Soy and Prostate Cancer Study Results Mixed

By Brian Vastag

In 1985, Herman Adlercreutz, M.D., and colleagues at the University of Helsinki discovered high levels of estrogen-like soy compounds in the urine of Japanese men. Given the low rate of prostate cancer among Japanese men and the anti–prostate cancer effects of estrogens, Adlercreutz hypothesized that high soy consumption protected against the disease.

More than two decades later, scientists are still trying to confirm the idea.

“It’s been a long road,” said Adlercreutz, who has published dozens of reports examining the two main soy phytoestrogens, daidzein and genistein—classified as isoflavones—and their effect on cancer development.

The latest study examining the issue, a large prospective report from Japan published in the March Cancer Epidemiology, Biomarkers & Prevention, paints a complicated picture. In the study population, high soy consumption protected against early prostate cancer, but it also was associated with an increased risk of advanced prostate cancer in some men.

“Consumption of isoflavones from traditional Japanese food might protect against prostate cancer,” said the study’s first author, Norie Kurahashi, M.D., of the epidemiology and prevention division of the National Cancer Center in Japan. “But we can’t recommend supplements with isoflavones because their relationship to advanced prostate cancer is unclear.”

Japanese men eat substantially more soy-based foods than Western men do, and the incidence of prostate cancer is much lower in Asian countries than in Western countries. But reviews of latent, or clinically insignificant, prostate cancer in autopsy reports reveal no differences between the populations, so Adlercreutz and others have theorized that isoflavones stop latent cancers from developing further.

Earlier, smaller epidemiological studies in Japan reached contradictory conclusions regarding the protective effect of soy, so the National Cancer Center researchers were hopeful that this latest study would resolve the issue, especially given the weighty animal evidence supporting a protective effect for soy isoflavones.

In Kurahashi’s study, the researchers surveyed 43,059 men aged 40–69 years about their consumption of 147 foods, including miso soup (made from fermented soybeans), natto (also a product of fermented soybeans), and tofu (made from soy milk). The Japanese consume miso soup more frequently than other soy foods, and miso, natto, and tofu account for about 90% of the population’s consumption of daidzein and genistein, according to the researchers.

Over the course of the study, 307 men were diagnosed with prostate cancer; 74 cases were advanced and 218 were local (confined to the prostate). Fifteen cases were of undetermined stage. The team calculated that the risk of developing localized prostate cancer was 50% lower in men who ate the most soy isoflavones compared to men who ate the least soy. Men in the top consumption group ate between two and three times more than men in the lowest consumption group.
Gut Bacteria May Be Key to Soy Benefit

The varied results in epidemiological studies of soy and cancer—some reports show that soy protects against prostate and breast cancers, whereas others don’t—has confounded researchers for nearly two decades. Accumulating research suggests that a gut check is in order.

In 1995, scientists at Michigan State University found that bacteria in the gut convert one of soy’s main isoflavones, daidzein, into an even more potent estrogen-like compound called equol. The team reported that bacteria cultured from some people made the conversion, but bacteria from others didn’t. More research confirmed that about half of the population has gut flora that can turn daidzein into equol.

Japanese researchers followed up with case-control studies looking at equol production in prostate cancer patients and healthy controls. In 2004, the team published a report in the Japanese Journal of Clinical Oncology showing that just 29% (38 of 133) of Japanese prostate cancer patients could make equol, compared with 46% (75 of 162) of controls. For Korean patients, the figures were 30% (18 of 61) and 59% (36 of 61), respectively. “These results suggest that the ability of producing equol ... is closely related to the lower incidence of prostate cancer,” the authors wrote.

And now researchers from the Fred Hutchinson Cancer Research Center in Seattle say that they’ve identified a bacterial “fingerprint” that distinguishes equol producers from nonproducers. “We’re hoping we can use this fingerprint to identify who might benefit from a high-soy diet,” said Meredith Hullar, Ph.D., who presented the research at the 2007 American Society for Microbiology annual meeting in May.

The team also found that the protective effect of isoflavone-rich foods was strongest in men aged 60 and older. “Isoflavones may be protective for localized prostate cancer only in men aged more than 60 years and may not have a protective effect in the early stage of prostate cancer in younger men,” the researchers write.

Kurahashi and her colleagues offered an array of possible explanations for the seemingly contradictory findings. The effect of soy compounds on prostate cancer development may really differ according to disease stage, possibly because the two tumor types respond differently to estrogen-like compounds. Or the findings could be a result of the few men who developed advanced prostate cancer in the study. Errors in estimated food intake, as self-reported by study participants, might also explain the discrepancy, they said. Or there could be no real association.

Adlercreutz, who was not involved in the Japanese study, said he was “a little surprised” by the association between high soy consumption and advanced prostate cancer. He pointed out that the risk of developing advanced prostate cancer was related to only one type of soy food, miso soup. Men who ate two or more bowls of miso a day had roughly twice the risk of developing advanced disease as did men who ate less than a bowl a day. High consumption of the other soy foods tracked in the study were not associated with increased risk of advanced cancer.

“Why would advanced cancer only be correlated to one type of soy food?” Adlercreutz asked. “It doesn’t make a lot of sense.”

In 2005, the Agency for Healthcare Research and Quality issued a report examining 178 prospective studies of soy foods, concluding that the evidence supporting a protective benefit against cancer was limited (see J Natl Cancer Inst 2005; 97: 1494).

The Japanese researchers plan to continue studying soy and prostate cancer, focusing on the ages when the most soy is consumed. “Given that Japanese consume isoflavones regularly throughout life, we do not know the period during which the effects of isoflavones on prostate cancer are preventive. We need well-designed clinical trials,” Kurahashi said.