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NCI To Study Review Group's Report Urging Restructure Of Prevention Program

NCI plans to appoint an internal committee to respond to the recommendations of an advisory group's report on the cancer prevention research program, Institute Director Richard Klausner said last week.

The report, by the Cancer Prevention Program Review Group, includes 43 recommendations to NCI for restructuring the program (**The Cancer Letter**, June 20).

"The point of this wonderful report is that it emphasizes that we need to have a very committed, robust, broad, and constantly validated, and therefore successful, program in prevention," Klausner said at a June 17 meeting of the National Cancer Advisory Board. "One thing that comes

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In Brief

Pass Joins Karmanos Cancer Institute; Nag President-Elect, Brachytherapy Society

HARVEY PASS, former head of the Thoracic Oncology Section and senior investigator of the NCI Surgery Branch since 1986, has joined the Barbara Ann Karmanos Cancer Institute. Pass will serve as chief of thoracic oncology at both Karmanos and the Veteran's Administration Hospital in Detroit. He will lead the institute's Aerodigestive Malignancies program, and serve as a professor of surgery and oncology at Wayne State University School of Medicine. . . . **SUBIR NAG** was elected president-elect of the American Brachytherapy Society. Nag is professor and chief of brachytherapy at the Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Research Institute. . . . **HSIENG-JIEN KUNG** was named Isador Jacob Goodman-Ruth Goodman Blum Professor in Cancer Research at Case Western Reserve University School of Medicine. Kung is professor of molecular biology and associate director of the Center. . . . **TUCKER LE BIEN** was named deputy director of the University of Minnesota Cancer Center. Le Bien is currently associate director for basic science at the University. . . . **ARIEL SORIANO**, of the University of Colorado Cancer Center, will receive the Richard C. Devereaux Outstanding Young Investigator Award from the Cancer Research Foundation of America. Soriano will study secondary prevention of lung cancer through nutritional supplements and chemical agents.

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Message Of Report: Prevention Must Be Integral To NCI

(Continued from page 1)
across very loudly is the need for prevention to be strong by being integrated with all of the activities of research and not to be viewed as something that is set off."

Klausner said he will ask members of NCI advisory groups for written comments on the prevention group's report. A committee of NCI staff will respond to the recommendations, he said.

Edward Bresnick, chairman of the prevention review group, said the report urged NCI to conduct more strategic planning and provide greater leadership and visibility to cancer prevention research.

"The key message is: cancer prevention must be an integral component of NCI," said Bresnick, vice chancellor for research and professor of pharmacology and medicine at the University of Massachusetts Medical Center.

The prevention review group consisted of 19 non-federal scientists and physicians and one cancer patient advocate. Klausner formed the review group in April 1996 to study the prevention program.

How Much Is NCI Spending?

Reacting to the report, NCAB members praised the review group's work, but some said they were concerned that the NCI budget for cancer prevention may not be adequate to make all the recommended changes.

"It's going to be almost impossible with the existing budget to probe all of these areas adequately, and have a balanced program, and yet these areas are very important," NCAB member Ellen Sigal said.

"It was very difficult for us to get a figure as to how much cancer prevention was in NCI," Bresnick said. "I think whatever the level of support for cancer prevention is within NCI, it should be more readily accessible to an individual or group who needs to know that figure."

According to the report, part of the prevention budget, about $188 million in fiscal 1996, is found in the NCI Division of Cancer Prevention and Control. "The Review Group's best estimate for the total NCI cancer prevention FY 1996 budget is about $400 million. To this figure could be added various components of physical, chemical and biological carcinogenesis, nutrition, observational epidemiology, and cancer control programs, which would increase the budget to approximately $740 million," the report said.

Bresnick said the funding may be adequate. "We have to evaluate how that $800 million is being dealt with," Bresnick said. "The programs we are recommending do involve new initiatives, but they can be done in the context of an evaluation of the expenditures from the existing budget."

Klausner said not all research can be neatly categorized. "We need to move away from an obsession with trying to put a dollar on what we spend on everything," he said to the NCAB. "We've gotten to a point where we divide our studies by 12% breast, 14% ovarian in order to make sure that we don't get yelled at by an interest group.

