Preface:

This book examines the root causes of three decades of disappointing progress in cancer treatment despite vast resources allocated towards its conquest since 1971 and the extraordinary advances in molecular genetics of the last 20 years. In so doing, this book identifies broad-based and far-reaching changes necessary to refocus clinical cancer research and redirect cancer management. The genesis of this book is the author's 30-year career as a researcher and clinician that witnessed the widening disconnect between momentous advances in cancer research and the stagnation of cancer care delivery. Scientists and clinicians of my generation began their career at an auspicious time. Advances in histopathologic classifications [1], new procedures to diagnose and stage cancer [2-4], and the advent of powerful radiotherapy-delivery systems and of new cancer drugs and administration schemes marked the dawn of an era when the conquest of cancer seemed an attainable goal. Growing interest in cancer led to the recognition of Medical, Surgical, and Radiation Oncology as distinct specialty fields. It also fostered the emergence of multi-institutional cancer study groups dedicated to optimizing cancer management through the objective assessment of outcomes of patients treated under strict protocol guidelines. Perhaps the most successful example of the benefits of these developments is the near conquest of Hodgkin's disease, spearheaded by Kaplan [5] and DeVita [6], a century and a half after its description by Thomas Hodgkin [7].

However, this momentous event was to remain nearly isolated. Indeed, little additional progress has been made towards the cure of most invasive cancers. In fact, in the last 20 years, only testicular cancer [8] has been added to the short list of malignancies routinely curable using chemotherapy. Analysis of cancer incidence and death rates in the United States since 1930 reveals two opposing trends. Ominously, there was a sharp and continuous rise in lung cancer incidence and mortality in men that peaked in 1991-1992, followed by a comparable and ongoing rise in women's that trails men's by 30 years, paralleling the smoking habits of both sexes. Alternatively, over the same period there has been a significant and progressive decline in death rates for stomach cancer in both sexes, and for uterine and colon-rectal cancers in women, and more recently lung cancer in men. However, these declines are largely attributable to prevention and early-stage detection, to food refrigeration, to better infection control and greater access to transfusion therapy, to enhanced nursing, social, and rehabilitation services, and to better \general medical support measures, rather than to advances in therapy. This is because the vast human and financial resources, unleashed by the National Cancer Act of 1971, were undermined by flawed hypotheses regarding the nature of cancer and by reliance on trial and error or serendipity as the main forces driving anti-cancer drug development. As a result, disease eradication is currently achievable in only 11 of over 200 human malignancies and meaningful survival prolongation is possible for another few [9,10]. These are meager achievements considering that the first remissions in acute leukemia was reported in 1948 [11], and the first cure of a disseminated solid tumor (choriocarcinoma) was achieved five years later.
Based on these sobering facts and on the principle of proportionality, it might be assumed that only patients with responsive cancers would be exposed to today's largely Inefficacious but toxic anti-cancer drugs. However, such an assumption would be erroneous for, unless contraindicated, most patients with disseminated or metastatic cancer undergo chemotherapy, often through the end of life. In the interim, the enormous progress in understanding cancer biology, genetics, and growth regulation made over the last 20 years has only recently began to find clinical applications. To

quote the President's Cancer Panel 1999 report, albeit in a different context, "*if we do not bridge the persistent disconnect between the research and delivery enterprises, our progress against suffering and mortality from cancer will continue to be slow, uneven, and incremental*" [12].

It is hoped that an analysis of the numerous and complex issues responsible for the stagnation in cancer therapies of the last 30 years will foster a critical awareness of the forces that drive and perpetuate the *War on Cancer* policies and patient care practices. In particular, it should lead to the recognition that cancer is not an undesirable growth that must be exterminated at all cost but a disease best controlled by prevention, early detection, and when these fail, by genetic manipulation. Implementation of this three-prong cancer control policy requires the enlightened cooperation and participation of health-care professionals, policymakers, and of the public at large. Halting and reversing rising cancer incidence and mortality rates, a goal not achievable under the current cancer cell-kill paradigm, and the 1,500 Americans who die of cancer each day, provide ample justification for implementing the evidenced-based three-prong cancer control approach proposed in this book.