Gene silencing with siRNA targeting E6/E7 as a therapeutic intervention against Head and Neck Cancer containing HPV16 cell lines

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INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) ranks sixth among human cancers worldwide and the incidence of HPV-associated cancer increased among white men and women aged 20-44 years, which paralleled an increase in the incidence of sexual activity associated with transmission of HPV16, have been known to cause cancers of the cervix and other anogenital tract sites. Molecular biologists have noted evidence as to the specific mechanisms involved in the HPV-related carcinogenesis. Epidermologist and molecular biologists have also suggested that HPV infection may be associated with cancers of the head and neck.

The oncogenic function of HPV16 has been primarily attributed to E6 and E7. These viral oncoproteins can inactivate tumor suppressor proteins such as p53 and pRb, leading to cell cycle disorder, telomerase activation, and cell immortalization.

The treatment of Head and Neck cancer is currently based on surgery, radiotherapy, and the use of chemotherapeutic drugs. The therapeutic advantage to control the progression of localized HNSCC, whereas chemotherapy has many side effects, induced by several mechanisms, including: interplay between target and normal cells or tissues. Novel therapeutic strategies target the HPV oncoproteins, E6 and E7, and cellular targets, such as p53, pRb (interactions between normal and transformed cells). They have shown that silencing both targets that cause cervical cancer HPV16 can induce target cell apoptosis. Therefore, strategies for achieving specific and selective to abrogate E7 and/or E6 function may be a rational therapeutic approach for treating HPV-positive head and neck cancer.

MATERIALS AND METHODS

HNSCC cell lines (UM-SCC47), have been confirmed to contain HPV16, was used for the present study. The double stranded siRNA sequences were prepared and annexed by Invitrogen RNAi Technologies. Two sequences were chosen and targeted the regions shown in the following table. A scrambled siRNA was used as negative control. The cell lines were transfected using Lipofectamine 2000. After transfection, the cells were returned to the incubator and cultured for 3 days. The cells were then used for experiments. The expressions of p53 and pRb proteins were assessed in both E6 and E7 siRNA and untransfected control samples, respectively.

CONCLUSIONS

These results indicate that siRNA E6/E7 may have potential as a gene-specific therapy for HNSCC-related Head and Neck cancers.

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