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Regression of prostate tumors after intravenous administration of targeted gene based nanomedicines

Christine Dufes

University of Strathclyde, UK

The possibility of using gene therapy for the treatment of prostate cancer is limited by the lack of safe delivery systems able to selectively deliver therapeutic genes to tumors by intravenous administration. Given that lactoferrin receptors are overexpressed on prostate cancer cells, we hypothesized that the conjugation of lactoferrin to generation 3 diamino butyric polypropylenimine dendrimer would improve its transfection and therapeutic efficacy in prostate cancer cells. In this study we demonstrated that the grafting of lactoferrin to the dendrimer led to an enhanced anti-proliferative activity of the dendriplex by up to 5.8-fold in PC-3 cells compared to the unmodified dendriplex *in vitro*. *In vivo*, the intravenous administration of lactoferrin-bearing DAB dendriplexes encoding TNF α resulted in the complete suppression of 70% of PC-3 and 50% of DU145 tumors over one month. Treatment with DAB-Lf dendriplex encoding TRAIL led to tumor suppression of 40% of PC-3 tumors and 20% of DU145 tumors. Tumor suppression was also observed for 20% of both types of prostate tumors following injection of DAB-Lf dendriplex encoding IL12. The treatment was well tolerated by the animals. Lactoferrin-bearing generation 3 polypropylenimine dendrimer is therefore a highly promising delivery system for the gene therapeutic treatment of prostate cancer.

C.Dufes@strath.ac.uk