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Inhalation Delivery of Nano-Aerosol Containing PEI-glucose-PTEN Complex Induced Change of Protein Translation in Kras Knock-Out Lung Cancer Model Mice

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Difficulties of long-term survival of lung cancer patients treated with conventional therapies require the need for novel approaches and gene therapy holds promise in this area. Several genes are known to have anti-tumor activities and have been used as a gene of delivery, however, a number of problems such as efficiency, specificity of the gene delivery hinder the application of gene therapy. Such traditional problems have re-emerged the aerosol gene delivery as a viable and a noninvasive approach to lung cancer therapy. In this study, glucose conjugated polyethyleneimine (PEI-Glu) was used as a carrier particle. After confirmation of carrier efficiency of transfection into the lung, we investigated changes of protein translation of the lung by PTEN, antitumor protein. Aerosols containing PEI-Glu and recombinant plasmid pcDNA3.0-PTEN complex were transferred into Kras knockout lung cancer model mice using nose-only inhalation system. Western blot analysis revealed that aerosol gene delivery carried out successfully. In PI3K/Akt pathway, PTEN as well as PI3K proteins were highly expressed. However, expression levels of PDK1, Akt-1, phosphorylated mTOR, 4E-BP1, p70S6K, and phosphorylated p70S6K were decreased. PTEN delivery increased expression levels of MEKK3, MEKK1, phosphorylated ERK, and phosphorylated p38 proteins. Our data strongly suggest that our carrier system is compatible with in vivo gene delivery and could be applicable to gene therapy. Supported by BK21 Korea

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