# CANCER 4

A COMPREHENSIVE TREATISE

## BIOLOGY OF TUMORS: Surfaces, Immunology, and Comparative Pathology

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# Preface

As was shown in the first two volumes of this series, great strides have been made in identifying many of the agents or classes of substances responsible for carcinogenesis and in delineating their interactions with the cell. Clearly, the aim of such studies is that, once identified, these agents can be eliminated from the environment. Yet, despite these advances and the elimination of some important carcinogenic agents, one major problem exists. It is a constant monitor of all oncologic study and diminishes the importance of every experiment and of every clinical observation. *As we noted earlier, that problem is our inability to define the malignant cell.* It is through studies of the fundamental biology of tumors that we seek this definition.

A vast amount of information has been gathered which describes *what* this cell does and—to a lesser extent—*how* it does it. But the *why* evades us. We have been unable to define the malignant cell, save in broad terms by comparing it to its normal counterpart. The major problem appears to be that the malignant cell does so much. It is a chimera, mystifyingly composed of normal activities and structures, of phenotypic schizophrenia with embryonic, fetal, and adult characteristics and, occasionally, a hint of an unclassifiable capacity unique to malignant cells.

The clues as to the *why* of cancer function must be derived directly or by induction from the *what* and *how*. Malignant cells replicate when replication is not required. Whether by escaping the normal inhibitory controls of the host, or by suprasensitivity to stimulation, or by some defect other than these, the tumor grows. The growth is noncompensatory and nonfunctional. The malignant cell also lives beyond its normal span. Together, growth and increased life span result in disruptive cellular accumulation. And what is more, malignant cells compete rather than participate with their normal neighbors and then competitively invade and destroy. The malignant cell itself evades destruction by humoral, immunological, and cellular defense mechanisms. It is therefore characterized by autonomous behavior, living off the host rather than with it. Are these abnormal activities the result of a single alteration or many? One integrated pattern or many? And what genetic or epigenetic or genetic–epigenetic alteration is responsible for this successful, this deadly capacity? An examination of the biology of

tumors presented in Volumes 3 and 4 serves many purposes. It may enable us to better understand normal cell biology. It may suggest crucial cellular alterations induced by carcinogenic agents. And, by understanding its aberrations of control and the advantages thus gained by the malignant cell, we may be better able to find a means of reversing them and halting their destructive processes.

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# Spread of Tumors

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# Surfaces of Normal and Transformed Cells

JAMES C. ROBBINS and GARTH L. NICOLSON

## 1. Introduction

Considerable data implicate events at the cell surface as having a primary role in the growth, development, and communication of normal animal cells and in the multiplication of cancer cells. For example, surface changes are of particular relevance in determining whether neoplastic cells provoke a host immune response and whether they survive or succumb to that response. Surface characteristics are also at least partially involved in the ability of cancer cells both to establish a primary growth site and to metastasize to secondary sites. A variety of additional factors are involved in each case, but progress in distinguishing neoplastic from normal cell surfaces will surely help to understand and to combat the development and growth of neoplastic cells.

Little detailed biochemical knowledge of animal cell surface structure and behavior has been available until recently. In the last few years, several new techniques and approaches—for example, freeze-fracture electron microscopy, lectin biochemistry, convalent labeling of cell surface molecules, and electron spin resonance spectroscopy—have produced vast quantities of data on normal and neoplastic cell surfaces. The data are still somewhat fragmentary, and in some areas contradictory, but a coherent picture of the cell surface is gradually emerging.

Actual tumors arise from unknown precursor cells, so most basic studies have relied on model systems such as tumor virus transformation of "normal" cells

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