LUNG
1. INTRODUCTION

Lung cancer is the leading cause of cancer deaths worldwide. It has overtaken breast cancer as the leading cause of cancer death in women, due largely to increased incidence of smoking among women, as well as adolescents of both sexes. Though the relationship between lung cancer and tobacco is well described, smoking cessation efforts have had limited success. Lung cancer incidence for 2002 was estimated to be 174,300; the projected number of deaths was 157,700 (1). Early detection methods have also been largely unsuccessful—no benefit of screening with chest radiographs or CT scans has been demonstrated, although studies are ongoing. Over the past 40 yr, the overall survival rate has improved only slightly as surgery, radiation therapy, and chemotherapy remain the mainstays of current treatment. Therapies with novel targeted agents are currently under active investigation in all settings of treatment. Primary lung cancer prevention efforts focus on educating people not to begin smoking; secondary prevention involves cessation efforts; and chemoprevention targets reversal of premalignant lesions and prevention of second primary tumors (SPTs) in patients with a prior history of cancer.

Chemoprevention uses natural or synthetic agents to interrupt the process of carcinogenesis and to prevent or delay tumor occurrence. Researchers in basic science and clinical settings collaborate to study lung cancer biology with the goal of uncovering the mechanisms of carcinogenesis and formulating new strategies for prevention and treatment. This chapter will review the biology of carcinogenesis, review completed clinical trials, and explore future strategies in lung cancer prevention.

2. BIOLOGICAL BASIS FOR LUNG CANCER

In 1912, researchers first proposed a potential role of tobacco in bronchogenic carcinoma (2), and observed that cessation of smoking could prevent lung carcinoma. In the 1930s, Ochsner and DeBakey hypothesized that increased cigarette sales might be related to the rising incidence of lung cancer (3). The carcinogenic link between smoking and lung cancer development is explained in terms of two concepts: field cancerization and the model of multistep carcinogenesis.

2.1. Field Cancerization

In the 1950s, Auerbach and others introduced the concept of field cancerization, which applies to cancers of the aerodigestive tract and states that carcinogen exposure results in diffuse injury to the epithelium throughout the aerodigestive tract (4). Genetic changes and premalignant and malignant lesions in one region of the field increase risk of cancer development in the entire field. Areas of carcinoma in situ and metaplasia occurring in the bronchial epithelium after prolonged exposure to...