COMBINATIONAL TREATMENT OF REOVIRUS AND NK CELLS AGAINST BLADDER CANCER CELLS USING AN INTRAVESICAL THERAPY MIMICKING IN VITRO ASSAY

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Background A variety of combination treatments have been investigated to overcome the low response rate and potential resistance of bladder cancer. Reovirus, one of the oncolytic viruses, has been studied for bladder cancer cells (BCC). While intravesical treatment with Reovirus serves as an efficient strategy, its monotherapy has often shown modest cytotoxicity against some BCC. Considering that natural killer (NK) cells have emerged as a key player in BC immunotherapy, it remains clear that a combination of reovirus with NK cells will be necessary to optimize therapeutic efficacy.

Methods We here investigated the anti-tumor effects of monotherapy and combination treatment at various concentrations in three types of BCC lines (5637, HT-1376, 253J-BV) using an in vitro experimental model mimicking intravesical therapy. To simulate the clinical treatment, we reduced the cytotoxicity duration to 2 hours followed by washing. In contrast, to enhance the anti-tumor effect, we utilized RP116, which is an attenuated reovirus with natural truncation of sigma 1, and interleukin (IL) 18/21-treated NK (eNK) cells expanded under stimulation with K562-mbIL-18/21 feeder cells and IL-2 and IL-15 from peripheral blood.

Results Monotherapy of RP116 or IL18/21-treated eNK cells exhibited effective cytotoxicity against the 5637 (grade 1 carcinoma), but not against HT-1376 (grade 2 carcinoma) and 253J-BV (derived from a metastatic site). However, combination treatment of IL18/21-treated eNK cells and RP116 showed effective cytotoxicity against HT-1376 and 253J-BV.

Conclusions Based on these findings, the combination therapy involving reovirus and NK cells could serve as an effective treatment strategy for bladder cancer.

REFERENCES

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