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Gold Nanorod-Embedded Electrospun Fibrous Membrane as a Photothermal Therapy Platform

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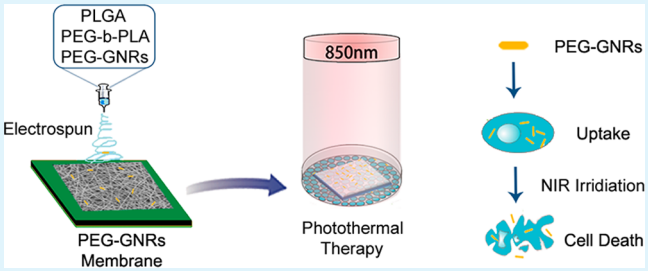
Supporting Information

ABSTRACT: A strategy of using a gold nanorod (GNR)-loaded electrospun membrane as a photothermal therapy platform of cancer is reported. The strategy takes both the advantages of the excellent photothermal properties of GNRs to selectively kill the cancerous cells, and the widely used biodegradable electrospun membrane to serve as GNR-carrier and surgical recovery material. PEG modified GNRs were embedded into the electrospun fibrous membrane which was composed of PLGA and PLA-*b*-PEG with an 85:15 ratio. After incubation with the cells in the cell culture medium, the PEG-GNRs were released from the membrane and taken up by cancer cells, allowing the generation of heat upon NIR irradiation to induce cancer cell death. We have demonstrated that the use of PEG-GNR-embedded membrane selectively killed the cancerous cells and effectively inhibited cancer cell proliferation though in vitro experiments. The PEG-GNRs-loaded membrane is a promising material for postsurgical recovery of cancer.



KEYWORDS: *PEGylated gold nanorods, electrospun, photothermal therapy, biodegradable membrane, cancer*

1. INTRODUCTION

In recent years, cancer has emerged as the leading cause of mortality in the world and severely affected public health.[1] Photothermal therapy, in which light is converted to heat to induce cell death via hyperthermia, holds great promise in cancer treatment.[2] Compared to radiotherapy and chemotherapy which have grievous adverse effects, photothermal therapy is advantageous in destroying cancerous cells with minimal damage to the surrounding normal cells, for the reason that tumors are more sensitive to heat-induced damage than normal tissues due to their poor blood supply.[3,4] Recent advances in the development of plasmonic nanomaterials with strong light absorption for localized hyperthermia have promoted the application of photothermal therapy. Among those nanomaterials, PEGylated gold nanorods (PEG-GNRs) have shown excellent properties including superior photothermal transfer efficiency at near-infrared wavelength regions (for deeper tissue penetration), facile synthesis with large quantity and uniform size, and low toxicity.[5,6] Besides the well-known enhanced permeability and retention (EPR) effect for the tumor accumulation of nanomaterials, it has been reported that gold nanorods have distinct intracellular trafficking pathway to target mitochondria of cancer cells but not normal cells which further enhances their tumor selectivity.[7] The feasibility of PEG-GNRs for photothermal tumor destruction has been verified in several in vivo experiments.[8,9]

However, to realize the potential clinical application of PEG-GNRs for cancer treatment, a suitable delivery platform is required. In previous studies, GNRs as well as other photothermal converters are generally administered by intravenous injection to systematic circulation, resulting in higher dosage and potential hazards due to their accumulation in liver and spleen.[10,11] Sustained releasing strategy, which has attracted increasing interest in cancer treatments and prevention,[12,13] has not been tried for GNRs neither. Ideally, the delivery system for PEG-GNRs should qualify these properties: (1) localized drug administration to the tumor; (2) possessing biocompatibility and biodegradability; (3) controlling the release and heat generation of PEG-GNRs.[14,15] Electrospun fibrous membranes with suitable polymer composition offer the opportunities for the development of such an ideal delivery system. Several biodegradable electrospun fibrous membranes have been broadly used in clinical postsurgical recovery for the purpose of antiadhesion and anti-infection.[16,17] Recent studies reported the incorporation of paclitaxel or doxorubicin as anticancer drugs in the electrospun fibers.[18,19] However, no nanomaterial-embedded biodegradable membrane for cancer therapy has been reported yet.