"What is prevention?," Klausner asked. "Is it not understanding the nature of cancer? How are we going to prevent it if we don't discover the cause?

"We need to be careful that this obsession with coding doesn't become something that removes from us the ability to have an intellectually correct conversation about what we really want to do and what we are and aren't achieving," Klausner said.

NCI's best estimate of the proportion of spending on cancer prevention is 38 percent, compared to 35 percent for treatment research, Klausner said. The estimate for prevention includes research in cancer causation, genetic disposition, and cancer development, he said.

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"That leaves 27 percent for training, education, and unclassified basic cancer biology," Klausner said. "And that 27 percent is essential for both prevention and treatment.

"While it's very attractive to argue we spend enough or we don't spend enough, I don't think that answers our responsibility to the nation, and that is, are we doing well enough?" he said.

NCAB Chairman Barbara Rimer said the report should be viewed as "part of a process and not the ultimate statement on prevention." Rimer served on the review group.

"This report had to be critical, because if you are asking where we need to go for the future, you have to take a hard look at the past and the present," Rimer said. "It could open a new dialogue in prevention."

Greenwald: Budget Needs To Grow

Peter Greenwald, director of the NCI Division of Cancer Prevention and Control, said the Institute would need an increase in funding for prevention to implement the report's recommendations. "Our first priority is to keep the payline [for extramural grants] up, and we all agree that is a very important priority," Greenwald said to **The Cancer Letter**. "But when you do that a time when you don't have substantial budget increases, then it is hard to do some of the applied research that you need to do.

"You begin to wonder, do we have the growth rate to accommodate all the opportunities in prevention as well as other areas?" Greenwald said.

Greenwald said he agreed with the report's recommendation that NCI recruit more scientists to the prevention program. "I didn't take it as being a criticism of the current leadership, but a need for additional leadership," he said. "We are spread thin, but the people we have are excellent.

"In order to recruit more staff and get the sort of people they are talking about, you need more resources," he said.

The report recommended that NCI decrease its funding for "large-scale demonstration projects." The report specifically mentioned the American Stop Smoking Intervention Study as one of the projects that should be cut. Another large-scale project funded by NCI is the 5-A-Day for Better Health project to encourage Americans to eat five servings a day of fruits and vegetables.

Greenwald said NCI is working with its ASSIST partners, the American Cancer Society and the Centers for Disease Control and Prevention, on a transition plan for the project.

"I believe programs like ASSIST and 5-A-Day should be expanded, not contracted," Greenwald said to **The Cancer Letter**. "However, these types of programs can best be run as partnerships. NCI's main role should be sponsoring the vanguard research, sharing in national leadership and public education, and supporting the research, evaluation, and periodic refocusing necessary to keep these programs strong.

"Obviously, all agencies taking part need to have the necessary resources to do this effectively," Greenwald said.

Summary Of The Cancer Prevention Review

Excerpts from the Executive Summary of the report follow:

The NCI Cancer Prevention Program Review Group strongly believes that prevention must be a principal component of the National Cancer Program if the cancer burden is to be reduced. A century-long experience with public health measures has shown that the prevention of disease is ultimately far more effective in reducing morbidity and mortality than is the treatment of already diagnosed disease. As such, it is apparent to the Review Group that over the next generation far greater reductions in cancer mortality will come from prevention than from the various treatments that are currently available or will be available in the coming years. In spite of this, a much smaller proportion of the NCI budget is committed to prevention than to various forms of treatment. Prevention must be well-represented in the programs of NCI, both intramurally and extramurally, and must have an appropriate budget. Furthermore, prevention, like all other elements of the National Cancer Program, must be founded upon excellent science, which originates from both the intramural and extramural research communities. It is through the application of excellent basic, clinical, and population-based research that effective preventive interventions can be mounted.

