AAV mediated VEGF gene therapy to control mandibular condylar growth

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Cell and gene therapy could attenuate or correct genetic disorders in bone and cartilage. However, correcting facial deformities caused by impaired growth through gene therapy is still uncharted territories. Objective: to establish a suitable in vivo gene delivery system to enhance condylar growth. Methods: We constructed a rAAV vector encoding VEGF164 cDNA amplified using RT-PCR from rat liver. The construct was then packaged in HEK293 cells to generate rAAV-VEGF164 virus particles. The cultured medium of transduced HEK293 cells was collected to quantify the VEGF secretion level by ELISA. Ninety 35 days female Sprague-Dawley rats were randomly divided into one experimental group, which was injected with rAAV-VEGF164 virus particles into both mandibular condyles; one control group which received a control vector encoding green fluorescent protein and the other control group which received PBS injection. Each group of rats was sacrificed on the following experimental days: 7, 14, 21, 30 &60. By means of in situ hybridization, immunohistochemistry staining, PAS staining, RT-PCR and morphological measurement, the delivered gene expression and new bone formation were investigated. Results: The level of VEGF164 protein in culture medium reached a peak after cultivation of HEK293 cells transfected with rAAV-VEGF164 virus 48 hours later. The in vivo results showed that exogenous gene expression was clearly detected in the deeper layer of mandibular condyle as early as 7 days postinjection by in situ hybridization. The thickness of hypertrophic layer significantly decreased and new bone formation increased in the experimental groups reaching a maximum at 30 days. In other organs (liver, kidney, spleen and heart), expression of the delivered transgene was not observed. Conclusions: This study first sought to confirm that foreign genes can be transferred to mandibular condyle in vivo. These exciting results strongly suggest that VEGF gene delivery is a promising approach to induce mandibular condylar growth.

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