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Study and Comparison of Different Multi-Nanostructures Applied for Laser-Induced Apoptosis of Breast Cancer Cells

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Short Communication

Cancer is a major public health problem which causes high rate of morbidity and mortality worldwide. It is well known that cancer therapy relies on chemotherapy and radiotherapy where most anticancer drugs are essentially taken up by cells with high proliferative rate, a distinct cancer cell characteristic. During the treatment process, however, normal tissue also suffers from chemotherapeutic actions, causing severe side effects [1,2]. Nan medicine has a great impact on the diagnosis, monitoring and treatment of diseases such as cancer and as well as control and understanding of biological systems. Advances in current technologies and the application of magnetic nanoparticles to deliver anticancer drugs to hypoxic zones of tumor have drawn considerable interest in the past decade [3]. Novel magnetic nana-formulations such as liposomes, metallic/nonmetallic, and polymeric nanoparticles has increased the ability to deliver drugs for which conventional therapy has shown limited efficacy [4-6]. Small magnetite nanoparticles (<15nm) is called Super Paramagnetic Iron Oxide Nanoparticles (SPION), which lacks a hysteresis loop and possess high field irreversibility, high saturation field and extra anisotropy contributions [7,8]. Over the past decades SPIONs with size and morphology dependent physical and chemical properties including biocompatibility, chemical composition, magnetic behavior, surface structure, adsorption properties, solubility, low toxicity, good magnetic response have attracted world-wide research attention [9,10]. These unique materials have been utilized successfully for number of applications including contrast-enhanced imaging [11] and drug delivery [12]. In magnetically guided nanoparticles (NPs), a constant external magnetic field is used to transport magnetic NPs loaded with drugs to a specific site within the body or to increase the transfect ion capacity. Functional groups play an important role in the production of organic shell around inorganic core to prepare uniform and stable suspension. Basically, a dendrite is composed of three architectural components: a core (I), an interior of shells (generations) consisting of repeating branch-cell units (II), and terminal functional groups (the outer shell or periphery) (III) [13,14]. One such example is poly (amid amine) (PAMAM), which acts as a template or stabilizer for preparation of inorganic nanocomposites. Dendrimers, especially PAMAM are capable of conjugating targeting ligands, imaging agents and drug molecules for targeted therapeutics. Intrinsic fluorescence of dendrite as surface modification can reduce the need for external fluorescent carrier, hence the final biocompatibility of delivery system will be improved [15,16]. The concept of dendrite nanocomposites is based on immobilization of pre-organized metallic ions [17,18]. Thus, a dendrite acts as a template or reactor to pre-organization of ions and small molecules [19]. In such cases, atoms and molecules could attach to internal space or external surface of dendrite [20,21]. Plasmatic nanoparticles exhibit unique optical properties such as strong Localized Surface Plasmon Resonance (LSPR), surface-enhanced scattering, non-linear optical properties, tunable resonance across the Vis-NIR due to adjustable nanoparticles size and shape [22-26], biocompatibility due to their inert surface, no toxicity, surface conjugation chemistry i.e., they can be linked to specific ligands for tumor targeting, imaging and therapies, lack of photo bleaching or blinking as with quantum dots, and very low oxidation [27,28]. As a result, Au NPs, nanoshells or nanorods have been extensively utilized for bioimaging [29,30], cancer cell diagnostics and therapeutics [31-33]. In addition to Enhanced Permeation and Retention (EPR) effect in passive targeting, tumor cells show higher concentration of receptors on their surfaces related to their enhanced mitosis rates. Thus, these receptors can be suitably targeted for active targeting by binding with for example ligands or antibodies. Receptors involved in endocytosis activity provide a pathway for the nanoparticles to

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Table 1: The above results indicate the importance of magnetic field guidance and encapsulated chemotherapy drug in nanoparticle cellular uptake and apoptosis. This does not, however, in any way mitigate the advantages of other techniques, as for example nanodendrimers have large number of dendrites and intrinsic fluorescent properties, which can play a leading role in biomedical engineering and clinical application.

