# Mucins in Lung Cancer

## *Diagnostic, Prognostic, and Therapeutic Implications*

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**Abstract:** Aberrant expression of mucins is associated with cancer development and metastasis. An overexpression of few mucins contributes to oncogenesis by enhancing cancer cell growth and providing constitutive survival signals. This review focuses on the importance of mucins both in the normal bronchial epithelial cells and the malignant tumors of the lung and their contribution in the diagnosis and prognosis of lung cancer patients. During lung cancer progression, mucins either alone or through their interaction with many receptor tyrosine kinases mediate cell signals for growth and survival of cancer cells. Also, stage-specific expression of certain mucins, like MUC1, is associated with poor prognosis from lung cancer. Thus, mucins are emerging as attractive targets for developing novel therapeutic approaches for lung cancer. Several strategies targeting mucin expression and function are currently being investigated to control lung cancer progression.

**Key Words:** Lung cancer, Mucins, MUC1, MUC4, MUC5AC, MUC7, Mucin vaccines, L-BLP25, TG4010, Aptamer.

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Mucins are high molecular weight, heavily glycosylated proteins that are expressed in the epithelial cells of various organs. The presence of a variable number of tandem repeats in the extracellular domain distinguishes mucins from other glycoproteins. The number of tandem repeats is unique to each mucin and contains several proline, threonine, and serine (PTS) residues, but is usually devoid of cysteine residues. This mucin domain/PTS region provides the acceptors for relatively short O-linked glycans (2–20 monosaccharides per chain).[1] The PTS region forms the densely packed filamentous carbohydrate-rich moiety that determines most of the biophysical properties of mucins. Mucins are classified into two major groups: membrane-bound mucins and the secretory mucins (Fig. 1). There are 11 membrane bound mucins, namely, MUC1, MUC3A, MUC3B, MUC4, MUC12, MUC13, MUC15, MUC16, MUC17, MUC20 and MUC21; and seven secreted mucins, MUC2, MUC5AC, MUC5B, MUC6, MUC7, MUC8, and MUC19.[2] Mucins are expressed during embryonic stages of lung development and are involved in the normal development of the lung.

Several reports suggest that mucins are overexpressed in non–small-cell lung cancer (NSCLC) and can be used as suitable biomarkers for identifying and monitoring the progression of lung cancer.[3–6] Under normal conditions, mucins serve as a protective barrier for epithelial cells of various organs including lung.[7] Deregulation of membrane-bound and secretory mucins is associated with cancer progression and metastasis by altering various signaling pathways.[8–10] Of the various mucins, membrane-bound mucin MUC1 and secretory mucin MUC5AC seem to be predominantly found in NSCLC and are correlated with disease progression.

Lung cancer is the most common cause of cancer-related deaths in the United States.[11] Mucins have not been extensively studied for their role in the pathogenesis of lung cancer. This may be due to the complexity of mucin biology and the existence of multiple mucins with differing functions within the cell. However, as our knowledge of mucins in other diseases is increasing, the role of various mucins in lung cancer too will be understood better. This review addresses the current knowledge about the expressional status and role of mucins in lung cancer cell, their significance as prognostic and diagnostic markers and their potential as therapeutic targets.

## EXPRESSION AND FUNCTION OF MUCINS IN NORMAL LUNG EPITHELIUM

Mucins secreted by the goblet cells in the respiratory epithelium form the mucosal coat of the apical epithelium and thereby protect the airways and alveoli from insults such as dehydration, pathogen invasions, and chemical agents.[12] In a normal airway, expression of MUC1 is weak, and a diffuse signal is observed in the tracheobronchial and collecting duct epithelium. MUC1 expression is not observed in the submucosal glands and bronchioles.[13] Weak MUC2 expression is observed in the entire respiratory epithelium; however, the basal pole of some goblet cells expresses MUC2 moderately.[13] MUC2 is undetectable in

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