ONCOLOGY

Arkadiusz Z. Dudek and Steven F. Powell
Division of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis, Minnesota

1 INTRODUCTION

Cancer is a devastating disease that is often fatal. Even with therapy, many patients will die. According to the World Health Organization (WHO), cancer was responsible for 7.8 million (13%) of 58 million deaths worldwide [1]. Due to this, it is no surprise that anticancer drug research is one of the most funded and vigorously pursued fields of research in the world today. Cancer remains a leading cause of morbidity and mortality throughout the world. In the United States, the pharmaceutical industry has exploded with the production of many new therapeutic agents. Anticancer drugs make up a great deal of these agents.

The quest for anticancer agents is fraught with difficulty. Anticancer drugs have typically been limited due to the severity and frequency of adverse effects seen in patients. *Chemotherapy*, as anticancer drugs are commonly termed, is often feared by patients. As research has progressed, we have been able to find more agents that are active against a variety of cancers. With improvement in our understanding of cancer, these agents have been designed to be less toxic to patients. Despite this, toxicity remains a major concern with anticancer agents.

The toxicity of anticancer agents can be attributed to the subtle differences in cancerous cells when compared to normal healthy cells. A cancerous or malignant cell is essentially a cell that has gone out of control. These cells grow, divide, and spread relentlessly. Their life spans are often infinite. In addition to this, they have the ability to invade other tissues and cause organ damage. Cancerous cells do not typically provide any beneficial biologic function and will replace normal healthy tissue. They aggregate as abnormal tissue, often called tumors. The spread of these tumors result in severe morbidity and mortality. The mechanisms behind the malignant cells erroneous processes often protect them from normal host defenses and chemotherapy. Anticancer agents are imperfect and cannot recognize all the subtle differences seen in malignant cells. They often can only target rapidly dividing cells. The result is damage to normal, healthy cells that reproduce more often. These are often the cells of the gastrointestinal tract, the bone marrow, and the sex organs. Additionally, some of these agents can have drastic effects on other normal healthy tissues, including the cardiovascular and neurological systems. Damaging these organ systems with drugs can cause further medical problems in already ill patients.

In addition to their ability to "hide" from the host's immune system, malignant cells have the ability to rapidly adapt to toxic conditions. For instance, a chemotherapy agent that might show activity in malignant cells at one point in time may eventually lose its ability to damage that cell type in the future. This is due to the resistance mechanisms present in malignant cells. These resistance mechanisms can be either innate or acquired. Alterations in drug transport mechanisms, drug targets, drug metabolism, DNA (deoxyribonucleic acid) repair, DNA synthesis, and apoptosis mechanisms can all contribute to resistance. A recurring problem in anticancer research is to find more agents to treat these resistant cells.

Pharmaceutical Sciences Encyclopedia: Drug Discovery, Development, and Manufacturing
Edited by Shayne C. Gad