

METHODS IN MOLECULAR MEDICINE™

Lung Cancer

Volume 1
Molecular Pathology
Methods and Reviews

Edited by

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Humana Press

Metastatic Orthotopic Mouse Models of Lung Cancer

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1. Introduction

A number of xenograft models have been developed for human lung cancer. These include subcutaneous (sc)-implant models and implantation under the renal capsule, but these models have not been sufficiently representative of the clinical situation (1). The studies of McLemore et al. (2,3) have utilized the orthotopic concept to develop more relevant lung-tumor models in nude mice. The first model developed by McLemore et al. (2) utilized the growth of human lung cancer cell lines in the bronchioloalveolar region of the right lung of nude mice implanted via an intrabronchial injection. Suspensions of disaggregated fresh tumor specimens were also implanted intrabronchially (ib) by this group. These tumors grew intrabronchially much more extensively than the same tumors inoculated sc. However, most of the tumors propagated ib were localized to the right lung, with only 1% metastasizing to the left lung, 2% to the trachea, 6% to the peritracheal area, and only 3% spreading distantly to lymph nodes, liver, or spleen. McLemore et al. (3) subsequently developed a second model by injecting lung tumor cells via an intrathoracic route into the pleural space. This model seems similar to the intrabronchial model in that extensive local growth occurs with little metastatic spread.

Ten years ago, we described a method that utilizes histologically intact tumor tissue implanted into the left lung by a novel thoracotomy procedure. We have demonstrated that this method results not only in extensive local growth in nude and severe combined immunodeficient (SCID) mice but also in development of regional and distant metastases (4-6). This corroborates the