Because of its prime importance to the central objectives of the National Cancer Program, it is imperative that NCI's prevention efforts have outstanding leadership that will develop a creative, discovery-based, and assertive prevention research program and will utilize the strengths of both the intramural and extramural communities. Senior administrators of the prevention division also must work effectively with the NCI leadership in formulating this program.

The major responsibility for the NCI cancer prevention program lies within the Division of Cancer Prevention and Control. Consequently, much of the activity of the Review Group centered on an analysis of this division's role in establishing the NCI cancer

prevention agenda, providing the necessary leadership, representing the research interests of cancer prevention, and serving as effective spokespersons for the intramural and extramural research communities.

After receiving oral and written testimony and conducting interviews with intramural and extramural scientists, the Review Group perceived: a) the need for a better delineated, scientifically sound, long-term strategy for directing cancer prevention research into the next century; b) a need for additional outstanding scientists in leadership roles within DCPC; and c) the need for all other NCI divisions to focus greater attention on research toward the prevention of human cancers.

The Review Group briefly considered the appropriateness of including cancer prevention *and* control within a single organizational unit, as currently exists within DCPC. Because of a lack of sufficient data and the existence of another NCI review group which has the responsibility for evaluating cancer control efforts, the separation of these research functions was not considered further. Nevertheless, the Review Group believes that either the inclusion of cancer prevention and control within a single unit or the separation of these research functions would be compatible with pursuing the goals of NCI.

In this report, the Review Group uses the phrase "prevention division" to describe an administrative unit that has the responsibility for directing and managing the NCI cancer prevention research agenda.

The Review Group considered the focus of cancer control to be on persons with clinically overt cancers, while that of cancer prevention to be directed at apparently healthy populations, including those at high risk and/or those with delectable precancerous lesions. Nevertheless, prevention, which develops basic scientific principles and control, which applies these principles, must be linked in some fashion to provide a continuum from bench to population.

Recommendations

Modifiable Risk Factors

•Increase the investment in developing effective interventions for prevention and cessation of tobacco use, particularly in populations where tobacco use has remained high, e.g., adolescents, women, and those with less education and income.

•Increase the proportion of the tobacco control investment in basic research (including behavioral research) and in the development of effective interventions, and decrease the investment in large-scale dissemination efforts, e.g., ASSIST.

•Identify respected senior scientists to assume major leadership roles within the prevention division for the development and coordination of the tobacco avoidance, diet/nutrition, and cancer prevention research agendas.

•Encourage methodologic research to clarify the most promising research designs and strategies for diet and cancer prevention research, and to streamline the conduct of dietary intervention trials.

•Encourage research to identify biomarkers of the consumption of key dietary components, particularly micro- and macronutrients and to develop objective markers of short- and long-term physical activity.

•Increase the investment in research aimed at understanding the biological mechanisms underlying putative associations between diet and cancer incidence, particularly concerning fruits and vegetables, fats, and total energy consumption, as well as determining the mechanisms whereby physical activity may reduce cancer risk.

•Develop an orderly process for the formulation and testing of dietary behavioral trials of hypothesized healthful eating patterns.

•Support intervention trials aimed at identifying behavioral strategies to enhance physical activity and to assess the impact of such enhancement on cancer risk factors.

•Emphasize basic and applied studies on the role of viruses and *Helicobacter pylori*, as factors or cofactors in the etiology of certain cancers, and initiate research on and development of appropriate vaccines.

Animal Models and Extrapolation to Human Cancer

•Continue to develop new *in vitro and in vivo* models for identifying and assessing the efficacy of chemopreventive agents that integrate present knowledge of genetic and molecular alterations involved in human carcinogenesis.

•Develop intermediate biomarkers for assessment of exposure and biological effects applicable in prevention studies and validate their use in parallel studies in animals and humans.

Genetic Predispositions to Cancers

•Expand identification of high-risk healthy populations based on genetic predispositions and the development of new molecular markers.

•Investigate diverse non-genetic factors influencing the expression of genetic predisposition and the response to interventions, including the contribution of environmental exposures (radiation, exogenous and endogenous chemicals, bacteria and viruses).

•Develop new molecular markers for the early detection of cancer.

