cancer cells to divide relentlessly, are

regulatory enzymes that attach phosphate chemically to other proteins, turning their activity up or down depending on the protein target.

Altered levels of phosphate could be tipping the balance of these chemical reactions in complex ways, Beck says.

Public health researchers say that phosphate dietary intake has increased over the last 30 years and also may be underestimated because of the increasing contribution of food additives. Phosphate is added to a variety of processed foods such as meats, baked goods and soft drinks to improve texture and durability.

The authors calculate that the human dietary equivalent of a mouse's high phosphate diet is 1,800 milligrams per day, an intake level that many humans match or exceed. The high-phosphate diet did not have a corresponding increase in calcium, which would reflect the equivalent of a dairy-rich diet. A low-phosphate diet in the mice corresponds to 500 milligrams per day for humans.

"Another way to look at it is that a low-phosphate diet may help prevent cancer," Beck adds. Previous research on the effects of a restricted-calorie diet in the same mouse model of skin cancer lowered the number of skin papillomas by a factor comparable to that obtained by limiting phosphate intake.

According to Department of Agriculture data from 2006, the average phosphate intake for American males and females over two years old is 1,334 mg. The Recommended Daily Allowance is 1,250 mg for pre-teens and teenagers and 700 mg for adults, with a maximum tolerable level set at 4 grams per day.

Researchers in Korea have recently found similar effects of high dietary phosphate on lung cancer in mice. Beck says he began studying

phosphate's influence on oncogenes in bone cells grown in the laboratory. He and his colleagues found that in the presence of high phosphate, bone cells divide more quickly and produce more osteopontin, a protein linked to the breakdown of bone, and other cancer-related proteins.

In this paper, Beck and colleagues also found that high phosphate activates the oncogene N-ras in skin cells, and that high phosphate in a mouse's diet increases the level of osteopontin in the blood.

He cautions that many foods naturally contain phosphate, but not all of it is absorbed equally, so the amount of phosphate consumed does not always reflect phosphate levels in the blood. In addition, phosphate requirements by the body may vary according to age, sex and daily activity, he says.

"Phosphate in the diet has been previously studied for its effects on bone formation and bone breakdown, as well as by cardiologists and kidney specialists," Beck says. "But outcomes and endpoints having to do with cancer have not been looked at. This is an area where we have to be careful about mechanism, because there are many influences on phosphate metabolism."

Provided by Emory University