Method	Laser (nm)	Cell Lines	Apoptosis %	Reference
1) MPIL-Tz	514 (CW) 532 (Pulsed)	BT-474	44.6 42.6	33
2a) Dox	514	MCF-7	35	41
2b) MPL			40	
2c) MPL-MF			50	
2d) MPL-Dox			75	
2e) MPL-Dox-MF			90	
3a) Laser only	514	MDA-MB 231	2	42
3b) MPDF-Hydr			5	
3c) MPDF-Hydr.-Laser)			35	
3d) MPDF-NP			5	
3e) MPDF-NP-Laser			15	

be accumulated within the cells rather than being restricted to the surface. From a photo thermal therapy perspective, the wave length of maximal absorption and the absorption cross-section are key features to consider when selecting a particle for hyperthermia. It is suggested if the temperature increases to about 42-45°C from the physiological temperature of 37°C, the induced heat heat can effectively destroy the cancer cells via cell-targeted uptake [34]. Meanwhile, size and surface characteristics of the nanoparticle are of prime importance in the bio distribution and rapid clearance of nanoparticle from the blood which affects nanoparticle delivery to target sites [35,36]. In recent years much interest has been shown for nanotechnology-based imaging, therapeutic and effective cancer therapy where one of the main goals is to deliver therapeutic agents to tumor sites, since most anticancer drugs cannot distinguish between healthy and cancerous tissues hence causing some undesirable results [37-44]. In this communication, the results of experience gained in recent years in relation to application of lasers and multilayer nanostructures to breast cancer cells hyperthermia are reported. The details of nanoparticles cytotoxicity, uptake and images can be obtained from the corresponding references.

The three major strategies that were designed, fabricated, characterized and optimized are:

1- Magnetoplasmonic immunoliposomes targeted by Trastuzumab-(MPIL-TZ)

2- Magnetoplasmonic liposomes containing doxorubicin (MPL-Dox)

(a) Doxorubicin only (Dox)

(b) Magnetoplasmonic liposomes only (MPL)

(c) MPL with applied magnetic field (MPL-MF)

(d) MPL containing doxorubicin (MPL-Dox)

(e) MPL-Dox with applied magnetic field (MPL-Dox-MF)

3- Magnetoplasmonic nanodendrimers targeted by folic acid (MPDF) Four methods for synthesis of gold nanoparticles were employed: sodium borohydroxide (NaBH4) and hydrazine sulfate (Hydr.) reducing agents, presynthesized 10-nm gold nanoparticles (AuNPs) and NaBH4 with 10 times concentration. Only MPDF-hydr. and MPDF-NP were used for hyperthermia experiments due to their higher rate of cellular uptake. Two cell lines of MDA-MB 231 and MCF 7 were used but only the former were reported because of over expressed folate receptors. The following groups were used. The results are shown in Table 1.

(a) Laser only

(b) MPDF-Hydr.

(c) MPDF-Hydr. with applied laser (MPDF-Hydr.-Laser)

(d) MPDF-NP

(e) MPDF-NP with applied laser (MPDF-NP-Laser)

The above results indicate the importance of magnetic field guidance and encapsulated chemotherapy drug in nanoparticle cellular uptake and apoptosis. This does not, however, in any way mitigate the advantages of other techniques, as for example nanodendrimers have large number of dendrites and intrinsic fluorescent properties, which can play a leading role in biomedical engineering and clinical application. Also, in terms of *In-Vivo* clinical practice, it is suitable to use an appropriate multimodal system such as pulsed or modulated near infrared laser wavelengths within the therapeutic window with higher tissue penetration depth as well as efficient engineered multifunctional contrast agents with accurate selective and tunable absorption peaks. In spite of advances in nanotechnology as a cutting-edge field and significant role in producing innovative solutions for cancer treatment, the treatment strategy of cancer has almost remained unchanged over the years i.e., surgical removal of the tumor, chemotherapy, radiotherapy or sometimes combination of both, which in any case some degree of undesirable damage to surrounding healthy tissue is inevitable due to for example over dose of ionizing radiation, unselective drug delivery or other factors. It seems, more research is moving in the direction of designing a multi-task theranostic platform to safely perform selective drug delivery, imaging and therapy of cancer known as "smart theranostic" where hopefully less or no harm is done to patients. For example, in the case breast cancer this implies even less discomfort caused by multiple and repeated palpation or by pressing plates during the screening process, which themselves can biomechanically provoke the target tissue.

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