•Develop and expand existing biorepositories and provide new access with appropriate consent to such materials for the testing of new molecular detection strategies.

•Develop and improve new high throughput technologies for implementation of promising molecular diagnostic approaches in clinical and population-based

trials.

•Perform comprehensive trials in targeted high-risk populations for validation and potential integration of novel prevention and detection strategies.

Chemoprevention Trials in Human Populations

•Ensure the conduct of randomized trials in human populations as the gold standard for scientifically demonstrating ways to reduce cancer incidence. Ensure the existence of a well-defined process of decision-making about target organ sites, appropriate populations, credible endpoints, and candidate chemoprevention agents for human trials. Large-scale studies should be preceded by extensive preclinical studies, epidemiological analyses, and toxicity assessment in humans.

•Design recruitment strategies to attract healthy people as participants in cancer prevention trials. High-risk but otherwise healthy people are identified as the following: individuals with predisposing genetic traits or a positive family history of cancer; persons engaging in high-risk behaviors; individuals with high exposures to occupational and environmental carcinogens and cancer-associated infections; and the elderly.

•Restructure the chemoprevention preclinical drug development effort.

a) Form an advisory committee as a subset of the NCI Board of Scientific Advisors, supplemented with other outstanding extramural basic scientists, clinical investigators, molecular epidemiologists, and staff of NCI and the Food and Drug Administration. Mandate the committee to define the drug discovery program, stimulate creative approaches in the development and use of new animal model systems, evaluate candidate chemopreventive agents for cellular and animal screening tests, assess the evidence of efficacy and safety from animal studies, and set guidelines for selecting agents for human trials.

b) Continue to upgrade the *in vivo* animal systems for screening of efficacy and safety of chemopreventive agents through the use of the RO I grant mechanisms in addition to the present contract mechanisms.

c) Continue to use the master agreement contract mechanism for routine preclinical toxicological testing and for routine screening for chemopreventive efficacy. However, there should be frequent, open, re-competition with clear opportunities for developers of new assay systems to also become master agreement contractors.

d) Develop and validate biomarkers and intermediate endpoints in concert with those being developed and assessed in humans.

•Restructure the NCI prevention division's program for Phase I, II, and III trials to reflect a stronger extramural component by establishing one multimodality cancer prevention trials group (patterned after the Oncology Therapy Trials Groups). This group will:

a) develop and solicit proposals for Phase II and III cancer prevention trials with one or multiple modalities, i.e., behavioral, dietary, pharmacological, immunological, and combinations thereof.

b) evaluate the scientific basis, recruitment strategies, statistical power, feasibility, and public health significance of competing proposals for trials.

c) make awards for Phase II trials, and work with NCI to obtain the necessary funding needed for Phase III trials

d) jointly sponsor trials, to prevent the appearance of new cancers and recurrences in patients, with established treatment trials groups to marshal the right combinations of experience and capability.

e) stimulate methodologic research on efficient, cost-effective prevention trials design.

f) provide to the scientific community administrative guidance regarding safety and efficacy monitoring boards, Food and Drug Administration Investigational New Drug applications, institutional review board policies, requirements for medical record and biological specimen retention, and how to achieve inter-institute collaboration on data collection for multiple endpoints.

•Form a special committee for biological studies which would stimulate and review proposals for ancillary biological studies on tissues and DNA of participants in prevention trials, and stimulate the use of the best available methods for validating intermediate endpoints to take better advantage of existing prevention trials. These functions could be incorporated into the recommended BSA subcommittee.

•Devise and implement a mechanism for collaboration between NCI and the other NIH institutes to incorporate non-cancer endpoints into cancer prevention trials and cancer endpoints into non-cancer trials initiated by other institutes.

Behavioral Research and Behavioral Intervention

•Incorporate behavioral research as an integrated but independent component of the NCI prevention program.

•Conduct behavioral research at multiple levels, ranging from laboratory-based behavioral research to small scale hypothesis testing research to larger studies with the power to assess efficacy.

•Pay special attention to the development of interventions that are ethnically and culturally appropriate.

