‘‘Cancer poses enormous personal, clinical, and societal challenges, but it is exciting to consider prospects for historic progress in treatment this decade based on developments emerging in many areas of the field. Here, I offer a personal perspective on core problems, emerging developments, and responses which investigators and their advocates may benefit from considering. This is the first of a series of editorials which will delve into the issues introduced below.’’

Two fundamental concerns that impact cancer as a personal and clinical challenge are the core problems of selection for therapeutic resistance and the degree to which microenvironmental and peripheral systems of the organism are modifiers versus roots in clinical disease. Disorders in microenvironment and peripheral systems that control cancer might increasingly be viewed as primary rather than secondary factors in the root nature of cancer as a clinical disease. These two concepts are inherently intertwined. Cancer is still viewed primarily as a problem of cancer cells, but a competing concept that is strengthening views cancer as a breakdown in tissue and system homeostasis that permits cancer cells to divide and invade. This is a crucial and radical distinction from prevailing thought, since it implies that cancer may be a symptom of an underlying clinical disorder, rather than the root problem itself that needs to be addressed. In this competing concept of cancer, immune and inflammatory phenomena are critical, harking back to early pathologic descriptions of cancer but also representing some of the most exciting areas of research in the field today. Tumor immunology is among the oldest parts of the field, periodically neglected by the mainstream of the field, but now quickly reassuming vigor.

Perhaps the most compelling challenges to mainstream thought are, experiments in transgenic immunocompetent animals suggest that the efficacy of cytotoxic therapies can no longer be incontrovertibly viewed simply as a function of cancer cell kill.

These ideas also impact the core clinical problem of selection for therapeutic resistance. With increasing sophistication in analytic methods to probe the genetic, epigenetic, and cellular diversity in tumors, the complexity being revealed is ever more astonishing, raising concerns about the breadth of success of approaches that only directly target cancer cells. The molecular face of tumor plasticity is very ugly and it enhances the specter of therapeutic resistance as the core challenge in clinical cancer treatment. Effective treatment of cancer may not necessarily entail understanding or addressing this complexity, but mastering the use of tissue or systemic systems that have the inherent ability to do so. However, if the competing view of cancer as a breakdown in tissue and systemic management systems is to be useful, it will need to establish how broadly effective targeting or restoring these systems might be. Combined immunochemotherapeutic approaches stimulated by
provocative preclinical studies that are now getting underway in clinic may offer an initial take on the standing of this direction.

Several major concerns impact cancer as a societal problem. The growth of ‘patient power’ will become an ever-greater factor in how cancer is addressed by oncologists and researchers should be aware of these trends to anticipate where needs and opportunities are arising. Unfortunately, in the United States, the National Cancer Institute (NCI) is responding weakly, if at all so far, to many emerging societal trends that will affect how cancer researchers must be positioned for the future. Great changes this decade are coming from the societal and political force of cancer survivors and advocates, many of whom increasingly view what has been restricted from them to date as a right. Controls on information from individual genetic testing, the availability of experimental drugs only in large formal trials, and government regulatory stances on the efficacy versus safety of new agents are just some of the areas in which the norms representing traditional boundary conditions on research activity appear to be breaking down. In the United States, the ACLU (American Civil Liberties Union) and other impactful political advocacy organizations concerned with individual freedoms are becoming involved, and these trends will continue, with both benefits and detriments to independent research. The internet has radically shifted knowledge-based power and influence toward patients and smaller institutions, weakening influential structures dominated traditionally in research by federal groups and clinical and academic guilds. Survivorship issues virtually untouched by laboratory researchers will come more to the fore. These trends point to a growth in entrepreneurialism, which will flower again with the eventual release of pent-up cash as markets recover slowly.

With regard to therapeutic discovery, coming trends may prompt the NCI to correct their failures to sufficiently explore repositioning opportunities in cancer for the thousands of existing approved drugs, generics, and late-stage development agents, and to prioritize supporting existing organizations who are engaged in promoting open-source drug discovery with pharmaceutical industry collaborators. The drug industry seems likely to continue to reduce effort in preclinical discovery this decade, increasing the incentive to employ for mutual benefit their huge collections of true medicinal compounds that are not only underutilized but also grossly undermonetized. Future editorials will delve more deeply into these emerging trends impacting the personal, clinical, and societal problems posed by cancer which will affect how cancer researchers need to orient and develop their work.

Disclosure of Potential Conflicts of Interests

The author is leading a company that seeks to serve as an agent to provide pharmacologic compound libraries to nonprofit screening laboratories.

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Perspectives on Emerging Trends in Cancer Research

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