
SIGNAL TRANSDUCTION IN CANCER

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PREFACE

Cancer is the second leading cause of death in developed societies, and epidemiologists predict that in a few years cancer will surpass cardiovascular disease to become the leading cause of mortality. After years of growth, the rate of death from many forms of cancer seems to be leveling off. However, most human cancers remain essentially incurable once they have spread, and relatively little progress has been made in this area since the dawn of the chemotherapy era over 50 years ago.

In contrast to the slow progress in treating cancer, our understanding of the physiology of normal and neoplastic cells has increased phenomenally in recent years. This has raised the hope that we can have a clearer understanding of the molecular abnormalities which distinguish a cancer cell from its normal counterpart, resulting in the development of targeted molecular approaches which will kill tumor cells while leaving normal cells unscathed. In the end, it is this issue of “therapeutic index” that makes treating cancer so difficult with current cytotoxic agents.

In designing such sophisticated treatments for cancer, it is necessary to consider the processes which govern normal cellular physiology. After the first few cell divisions in embryogenesis, the biological program of a cell is directed by extracellular cues, such as soluble molecules (e.g., cytokines or hormones), cell-cell interactions, and cell-matrix interactions. The information triggered by these stimuli must be conveyed into the cell, to both nuclear and cytoplasmic targets, to direct the cellular response. The transmission of this information, or signal transduction, is critical to the appropriate response of a normal cell. However, these signaling pathways can often be subverted in malignancy. One of the consequences of the mutations which characterize cancer is the activation of signaling cascades leading to survival, proliferation, or pluripotency (blocked differentiation) of a cell which is inappropriate for its physiological circumstances.

If nothing else, the recent advances in understanding how signaling pathways control normal cellular function, and how these pathways become deranged in cancer, would make this a perfect time to review signal transduction in this context. However, in addition, we are now at the dawn of a new age in the treatment of cancer based on molecular strategies. New therapeutic approaches are targeting growth factor receptors which are over-expressed, oncogenic tyrosine kinases resulting from chromosomal translocations, or pro-survival proteins whose expression is being driven inappropriately. It seems clear that the next major advances in the therapy of cancer will arise from strategies targeting the molecular abnormalities of the tumor cells and its environs.

Thus, the goal of this volume is to explore signal transduction pathways of particular importance to human cancer. While it is impossible to be fully comprehensive in a fast-moving field which encompasses most aspects of cellular physiology, the 14 contributions in this volume were chosen to reflect major areas of signaling research. Although one cannot draw rigid boundaries as to where signaling pathways reside, the volume has been divided into four sections reflecting physiological groupings. These focus on receptors at the cell surface, intracellular signaling cascades, transcription factors functioning in the nucleus, and pathways triggering programs of cell death. These chapters provide a panoramic view of signaling pathways which control critical cellular events, and which are commonly subverted in human cancers.

Without question, the contributions in this volume reflect the state of the art of one of the most exciting areas of cell biology, biochemistry, and molecular genetics. However, "signal transduction" is no longer a topic restricted to sophisticated scientific discussions. It is on the minds of practicing oncologists around the world as a leading hope for the future of cancer therapy. As such, these 14 chapters also represent a blueprint for strategies which can be translated into the clinical arena with relatively brief development times. In this exciting era in which scientific advances and medical practice are rapidly converging, the goal of this volume is to inform and inspire scientists and physicians alike.

David A. Frank, M.D., Ph.D.
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