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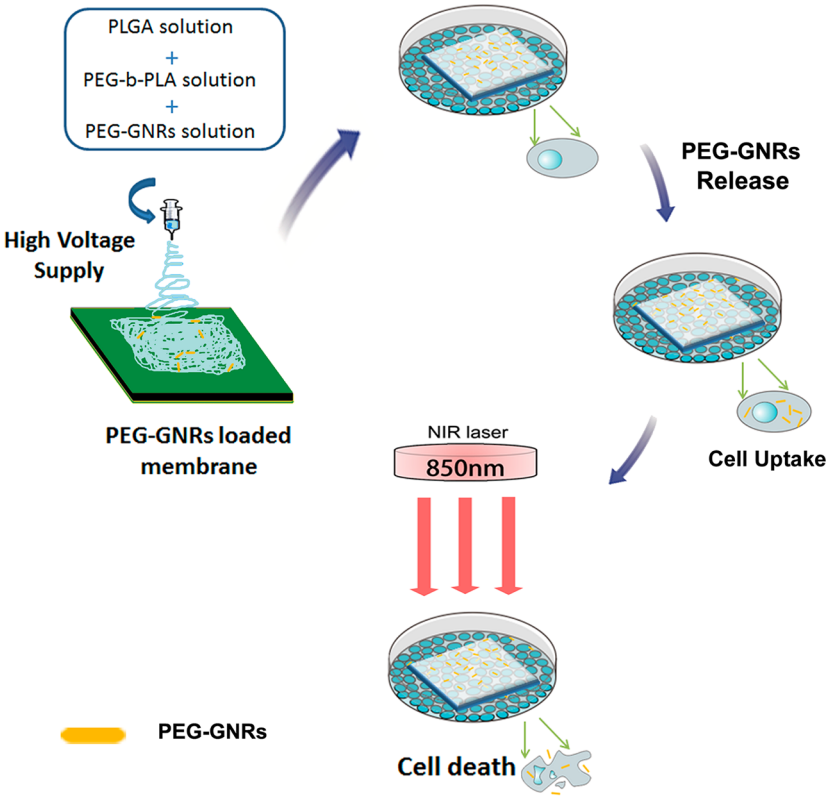
Scheme 1. Schematic illustration Depicting the Strategy of Using PEG-GNRs Membrane for the Photothermal Therapy of Cancer Cells in Vitro[a]



[a]The cells were grown in a vessel and covered by the PEGylated gold nanorod-loaded membrane that was prepared by electrospinning. After the cell uptake of the released PEG-GNRs, the cells were irradiated with an 850 nm NIR illuminating apparatus to induce hyperthermia for cancer cell ablation.

In this work, for the first time, we have designed and prepared PEG-GNRs-loaded electrospun membrane as a sustained photothermal platform for cancer therapy. It takes advantage of both the excellent photothermal properties of GNRs to selectively kill the cancerous cells, and the widely used biodegradable electrospun membrane to serve as GNR-carrier and surgical recovery material.[20] With the PEG-GNRs embedded membrane, the efficient and selective ablation of cancer cells via hyperthermia has been demonstrated. We expect this membrane could be placed on the lesion after primary tumor surgery to not only promote cancer surgical recovery, but also realize long-time antirecurrence effect with the help of NIR irradiation.

2. MATERIALS AND METHODS

2.1. Materials. PLGA (M_w = 60 000, LA/GA = 75/25) and PLA-b-PEG (M_w = 10 000, LA/EG = 50/50) were obtained from Jinan Haidai Biological Technology Co. (Shandong, China). *N*,*N*-Dimethylformamide (DMF) and acetone were obtained from Beijing Chem. Co. (Beijing, China).