•Include as priorities for behavioral research a focus on preventing tobacco use in children and teenagers, encouragement of cessation among heavy smokers and women, increasing use of recommended early detection tests, and improvement of the behavioral outcomes of genetic testing for cancer susceptibility.

•Include the following components within an outstanding behavioral research program in prevention: epidemiologic foundations, expertise in measurement and evaluation, national data on key behaviors, knowledge of theories of behavior, understanding of behavior change, expertise in cancer risk communication, strength in

intervention design, expertise in cost-effectiveness and mechanisms for dissemination.

•Conduct behavioral research initiatives through mechanisms which crosscut NCI as well as the National Institutes of Health, depending upon the focus of effort.

•Create training programs for behavioral scientists to function in the new scientific paradigms, including genetics, chemoprevention, diet/nutrition, addiction and other pertinent areas.

Training of Health Professionals

•Develop and support new mechanisms for already trained health professionals to Familiarize them with the field of cancer prevention and to provide them with opportunities to expand their skills to contribute to the science of prevention.

•Develop a data base of professional resources and deficiencies in the field of cancer prevention to assess current and future personnel needs, similar to that currently used to project needs for physician training.

•Form a working group to make recommendations for multidisciplinary training of prevention researchers in the new scientific paradigms and for evaluating the effectiveness of this training.

•Encourage the development of innovative training opportunities for prevention researchers to augment their training in areas such as genetics, pharmacologic intervention in prevention, epidemiology, and behavioral science.

Organization & Infrastructure of NCI Prevention Div.

•Ensure appropriate interactions among units that have the responsibilities for cancer prevention and control in order to facilitate translation of prevention principles into action.

•Establish a restructured cancer prevention division within NCI that has the responsibility and resources for formulating and implementing the cancer prevention agenda through the development and application of outstanding science. Enhance the senior management of the prevention division by recruitment of outstanding cancer prevention investigators who would assist in formulating and implementing a strategic plan, prioritize scientific goals, assess required resources, and facilitate interactions among the intramural and extramural research communities.

•Stimulate more effective interaction among intramural cancer prevention researchers, who are currently located in disperse laboratories and scattered across the prevention division.

•Expand the current NCI Board of Scientific Advisors to include additional prevention research investigators and form a subcommittee of BSA, supplemented by other extramural experts, as an advisory group specific to the prevention division.

•Perform an in-depth evaluation of the Community Clinical Oncology Program to ascertain its contribution to the prevention effort and consider its relocation to the Division of Cancer Treatment, Diagnosis, and Centers.

•Continue to re-evaluate and modify, if appropriate, the programs for preclinical drug development and form a subcommittee of the Board of Scientific Advisors, supplemented by extramural cancer prevention investigators, and staff of the prevention division and the Food and Drug Administration, to assist and monitor the decision process in the preclinical and prevention trials phases.

•Form an extramural multi modality prevention trials group, patterned after the Oncology Therapy Trials Groups, which would set guidelines, make funding recommendations, and monitor the progress of prevention trials.

•Develop a mechanism to rapidly respond to new research developments, and to evaluate and fund outstanding ancillary research spin-off studies in populations represented within an ongoing prevention trial.

•Develop databases of. a) clinical cancer prevention trials, their objectives, target population, methodologies, successes, and failures; and b) the availability of blood and tissue products from clinical trials which could be accessed by all prevention researchers through a peer-reviewed mechanism.

•Strengthen collaborative relationships with other groups also involved in cancer prevention, such as the Centers for Disease Control and Prevention, the American Association for Cancer Research, the American Society of Clinical Oncology, and the American Cancer Society.

•Work more closely with the Food and Drug Administration on matters that affect cancer prevention, e.g., utilization of fully validated intermediate biomarkers in prevention trials.

