

■ FROM THE DIRECTOR

Cancer Prevention Think Tank: Fulfilling the Potential for Disease Control

The broadest measure of cancer prevention research is finding ways to reduce the incidence, progression, recurrence, and metastasis of the disease. This comprehensive, global “reach” of prevention was examined at the first Cancer Prevention Think Tank on December 8, 2006, at NCI-Frederick. Hosted by CCR and organized by Nancy Colburn, PhD, Chief of the Laboratory of Cancer Prevention (LCP), the forum engaged scientists and clinicians from CCR, NCI’s Division of Cancer Prevention (DCP), Baylor College of Medicine, and Brigham and Women’s Hospital for a day-long exchange of information, insights, and strategies.



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The objective of the Cancer Prevention Think Tank was to identify the most promising, novel molecular targets and interventions to reduce the burden of cancer at every juncture for the general population, high-risk groups, and patients. The meeting was also an opportunity to strengthen collaboration and foster communication among members of the LCP, the Molecular Targets Development Program (MTDP), the Mouse Models of Mammary Cancer Collective (MMMCC), the Animal Models Initiative (AMI), the Inflammation and Cancer Initiative (ICI), and the DCP.

In my opening remarks, I highlighted cancer prevention as one of CCR’s core competencies in delivering meaningful advances that benefit at-risk populations and patients. Our efforts to discover molecular targets and pioneer novel interventions effectively combine and leverage expertise from diverse fields to speed progress from elucidation to translation to treatment. The Cancer Prevention Think Tank is an acknowledgement of how important an integrated, multidisciplinary approach is for accelerating our progress toward reducing cancer incidence and mortality.

The day began with Powel Brown, MD, PhD, from the Breast Center at Baylor College of Medicine, discussing novel molecular targets for the prevention of breast cancer. Based on his clinical perspective of breast cancer prevention, risk management, and genetics, combined with his research in cancer preventive agents, Dr. Brown stressed the need for combination therapies and effective agents for preventing estrogen receptor (ER)–negative

breast cancer. He focused on receptor-selective retinoids, particularly retinoid bexarotene, for inhibiting growth in breast cancer and premalignant cells; receptor tyrosine kinase inhibitors (TKI); and activator protein-1 (AP-1) transcription factor inhibitors. Dr. Brown's discussion of validated and potential targets concluded with stem cell inhibitors as an exciting prospect for breast cancer prevention research.

Think Tank participants then shared findings on molecular targets for cancer prevention, including targeting translation initiation to prevent tumorigenesis and invasion, the therapeutic potential of programmed cell death (Pcd) 4 designer drugs, ER zinc finger interventions for the treatment of breast cancer, the role of Lsh and genomic demethylation in tumor progression, and selenoproteins as anticarcinogenic agents. The roundtable discussion that followed focused on targeting the microenvironment for tumor suppression. Angiogenesis, macrophages, and basophils were cited as high-impact targets, in addition to stromal epithelial interactions, epithelial-mesenchymal transition, and myofibroblasts. The consensus was that infection, cytokines, signaling molecules, and transcription factors are critical avenues for studying microenvironment targets. The participants also tackled prospects for targeting cancer stem cells without harming normal stem cells, with Dr. Brown noting the importance of identifying differences between a normal stem cell and a quiescent stem cell undergoing transformation. Insights were also shared about humanizing mice for enhancing physiological responses to drugs.

The afternoon guest speaker was Monica Bertagnolli, MD, a surgeon from Brigham and Women's Hospital, whose clinical practice is integrated with her research to identify markers of colon carcinogenesis and to exploit those targets for tumor prevention and treatment. Dr. Bertagnolli discussed selective cyclooxygenase-2 (COX-2) inhibition for prevention of colorectal adenomas from her standpoint as principal investigator of an NCI-sponsored multi-institutional clinical trial testing this drug. She then described 15-hydroxyprostaglandin dehydrogenase (PGDH) as a new target for chemoprevention and elaborated on prospects for targeting the Indian Hedgehog (*IHH*) gene and prostaglandin E2 (PGE2) for cancer prevention.

The second half of the Think Tank workshop featured presentations on dietary interventions for the prevention of colorectal and other cancers, as well as the inhibition of basic leucine zipper (bZIP) protein transcription factors. Critical points for intervention were identified, including detection of micrometastases and tumor cell dormancy prior to a proliferative phase. During the roundtable discussion, Dr. Bertagnolli stressed the need for "on/off" mechanisms to avert toxicity and drug resistance when a major pathway is chronically suppressed. The participants agreed on the need for more tissue-based studies in people at high risk, with the results subsequently correlated with animal studies. The exchange culminated in a suggestion that CCR basic and clinical researchers team up to study organ-specific cancers, which would complement ongoing investigations focused on transcription factors and signal transduction, for example.

The 2006 Cancer Prevention Think Tank highlighted the value of CCR's efforts toward cancer prevention. The event brought together molecular biologists, mouse geneticists,

developmental biologists, epidemiologists, clinical oncologists, and others to prioritize opportunities that have emerged from recent discoveries of molecular events in carcinogenesis, and to guide efforts for exploring new ones. Through initiatives such as the Think Tank, CCR's research strengths are being leveraged and optimized so that, ultimately, no segment of the population will have unmet needs related to cancer.

For more information on CCR's cancer prevention research, visit LCP's Web page at <http://ccr.cancer.gov/labs/lab.asp?labid=169>. Plans are under way to develop an interactive Web site to further stimulate ongoing communication and interaction between Cancer Prevention Think Tank researchers and current and future collaborators.

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