Title: Intratumoral injection of plasmid-encoded flagellin inhibits growth of NSCLC-cells in murine lung cancer model

Body: Lack of progress in the treatment of NSCLC urges to look for experimental therapeutic methods, such as gene therapy. Currently used therapeutic vectors can cause adverse effects, or have a limited potential to transduce cells. The aim of this work was 1) to construct a vector suited for gene therapy allowing for selective transduction of only tumor cells 2) to assess therapeutic potential of Salmonella flagellin (FliC). Engineered plasmid vector was obtained by PCR synthesis. For the purpose of tumor-specific transcriptional activity it was necessary to design a two-step promoter unit system based on telomerase minimal promoter. Influence of FliC on NSCLC cells was assessed by measuring proliferation of transfected cells and by phenotyping of maturation markers on DCs incubated with A549 cells. NSCLC tumors in mice were injected with empty or FliC-coding vector. Tumor growth and survival of the mice were analyzed. FliC-transfected A549 cells had significantly lower proliferative potential. Such cells enhanced maturation of MoDC as suggested by higher expression of CD80 and CD83. NSCLC-inoculated mice administered with a vector containing FliC gene had a significantly longer survival time (p<0.002) and slower tumor growth (p<0.01) comparing to the control group. Designed two-step promoter unit allows for efficient and tumor-selective expression of therapeutic gene. Results suggest that NSCLC transduction with FliC gene may inhibit its proliferation in vitro and tumor growth in vivo and increase survival rate. Due to ambiguous results obtained in co-culture of transfected A549 and DC antitumor properties of FliC other than induction of DC maturation need to be considered.