

Highlighting the Science of Cancer Prevention

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As incoming President of the American Association for Cancer Research (AACR), I am delighted that the AACR publishes the journal *Cancer Prevention Research* and that this journal is meeting with great success, because I believe the AACR should continue to increase its efforts in the arena of cancer prevention. The past few decades in particular have seen breathtaking advances in the understanding of the biological underpinnings of cancer: how it begins, progresses, and ultimately can kill. Although huge effort has rightly gone into understanding and treating the later stages of cancer, producing advances that often turn cancer from a death sentence into a manageable chronic disease, still, too often such therapeutic approaches ultimately can do little to help the patient. Simply put, once the cancer horse is out of the stable, treatment comes too late.

What does the term “cancer prevention” encompass? In the popular press, cancer prevention often means something as simple as cessation of smoking or adoption of dietary habits. But cancer prevention does and should mean much more. We owe our understanding of the mechanisms of cancer, and therefore of cancer therapeutics and of how to treat clinically apparent cancers, to cancer research. Such research has also had the effect of changing the picture for cancer prevention: now a real potential exists for extending hard-won scientific knowledge of cancer more broadly into cancer prevention itself, forestalling the great human and other costs of treating cancer at its late stages.

This perhaps requires redefining cancer prevention. A definition from the view 40,000 feet up is that cancer prevention is simply earlier and earlier treatment, blocking the risk and progression of cancers by beginning at stages very much earlier than traditionally done. Cancerous cells and cells at a high risk for progression into cancer are generated and progress much earlier than the stage at which cancer is usually treated: at the onset of the clinically manifest tumor. Therefore, cancer prevention can be divided into primary, secondary, and tertiary prevention. Primary prevention involves avoiding exposure to carcinogenic agents or behaviors and frequently is applied to broad populations. Secondary prevention targets existing, more specific risks in more closely defined higher-risk populations. Tertiary prevention primarily aims to prevent or control the symptoms and morbidity of established cancer, or the morbidity

caused by cancer therapy. Although tertiary approaches do not involve preventing (or treating) cancer at the outset, it is important to note that prevention of recurrence of a preexisting cancer or of a subsequent, different cancer following definitive treatment of early-stage cancer patients also can be included in the definition of tertiary cancer prevention. All these modes of prevention are on a gradient of increasing risks and are directed at successive stages of advancement to cancer, which can take many years.

Because so much is now understood about the cellular, molecular, and contextual changes of these stages, they are ripe for attack by cancer researchers who would not traditionally define themselves as cancer prevention researchers. For example, the explosion of studies in genetically engineered mice may be as (or more) relevant to prevention study of early carcinogenesis and targeted drug development as it is to therapy, where it originated. Recent such studies have shown that inhibitors of mammalian target of rapamycin, nuclear factor- κ B signaling, and vascular endothelial growth factor receptors have strong activity in genetically engineered *K-ras* mouse models of lung carcinogenesis at the level of premalignant stages; this work reflects the importance of targeting angiogenesis and other microenvironmental or stromal interactions with neoplasia not only for cancer therapy but for prevention as well. Another study found that intravesical delivery of a mammalian target of rapamycin inhibitor strongly suppressed bladder tumorigenesis in a novel mouse model involving targeted deletion of the phosphatase and tensin homolog gene and *p53*. Also, the science of endogenous tumor-antigen vaccines began in advanced cancer therapy, where the vaccines did not work, and has begun to shift to cancer prevention, where the vaccines are showing promise in genetically engineered mice (e.g., MUC1 vaccination for treating inflammatory bowel disease and preventing colon cancer), and to clinical trials in early, low-volume disease.

In sum, we as cancer researchers have an unprecedented opportunity before us. The breadth and excitement of current opportunities in the science of cancer prevention have never been greater. By putting stress on the importance of solid science and improving communications among the various prevention science disciplines, we can hasten the ability of cancer prevention to achieve new clinical impact by reducing cancer risks associated with important factors such as molecular signaling pathway alterations, obesity, smoking, stress (and even, dare I say, telomeres and telomerase).

Disclosure of Potential Conflicts of Interest

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