In Vivo Cancer Cells Elimination Guided by Aptamer-Functionalized Gold-Coated Magnetic Nanoparticles and Controlled with Low Frequency Alternating Magnetic Field

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This work proves the biomedical applications of magnetic nanoparticles under the influence of a magnetic field in cancer therapy. This study presents magnetodynamic nanotherapy using DNA aptamer-functionalized 50 nm gold-coated magnetic nanoparticles exposed to a low frequency alternating magnetic field for selective elimination of tumor cells in vivo.

SITUATION

Medical nanotechnologies are becoming promising for cancer treatment.
The main drawback is that nanoparticles accumulate in healthy tissues causing harmful effects. Targeted delivery requires functionalization of nanoparticles with molecular probes such as antibodies or aptamers that bind specifically to unique or overexpressed biomolecules on cancer cells.

APPROACH

Aptamer-modified gold-coated magnetic nanoparticles (AGMNPs) are applied to target tumor in vitro and in vivo.
For the selective targeting it is used aptamer AS14 to mouse Ehrlich carcinoma fibronectin (Fn).
Fn plays a major role in cell growth, differentiation, migration, wound healing, blood coagulation, embryonic development, and also in oncogenic transformation.

RESULTS

A significant therapeutic effect was observed in tumor tissues after treatment with AS-14-GMNPs in the low frequency alternating magnetic field (LFAMF) This treatment caused significant immune response as there was visible inflammatory infiltration of segmented leukocytes on the boundaries of necrotic areas.
Swelling and destructive changes of the tumor tissue's microenvironment were also observed (Figure 1).
Toxicity of aptamer-functionalized GMNPs was estimated by changes in blood serum biochemistry (Table 1).

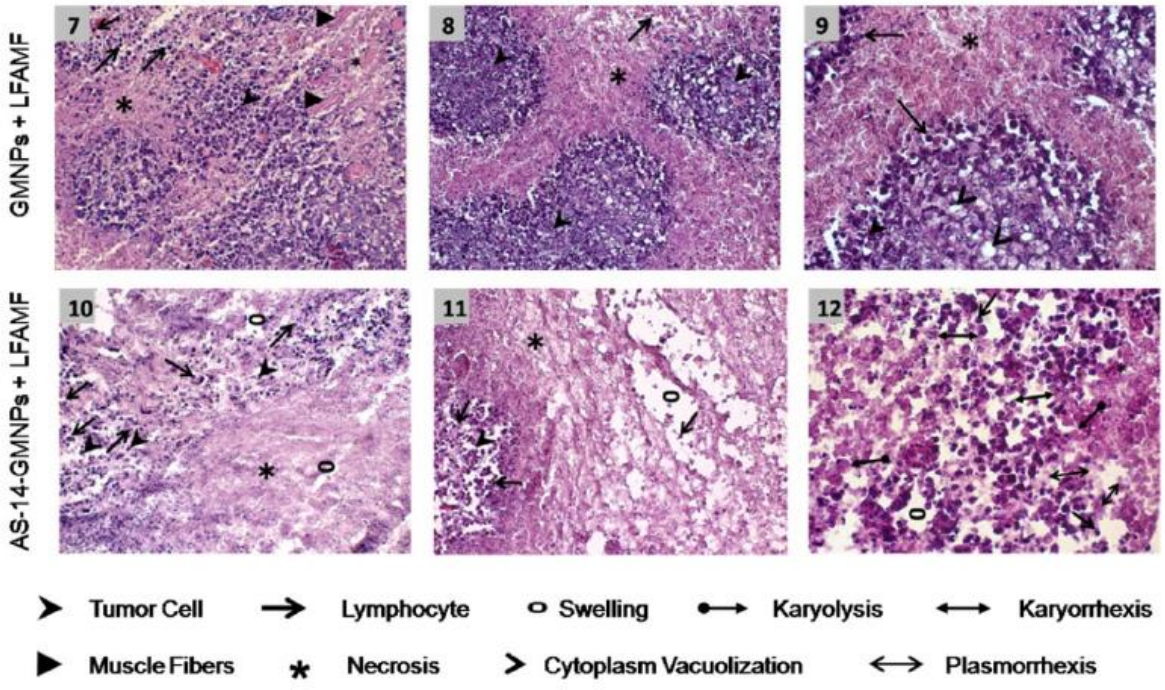

Figure 1_ Histological Structure of the Treated Tumor, part B.
B7-B9– GMNPs and LFAMF treated carcinoma displays scattered tumor necrosis with weakly expressed inflammatory infiltration, tumor tissue remains in the form of "islands" in which the majority of cancer cells are with cytoplasm vacuolization and signs of karyolysis. **B10-B12** – AS-14-GMNPs and LFAMF treated carcinoma shows large tumor necrosis areas, swelling, destructive changes of tumor tissue microenvironment and inflammatory infiltration of segmented leukocytes. On the periphery remaining tumor cells are dead with karyorrhexis, karyolysis, plasmorrhexis. Magnification: (B1) ×100; (B2, B4, B5, B7, B8, B10, B11) × 200; (B3, B6, B9, B12) x 400.

Sample	Cholesterol, m mole L^{-1}	Total protein, g L^{-1}	Alanine amino-transferase, IU L^{-1}	Alkaline phosphatase, IU L^{-1}	Total bilirubin, µ mole L^{-1}
AS-14-GMNPs					
Female (N=5)	1.45±0.01	50.75±3.32	18.40±3.67	214.30±74.81	5.67±0.38
Male (N=5)	1.56±0.48	55.97±6.21	31.90±13.17	254.87±122.29	6.05±0.21
DPBS					
Female (N=5)	2.30±0.28	53.90±1.27	13.55±4.78	177.67±27.13	6.25±0.70
Male (N=5)	2.32±0.26	55.90±2.76	20.93±6.9	251.40±71.13	6.20±0.53

Table 1_ Blood serum biochemistry parameters performed separately for male and female mice treated with AS-14-GMNPs in phosphate buffer (DPBS) or DPBS alone. All data are presented as the mean ± standard error of mean.

Gold nanoprisms could be appropriate candidates for *in vitro* cellular thermoablation due to their efficient internalization and heating capacity