

GP73-regulated oncolytic adenoviruses possess potent killing effect on human liver cancer stem-like cells

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Cancer stem cells (CSCs), also known as tumor-initiating cells, are highly metastatic, chemo-resistant and tumorigenic, and are critical for cancer development, maintenance and recurrence. Oncolytic adenovirus could targetedly kill CSCs and has been acted as a promising anticancer agent. Currently, a novel GP73-regulated oncolytic adenovirus GD55 was constructed to specifically treat liver cancer and exhibited obvious cytotoxicity effect. However, there remains to be confirmed that whether GD55 could effectively eliminate liver CSCs. We first utilized the suspension culture to enrich the liver CSCs-like cells, which acquires the properties of liver CSCs in self-renewal, differentiation, quiescence, chemo-resistance and tumorigenicity. The results indicated that GD55 elicited more significant cytotoxicity and stronger oncolytic effect in liver CSC-like cells compared to common oncolytic virus ZD55. Additionally, GD55 possessed the greater efficacy in suppressing the growth of implanted tumors derived from liver CSC-like cells than ZD55. Furthermore, GD55 induced remarkable apoptosis of liver CSC-like cells *in vitro* and *in vivo*, and inhibited the propagation of cells and angiogenesis in xenograft tumor tissues. Thus, GD55 may virtually represent an attractive therapeutic agent for targeting liver CSCs to achieve better clinical outcomes for HCC patients.