Targeted Gene Therapy for Human Lung Adenocarcinoma with a Suicide Gene Driven by a Lung-specific Promoter Delivered by the JC Virus-like Particles

Chun-Nun Chao[1*], Mien-Chun Lin[2], Chiung-Yao Fang[3], Cheng-Huang Shen[4], Pei-Lain Chen[5], Meilin Wang[6], Deching Chang[7]

[1.] Institute of Molecular Biology, National Chung Cheng University, Chiayi, Taiwanj; Department of Pediatrics, Chiayi Christian Hospital, Chiayi, Taiwan, [2.] Institute of Molecular Biology, National Chung Cheng University, Chiayi, Taiwan; Department of Urology, Chiayi Christian Hospital, Chiayi, Taiwan, [3.] Department of Medical Research, Chiayi Christian Hospital, Chiayi, Taiwan, [4.] Department of Urology, Chiayi Christian Hospital, Chiayi, Taiwan, [5.] Department of Medical Laboratory Science and Biotechnology, Central Taiwan University of Science and Technology, Taichung, Taiwan, [6.] Department of Microbiology and Immunology, Chung Shan Medical University, Taichung, Taiwan, [7.] Institute of Molecular Biology, National Chung Cheng University, Chiayi, Taiwan

Background/Objective

Currently, it is still difficult to treat the patients with lung adenocarcinoma because most of the patients present with advanced stage of the disease and with poor prognosis. Surfactant protein B (SP-B) expressed exclusively in lung epithelium and over-expressed in lung adenocarcinoma. In addition, JC virus (JCV) has been detected in human lung carcinomas, indicating cellular susceptibility to JCV infection. In this study, JC virus-like particles (JC VLPs) packaged a suicide gene driven by human SP-B promoter were employed for targeted gene therapy of human lung adenocarcinoma.

Method

Human SP-B promoter DNA was cloned into a plasmid harboring GFP reporter (pSPB-gfp) or thymidine kinase gene (pSPB-tk). Tissue-specificity of SP-B promoter was demonstrated by transfection. The expression plasmids were then packaged into the JC VLPs.

Result

The VLPs were able to deliver reporter gene into human lung adenocarcinoma cells with high efficiency. Selective cytotoxicity of pSPB-tk delivered by the VLPs on human lung adenocarcinoma cells were also demonstrated in vitro. In the xenograft mouse model, treatment with pSPB-tk-VLPs in the presence of GCV resulted in about 80% growth inhibition of human lung adenocarcinoma tumor nodule.

Conclusion

In conclusion, the JC VLPs are able to package and deliver pSPB-tk plasmid into human lung adenocarcinoma cells with high efficiency, resulting in growth inhibition of the cancer cells in vitro and in vivo. Therefore, it is possible to employ the pSPB-tk-VLPs to treat human lung adenocarcinoma in the future.