Lung cancer: active therapeutic targeting and inhalational nanoproduct design

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ABSTRACT

Introduction: Pulmonary drug delivery is organ-specific and benefits local drug action for lung cancer. The use of nanotechnology and targeting ligand enables cellular-specific drug action. Combination approaches increase therapeutic efficacy and reduce adverse effects of cancer chemotherapeutics that have narrow therapeutic index window and high cytotoxicity levels. The current progress of inhaled cancer chemotherapeutics has not been examined with respect to targeting strategy and clinical application potential.

Areas covered: This review examines the state of the art in passive (processing and formulation) and active (targeting ligand and receptor binding) technologies in association with the use of nanocarrier to combat lung cancer. It highlights routes to equip nanocarrier with targeting ligands as a function of the chemistry of participating biomolecules and challenges in inhalational nanoproduct development and clinical applications. Both research and review articles were examined using the Scopus, Elsevier, Web of Science, Chemical Abstracts, Medline, CASREACT, CHEMCATS, and CHEMLIST database with the majority of information retrieved between those of 2000–2018.

Expert commentary: The therapeutic efficacy of targeting ligand-decorated nanocarriers needs to be demonstrated in vivo in the form of finished inhalational products. Their inhalation efficiency and medical responses require further examination. Clinical application of inhaled nanocancer chemotherapeutics is premature.

1. Introduction

1.1. Lung cancer

Lung cancer is the main and second causes of cancer-related death among men and women, respectively, worldwide [1]. With the current treatment options, the survival rate of lung cancer patients is still very low [2,3]. Lung cancer is broadly categorized into primary and secondary cancers. The primary lung cancer is characterized by carcinoma cells originating from the lung tissues. The secondary lung cancer is contracted via metastasis of carcinoma cells to the lung tissues through blood or lymphatic system. Histologically, the lung cancer is divided into five types with small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC) representing about 96% of the lung cancer. Mesothelioma, carcinoid, and sarcoma are the other very rare types of lung cancer [4].

SCLC (20%) and NSCLC (80%) differ from each other in the sizes and locations of their cells [5]. SCLC locates in the central area of the lungs mainly in the bronchi [6]. SCLC is an aggressive, fast-growing lung cancer. It can be further classified into oat cell cancer and combined small cell carcinoma. NSCLC is available in four subtypes: large cell undifferentiated carcinoma (10–15%), squamous cell carcinoma (30%), adenocarcinoma (40%) [7], and pancoast tumor (<5%) [8]. The lung adenocarcinoma has heterogeneous histological profiles. It can constitute of two or more of the following variants: acinar, papillary, bronchioloalveolar, or solid with mucin. The adenocarcinoma may be originated from bronchiolar or alveolar tissues, but it tends to locate in the peripheral parts of the lungs [9–11]. The squamous cell lung carcinoma is classified as keratinizing, nonkeratinizing, and basaloid variants [12]. Seventy percent of squamous cell lung carcinoma occurs as central tumors, whereas 30% as peripheral tumors [13,14]. Large cell undifferentiated carcinoma is a rapid growing cancer with a high spread rate. It cannot be identified histologically as one of the NSCLC. All large cell undifferentiated carcinoma variants tend to be located in the peripheral lung except basaloid carcinoma [11]. Pancoast tumor is formed when the squamous cells are located in the lung superior sulcus and start to spread to the posterior ribs and bones of the spine and can cause Horner’s syndrome [8,11]. Surgery is not opted for this lung cancer type because it is very close to the nerves and spine.

2. Molecular biology

Profound molecular changes of cells bring about cancer. With reference to lung cancer, the normal epithelial cells of deep...