Review Group Membership

Besides Bresnick, members of the Cancer Prevention Program Review Group were: David Alberts, Arizona Cancer Center; Clara Bloomfield, Roswell Park Cancer Institute; Zora Brown, Cancer Awareness Program Services; Pelayo Correa, Louisiana State University Medical Center; Mary Daly, Fox Chase Cancer Center; Eric Fearon, University of Michigan; Suzanne Fletcher, Harvard Medical School; Marc Garnick, Pharmaceutical Peptides Inc.; Max Gottesman, Columbia University; Barbara Hulka, University of North Carolina; Robert Mayer, Dana-Farber Cancer Institute; Gilbert Omenn, University of Washington; Ross Prentice, Fred Hutchinson Cancer Research Center; Barbara Rimer, Duke University Medical Center; David Sidransky, Johns Hopkins University; Jane Weeks, Harvard Medical School; Robert Weinberg, Massachusetts Institute of Technology; Alice Wittemore, Stanford University Medical Center; and Gerald Wogan, Massachusetts Institute of Technology.

In Congress

Broccoli v. Basic Science: Bailar, Klausner Disagree

Testifying on Capitol Hill last week, biostatistician John Bailar said the publicity generated by his recent paper in the New England Journal of Medicine went far beyond his comfort level.

As Sen. Arlen Specter (R-PA) held up a copy of a USA Today cover story about Bailar's paper, Bailar said he did not agree with the newspaper headline summation of his message: "$30 Billion War On Cancer A Bust?"

"I did not write that headline," Bailar said at a June 19 of the Senate Labor, HHS & Education Appropriations Subcommittee. "There are some things we need to be concerned about, but that is a statement that I think is inappropriate."

Still, at the hearing, Bailar reiterated his principal recommendation: NCI should emphasize prevention programs at the expense of basic science and treatment.

The Institute should devote two-thirds of its resources to prevention, Bailar said. According to NCI officials, 38 percent of the Institute's budget goes to prevention programs.

While Bailar's paper in the New England Journal of Medicine was a national story, the hearing was not (**The Cancer Letter**, June 6).

There were no television crews, no overzealous headlines. In fact, about half of the reporters slipped out after Specter completed Item 1 on the agenda: the Health Care Financing Administration's plan for revising the Medicare relative value scale for physicians.

After the HCFA item was done and Bailar and NCI Director Richard Klausner sat down at the witness table, subcommittee chairman Specter and ranking member Tom Harkin (D-IA) showed no signs of having become true believers in the virtues of prevention and the futility of treatment and basic science.

Quite the opposite, Harkin appeared to be having good, clean, Socratic fun, drawing out Bailar on the subject of what the biostatistician means when he says "prevention."

Bailar: No Need to Know the Cause

An edited transcript of the exchange between Harkin and Bailar follows:

HARKIN: What causes cancer?

BAILAR: That's an extremely complicated, technical question, as you recognize. On the other hand, I'm not sure that we have to understand the causes in order to prevent cancer. [We can] identify carcinogens and remove them from the environment. By strengthening body defenses, with the chemopreventive agents [we] can act without any real understanding of the individual causes of cancer. We don't have to deal with cancer as a collection of 100, 200, 300, 400 diseases if we can work effectively along those avenues of attack.

HARKIN: If we don't know the cause, how are we going to get into prevention? If we didn't know the cause of small pox, if we didn't know the cause of polio, we couldn't prevent it.

BAILAR: We were preventing small pox before we knew the cause. A century or more before we knew about the small pox virus, vaccination was being perfected. Acute clinical observation showed that persons who had been infected with a related disease called cow pox, didn't get small pox.

HARKIN: What about polio?

BAILAR: Polio, we didn't know about the virus at the time the vaccine was developed.

HARKIN: Can you show me, or can you give me any idea of any study that has been done to show, if you do A, B, and C, you are not going to get cancer? I know no valid scientific study that shows it. I don't know how you would ever settle up.

BAILAR: Our understanding about the relation between cigarette smoking and lung cancer is an example of that. It was clear that there was a cause-and-effect relation before the surgeon general's report in 1964. Nobody knew what the cause was; there was educated guessing that it was tar or nicotine, or possibly just the heat in tobacco smoke. We didn't know what was going on, on a molecular, cellular level. What we knew was, if you got people to stop smoking, the rate of lung cancer would in time start going down. And that has happened.

