AB025. The effects and mechanisms of magnetic nanomaterials in prostate cancer diagnosis and therapy

Li Zhang

Department of Urology, the First Affiliated Hospital of Anhui Medical University, Institute of Urology, Anhui Medical University, Anhui Province Key Laboratory of Genitourinary Diseases, Anhui Medical University, Hefei 230000, China

Background: Take iron oxides (Fe_3O_4) nanoclusters for instance, to explore the effects and mechanisms of magnetic nanomaterials in prostate cancer diagnosis and therapy.

Methods: Fe_3O_4 nanoclusters (Fe_3O_4 NCs) were synthesized by using hydrothermal method through iron (III) acetylacetonate. The as-prepared Fe_3O_4 NCs were characterized by transmission electron microscopy (TEM), dynamic light scattering (DLS), X-ray powder diffraction (XRD), and Fourier-transform infrared spectroscopy (FTIR). The T_2-weighted image was obtained with a 3.0 T clinical MRI scanner. To establishing PC3-GFP-LC3, a PC3 cell line stably expressing green-fluorescent-protein-tagged microtubule-associated protein 1 light chain 3 (GFP-MAP1LC3), and then evaluate the effect of Fe_3O_4 NCs upon cell proliferation. To use 4 W/cm^2 near infrared laser (NIR, 808 nm), the light-thermal conversion of Fe_3O_4 NCs was assessed. GFP-LC3 punctate dots were observed by an invert microscope and LC3-I/LC3-II conversion was detected by western blotting. Autophagosome formation was observed by TEM. The tumoricidal effects to PC3 were evaluated by cell proliferation assay *in vitro* and xenograft volume curve *in vivo* under NIR in the presence or absence of autophagy inhibitors.

Results: The as-prepared hydrophilic and magnetic Fe_3O_4 NCs were 100 nm in uniform size. XRD and FTIR analyses showed the NCs possessed the characterized peak and functional motifs, r_2 value could reach 143 $mM^{-1}S^{-1}$, after magnetic targeting, the r_2 value could further shorten. Fe_3O_4 NCs did not affect the cell proliferation at 0–400 μg/mL, indicating the good biocompatibility. Fe_3O_4 NCs could induce the medium temperature elevated in a time- and dose-dependent manner under 808 nm NIR irradiation. Besides, Fe_3O_4 NCs could induce complete autophagic flux in PC3 cells, which effect could be inhibited by 3-MA or CQ administration. Under 808 nm NIR, Fe_3O_4 NCs could elicit 40% cell viability reduction, this reduction could be further enhanced when co-treated with 3-MA or CQ. *In vivo* study showed that under 808 nm NIR, tumor volume in NS, 3-MA, CQ group increased with prolonged time, while Fe_3O_4 NCs administration could inhibit the volume increase, when 3-MA or CQ was administrated simultaneously, the tumor volume was sustained with the initial treatments, the body weight of mice in each group did not alter significantly.

Conclusions: Fe_3O_4 NCs are safe T_2-MRI contrast nano-contrast agents, could enhance the sensitivity of prostate cancer diagnosis. The NCs possess outstanding light-thermal conversion capacity, could induce autophagy in PC3 cells. More importantly, Fe_3O_4 NCs could further enhance the tumoricidal effects under 808 nm NIR when the autophagiy-inducing effects are inhibited in PC3 cells.

Keywords: Magnetic nanomaterials; prostate cancer; diagnosis and therapy

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