Development of a tumor-homing peptide-mediated drug delivery method for magnetic hyperthermia

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Hyperthermia is a cancer therapy approach that kills tumor cells by heating up the affected area to 40-43 ºC.[1] During hyperthermia, the blood vessels of the tumor tissue cannot expand, and the blood flow rate is lower than normal tissue, so the heat cannot be dissipated to the environment for a short period of time and thus induces cell death.[2] Mmagnetic hyperthermia is one way of hyperthermia that magnetic nanoparticles (MNPs) witch injected into body and exposure to an alternating magnetic field (AMF) for heating target area.[1] MNPs are widely used in biomedical fields such as MRI diagnosis, drug delivery, and magnetic hyperthermia because of their superior properties such as biocompatibility and superparamagnetism.[3] However, one problem is that the innate immune system quickly recognizes and eliminates MNPs administered to the human body. Furthermore, providing sufficient heat to the affected area is difficult due to insufficient amounts of MNPs, uneven distribution of MNPs throughout the tumor, etc. In addition, it is not easy to accumulate MNPs in the bloodstream at the target site. Therefore, it is necessary to develop a high specificity delivery technique and inhibit the capture of MNPs by macrophages of the reticuloendothelial system to sufficiently increase the residence time of MNPs in the tumor tissues. In this study, to improve the stability of magnetic nanoparticles in vivo and the delivery efficiency to cancer cells, we selected Synomag-D50 coated with polymer dextran with excellent biocompatibility, and applied it on its surface. Two THPs, PL1 or PL3, are loaded to synthesize the MDT complex, and these polypeptides can specifically recognize and bind to specific receptors on the surface of tumor tissue or blood vessel contacting cells. We prepared MDT complexes modified by THP PL1 or PL3 (MDT1 and MDT3). Particle sizes of MDT1 and MDT3 were 57.3 and 102 nm, respectively, which are suitable for accumulation in tumor tissues. As assessed by cell specificity, the combination of U87MG cells and MDT3 showed the highest cell specificity. After being treated with 200 μg/mL MDT3 and applying an AMF, the cancer cell-killing efficiency was 71%. MDT3 is expected to be applied in the delivery of drugs for magnetic hyperthermia.

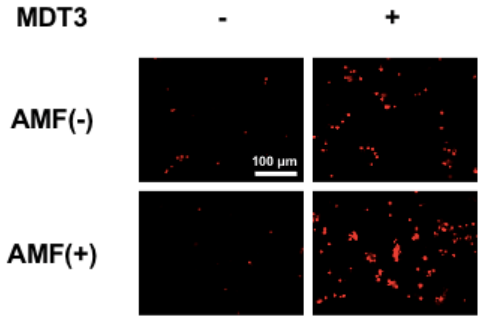

Figure 1. Cancer cell-killing efficiency by MDT3 and AMF treatement.

References

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