The potential of targeted paclitaxel immunonanoparticles conjugated to EpCam or cetuximab for lung cancer treatment by inhalation and intravenous administration.

Jürgen Borlak

Center of Pharmacology and Toxicology, Hannover Medical School, Germany
borlak.juergen@mh-hannover.de

Keywords: anti-EpCAM MAb, nanoparticles, lung cancer, inhalation, paclitaxel palmitate, covalent conjugation.

Pulmonary delivery of nanoparticles is a widely investigated and promising approach for lung cancer treatment. Among the various advantages of nanoparticles (NPs) over traditional treatments is their ability to provide prolonged and high local drug concentrations at the tumor tissue. The conjugation of the NP to a vector molecule recognizing unique cancer antigens may further promote the specific binding to the target antigen while avoiding indiscriminate drug distribution and systemic toxicity. In addition, the conjugated ligand can enhance the internalization of the delivery system and its therapeutic cargo into cancer cells. For example, the epithelial cell adhesion molecule (EpCAM) has been reported to be highly over expressed in many adenocarcinomas, including those of the lung.

In my presentation I will discuss the c-Raf transgenic lung cancer disease model and the *in vivo* tolerability and potential efficacy of pulmonary delivered paclitaxel palmitate loaded NPs which were covalently conjugated to an anti-EpCAM monoclonal antibody. Formulations were delivered by endotracheal administration to c-Raf transgenic EpCAM positive lung tumor bearing mice. Animals' survival, body weight changes and bronchoalveolar lavage biochemistry demonstrated the general safety of the delivered formulation as compared to the free drug solution. Additionally histopathology and *in vivo* µCT imaging results suggest that EpCAM based therapies can be considered as a promising strategy for improving lung cancer treatment using the inhalation administration approach. I will also discuss the results of a cetuximab-conjugated poly lactic-co-glycolic acid (PGLA) nanoparticle formulation for targeted delivery of the lipophilic paclitaxel palmitate (pcpl) prodrug in a mouse xenograft lung cancer model.