

4th World Congress on

Cancer Science & Therapy

October 20-22, 2014 DoubleTree by Hilton Hotel Chicago-North Shore Conference Center, USA

In vivo transformation of lung cells with apoprotein E derived peptide conjugated to polylysine (apoEdp-PLL): A non-viral vector for gene therapy

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Gene therapy is defined as the technology by which genes, small DNA or RNA molecules are delivered to human cells, tissues or organs to correct a genetic defect, or to provide new therapeutic functions for the ultimate purpose of preventing or treating diseases. It is an exciting field of biomedicine that has the potential to benefit patients affected by particularly complex diseases like cancers. A wide range of viral and non-viral vectors have so far been used each with specific strengths and weaknesses, and numerous attempts have been made to overcome these hurdles in order to optimize gene therapy protocols. For diseases with challenging current treatment the innovative strategies like gene therapy is highly demanded. Two diseases, cystic fibrosis (CF) and α 1-antitrypsin (α 1-AT) deficiency are relatively common single gene disorders for which the genetic basis is known and for which current treatment strategies are not curative. On the other hand lung cancers with multifactorial nature are a complex genetic and environmental factor interaction. Attempts have been made to treat both categories by gene therapy. For any sort of gene therapy we need to develop a non toxic, non-immunogenic, cost effective with good transformation/expression efficiency for target organ. Here we report the development of a non-viral vector using LDL receptor mediated pathway for transporting genetic materials to the lung tissue. A tandem dimmer sequence of apoprotein-E conjugated to polylysine was used as DNA delivery vector for *in vivo* transformation of lung. pCDNA3.1 plasmid complexed with apoEdp-PLL harboring beta-galactosidase reporter gene was injected to the tail vein of 5 male Balb/c mice. Frozen sections were prepared two days after injection from lung tissue and stained with X-gal for transgene activity assay. Beta-galactosidase reporter gene activity detection kit was used for quantitative assessment of gene expression. The beta-galactosidase activity level of 180 ng/mg of protein was detected which is indicative of acceptable transformation and activity of the transgene in the lung tissue. In all control tissues tested the values were 0.05ng/mg. The results are very encouraging for *in vivo* targeted transformation using the constructed vector for gene delivery to the lung. Using specific promoter for exclusive gene expression in lung tissue virtually any gene, for cancer or monogenic diseases, could be targeted to the lung tissue.

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