2.2. Preparation and Characterization of PEG-GNRs. Procedures for the preparation of PEG-GNRs were the same as those described previously.[21] In brief, the GNRs were synthesized according to Murphy's method. NH_2-PEG2000-NH_2 (2000 Da) was used for PEGylation of GNRs by in situ dithiocarbamate formation. To remove excess reactants, the synthesized PEG-GNRs were dialyzed by dH_2O with 7000 Da molecular weight cutoff dialysis bags. The morphology of PEG-GNRs was observed by transmission electron microscopy (TEM, JEM-2100F, Japan). A zetasizer (Nanov510, Malvern, U.K.) was used to determine the surface charge of GNRs dispersed in phosphate buffered saline (PBS) at room temperature. The maximum absorption of PEG-GNRs was determined via UV–visible absorption spectrum (UV-2500, SHIMADZU).

2.3. Fabrication of PEG-GNRs-Loaded Electrospun Fibrous Membranes. PLGA and PLA-*b*-PEG were dissolved in a mixed solvent of DMF and acetone ($V_{DMF}/V_{Acetone}$ = 5/5) to prepare the polymer solutions. The weight ratio of PLGA/PLA-*b*-PEG was 85:15. The PEG-GNRs were dispersed in DMF (34.8 μg/mL), and the total polymer content was 50 w/v% (w in g and v in mL). The membranes were prepared by the electrospinning device (The Beijing Machinery & Electricity Institute, China) at 20 kV voltage and a steady flow rate of 10 μL/min. The thickness of membranes was 100 ± 10 μm after 40 min electrospinning. The resulting electrospun fibrous membranes were dried under vacuum for 72 h at room temperature. The morphology of the electrospun membrane was observed by a scanning electron microscopy (SEM, JEOL JSM-6700F, Japan) at an accelerating voltage of 5 kV. The samples were sputter-coated with platinum before SEM analysis.

The surface PEG-GNR content of the membranes was measured by high resolution X-ray photoelectron spectroscopy (XPS, ESCALa-b220i-XL, VG Scientific). The angle of analyzer was 90° to the sample's surface.

2.4. Cell Culture. A549, HBE, MCF-7, and HeLa cells (Cell Resource Center, IBMS, AMS/PUMC) were all cultured in Dulbecco's modified Eagle's medium (DMEM, Gibco) containing 10% fetal bovine serum (Hyclone), 1% Pen Strep (10 000 IU/mL penicillin and 10 000 μg/mL streptomycin solution, Invitrogen) at 37 °C in a 5% CO_2 atmosphere incubator.

2.5. In Vitro PEG-GNRs Release and Uptake Study. For PEG-GNRs release study, the dried PEG-GNRs-loaded electrospun membrane was cut into 2 × 2 cm^2 pieces. The cut specimen was weighted and put in a centrifuge tube containing 10 mL of DMEM

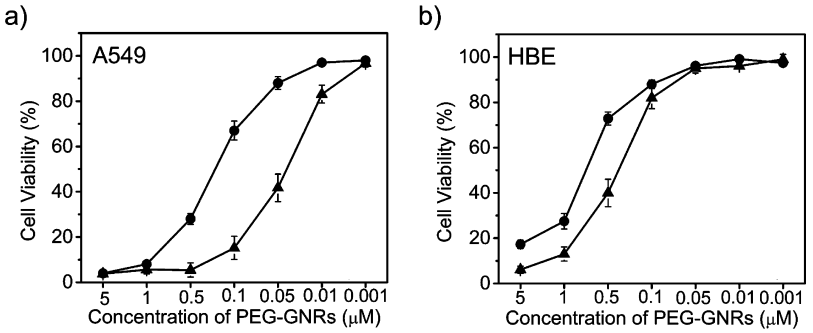


Figure 1. Effect of PEG-GNRs concentration on the viability of (a) A549 cells and (b) HBE cells. Cells were irradiated with (triangle) or without (sphere) a light dose of 0.4 W/cm^2 for 20 min.

with 10% FBS. At different time intervals, 2.0 mL of solution was taken out as the medium samples, and 2 mL of fresh DMEM with 10% FBS was added back to the incubation medium.

