Radiation sensitization, using targeted anti-CD 47 siRNA nanoparticles via radiotherapy

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Abstract

We investigated the use of protamine-hyaluronic acid nanoparticles (PH-NP; 164 ± 2.7 nmϕ) encapsulated in microcapsules (1.1 ± 0.3 μmϕ) that released their contents upon exposure to radiation together with two sessions of radiotherapy for tumor treatment.

Nanoparticles prepared via self-assembly with anti-CD47 siRNA were mixed with 1.0 ml of a solution containing 4.0% alginate, 3.0% hyaluronate, 1 mg ascorbate, and then sprayed into 0.5 mmol/l $FeCl_2$. MM48 murine breast cancer cells were inoculated into the left hind legs of C3He/N mice. Microcapsules were subcutaneously injected around the tumor. One hour after the injection of microcapsules, 10 or 20 Gy 140 KeV X-ray-radiation was locally administered to the tumors. Twelve hours after the completion of radiation, mice were exposed to 4cGy of whole-body ^{60}Co γ-radiation at 24 h intervals for 5 days.

The microcapsules released anti-CD47 siRNA nanoparticles that delivered anti-CD47 siRNA into the tumor cells. Macrophages and CD 8+ T-cells were activated by whole-body radiation. This treatment had a significant antitumor effect.

Our results indicate that targeting tumors with nanoparticles together with low-dose, whole-body radiation provides improved treatment of tumors.