HARKIN: We know that smoking does cause lung cancer. But cancer affects people who never drink, never smoke, eat the best kinds of foods. I don't know of any cohort of individuals that were immune from cancer.

BAILAR: I agree with you. I am not sure to what extent this is a result of random chance. You might have a group of persons for whom the risk of cancer is increased, perhaps quite a lot but still not 100 percent, so some will get the disease and some

won't. There may also be some substantial element in individual variation efforts that we do not know about and might be able to exploit if we did know. There has been research to try to identify reasons why some people are high risk and others who aren't. I don't think it has been applied across the board the way that it might, but there's certainly some kinds of cancer where we know a good bit about risk of individuals.

HARKIN: I tend to agree a certain amount that diet does have something to do with it.

BAILAR: There have been a number of studies of populations that have migrated from one area to another, and what is generally found is that within 15 to 25 years, those who migrate begin to observe cancer risks of the place they went to. They've been compared with siblings and others who stayed back in the country of origin, and if they took off that long before, there are major changes in cancer risk. I think that's abundant evidence that there is something in our environment that is determining most of our cancer risk. We don't know what it is in most cases.

HARKIN: I'm all for prevention, but it seems that we still have to know what we are going to prevent. You can take shots in the dark, that's fine. We can all change our lifestyles, change our diets, and hope for the best; it will help us live better, it will help us feel better, our lives would be healthier, our hearts would be better, and we would probably live longer and have a better life. But I'm not so certain that that alone is where we ought to focus as much attention as I think you're wanting.

BAILAR: We already have many indications that a class of vegetables, that includes cauliflower, broccoli, Brussels sprouts, and so forth, is in some way, somewhat protective. That may be information that may need to be more thoroughly checked. I don't regard it as absolutely established. But if we learn that there is that kind of correlation, there is something that we could recommend right now in a much more vigorous way than we can. Without understanding the mechanisms…

Klausner: We Need To Know How Cancer Works

After drawing out Bailar's views, Harkin asked NCI Director Klausner to respond:

"Well, you heard it, Dr. Bailar thinks that the [search for the] cause of cancer only means molecular cause, or subatomic cause," Klausner said. "What [we] look for [are] mechanisms at the level of cause that tells us how to intervene effectively.

"The reality is, the more we know about the components of tobacco, the better we are at prevention.

"Knowing that nicotine is in tobacco's delivery system, and that it's addictive is extremely important in effective prevention.

"We've known that tobacco is a cause of cancer for quite some time. First case control study was in1939, published in Germany. What you have to do to effect that prevention is very difficult, and the more we understand about who is at risk and why, including aspects of the mechanism, gives us more and more powerful tools of intervening. Whether it's intervening with addiction or intervening behaviorally. This takes research.

"If we try to turn this discussion into this type of black-and-white: you either just 'prevent,' sort of magically, whether you know or don't know [the cause]. Scientists work [by] establishing definitively connections that will allow you to predictably act, whether that means you totally understand the mechanism, or you vaguely understand the mechanism, or you understand enough that your intervention is predictable in terms of the outcome.

"Dr. Bailar mentioned chemoprevention, as though we would just throw chemicals at people, without knowing why and how they work. Now, there are chemicals, that we give because of observational studies, such as aspirin to prevent colon cancer. That's a great example where studying a molecular mechanism gives us what appears to be the precise molecular target of aspirin in that pathway.

"Now that allows us to say, aspirin does it, since that's not a specific inhibitor, only an inhibitor of that enzyme. If that is the enzyme that gave that observational effect, knowing that connection allows us now to design, in tests which we're now doing, chemopreventive agents to prevent colon cancer that may well be 1, 2 or 5 sets better than the information that we get out of the observational studies.

"It's just another example that what we want to do, we want to do well, and we want to make sure that we optimize it.

"It's not black-and-white, we need to know how everything works, but all of our history tells us, the better we know how it works, the better we can intervene with fewer side effects, and directed at the people who most need it. That's really what we're talking about.

"We need to know things to the point where we can successfully intervene."