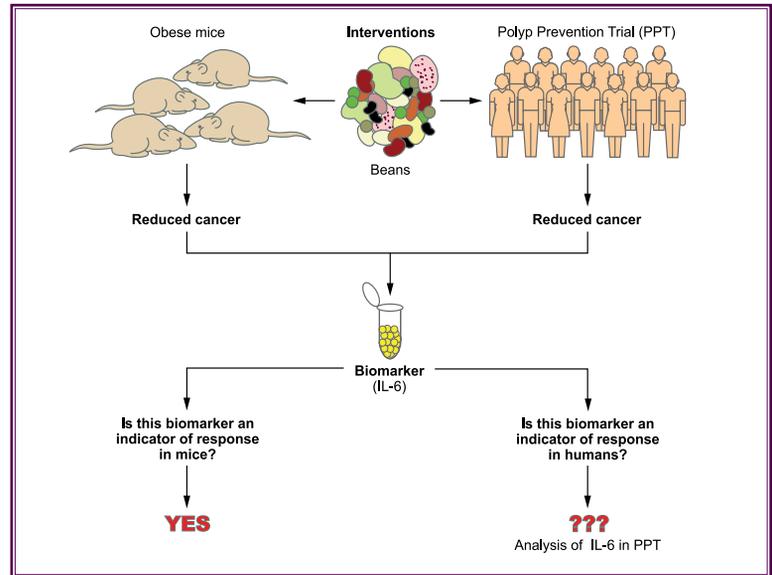


A Diet That Works:

New Study Shows Early Response of Colon Cancer to Dietary Change

Lifestyle plays an important role in human health, and conscious choices such as adopting healthier dietary habits have become especially crucial in 21st century healthcare as one means to reduce spiraling costs. Growing support exists to better understand diet and disease relationships. But setting up a trial to test a dietary intervention is often challenging since it is difficult to measure how well the intervention is working before actual disease onset.



(Image: J. Kelly)

Discoveries from the Polyp Prevention Trial suggested that a diet rich in beans would reduce the risk of colon cancer. Follow-up studies in mice proposed interleukin-6 (IL-6) as a biomarker of this response. Will IL-6 levels also reflect the efficacy of dietary intervention in humans?

In one of the first studies of its kind, Nancy Colburn, Ph.D., Chief of the Laboratory of Cancer Prevention at CCR, published research in the January 2009 issue of *Cancer Prevention Research* that identified biomarkers of early response to an efficacious dietary intervention—whole navy beans and bean extracts—for reducing the development of colon cancer in genetically obese mice.

In a previous study, Dr. Colburn and colleagues designed an experiment based on what had been observed in the Polyp Prevention Trial (PPT)—a human study that set out to determine whether or not a diet high in fruits and vegetables could reduce the recurrence of colon polyps (abnormal, potentially cancerous tissue growth) in at-risk individuals. The results of that trial revealed that those who ate the highest amount of beans showed only a one-third recurrence rate. Taking this information, Dr. Colburn designed a study using genetically obese mice injected with azoxymethane to induce colon carcinogenesis, placed them on a navy bean diet (whole bean, bean residue fraction, or bean extract fraction), and

found reduced tumor growth in all three groups as compared with controls.

The present study examines the serum and colon mucosa collected from these same mice and tests them for biomarkers that correlate with the efficacy of the intervention. The research team found that the proinflammatory cytokine interleukin-6 (IL-6) was an indicator of response in both the serum proteins and the gene transcripts of the colon mucosa in mice. Bean-fed mice had significantly lower levels of IL-6 in serum and had changes in many inflammation-associated genes in mucosa. Inflammation plays an important role in colon carcinogenesis, so these changes in inflammation-associated molecules likely play a functional role in modifying the disease process. It was noteworthy that the bean diet counteracted the effect of the carcinogen on colon IL-6.

“Biomarkers of response are important because we would like to match the intervention with those likely to respond. If we can identify after short-term exposures to the intervention those likely to respond, we can save a lot of time and money in human studies,” said Dr. Colburn.

Following the recommendation of the NCI Translational Research Working Group (TRWG) (<http://www.cancer.gov/trwg>) to connect mouse to human trials, Dr. Colburn and colleagues have discovered a mouse-human correlation between a dietary change and a reduction in colon cancer risk. Using an obese mouse model, the team validated the effectiveness of a dietary intervention and then identified a biomarker indicative of healthful changes in mouse colon mucosa. Next the researchers went back to a human clinical trial (the PPT) to validate the biomarkers they identified in their mouse study. The data for this trial, which was presented in April 2009 at the American Association for Cancer Research Annual Meeting, showed that diet may reduce the recurrence of colon polyps in humans by attenuating IL-6, so IL-6 appears to be a predictive biomarker of response to dietary prevention of colon carcinogenesis.

To learn more about Dr. Colburn's research, please visit her CCR Web site at <http://ccr.cancer.gov/staff/staff.asp?Name=colburn>.