For cellular uptake study, the dried PEG-GNRs-loaded electrospun membrane was cut into 2 × 2 cm^2 pieces, weighted, and then placed in the cell culture mediums where the A549 cells and HBE cells were incubated. After 24 h, cells were digested by trypsin and lysed as the cell lysates samples.

All the samples (medium samples and cell lysates samples) were diluted with 2% HNO_3 to 10 mL. Inductively coupled plasma mass spectroscopy (ICP-MS) was used for the quantitative analysis of Au against the standard Au samples. All experiments were performed in triplicate, and the quantitative value was expressed as the mean ± standard deviation.

2.6. Photothermal Therapy and Cell Viability Assay. Different types of cells (cervical cancer HeLa cells, human lung carcinoma A549 cells, breast cancer MCF-7 cells, and human bronchial epithelial HBE cells) were seeded in 96-well plates with a density of 10 000 cells/well and allowed to attach for 24 h at 37 °C in a 5% CO_2 incubator before the treatment. For photothermal therapy using NIR radiation, we used a continuous-wavelength diode laser operating at 850 nm as a light source for irradiation. Cell viability was determined 2 days later after photothermal treatment, using a cell count kit-8 (CCK-8) (Kumamoto Techno Research Park, Japan). Each experiment was repeated three times, and data represented the mean ± standard deviation.

2.7. Fluorescence Imaging. A549 and HBE cells were washed with PBS for three times and stained with 5 μg/mL propidium iodide (PI). Cells were then washed and observed under a confocal microscope (FluoView FV1000, Olympus) with excitation at 561 nm.

2.8. Flow Cytometry Analysis. The cells were rinsed with PBS and then harvested by the use of trypsin. The suspension of cells was collected in a tube for flow cytometry analysis. Annexin-V-fluorescein isothiocyanate (FITC) and PI were used to stain apoptotic and dead cells. The cellular suspension (500 μL) was treated with PI (2.5 μL, Molecular Probes, 1 μg/mL stock, in dH_2O) and then analyzed by using a flow cytometer (Accuri C6, BD). The PI fluorescent signal was collected using a 625/25 BP filter. The data were analyzed using the CFlow software.

2.9. Statistical Analysis. The values were expressed as mean ± standard deviation (SD). Two-tailed Student's *t* test was used to discern the statistical difference between groups. A probability value (p) of less than 0.05 was considered statistically significant.

3. RESULT AND DISCUSSION

3.1. Selective Photothermal Effect of PEG-GNRs on Cancer Cells. Our strategy of preparing PEG-GNRs embedded membrane to selectively kill cancer cells is shown in Scheme 1. First, the PEG-GNRs were synthesized and characterized to examine their photothermal property and determine the proper amount of PEG-GNRs to be loaded in the membrane. Subsequently, the PEG-GNRs were embedded into the electrospun fibrous membrane. Their release and cell uptake profile were examined. Finally, the PEG-GNRs embedded membrane was evaluated upon NIR irradiation via in vitro experiments.

Herein, PEG-GNRs were synthesized as previously reported.[21] The PEG-GNRs had a uniform size (length 52 ± 7 nm, diameter 10.8 ± 1.5 nm) and exhibited the Zeta potential of +22.5 mV (Figure S1a, Supporting Information). As the zeta potential of the GNRs before PEG-modification was −8.9 mV, the successful conjugation of PEG was approved. The positive surface charge of PEG-GNRs promoted not only their cellular uptake but also stability in solutions.[22] The PEG-GNRs showed excellent water-solubility. They did not aggregate for at least 3 months in PBS containing 10% fetal bovine serum. Meanwhile they were dispersed well in DMF and acetone, the organic solvents for electrospinning. The maximum surface plasmon resonance absorption wavelength of the PEG-GNRs in the cell culture medium is 850 nm (Figure S1b). The absorption is at near-infrared region (NIR), where blood and soft tissue could be easily penetrated, making it possible to apply to inner tissues.[23]

The purpose of any cancer therapy is to destroy malignant cells without harming healthy cells. We then evaluated the cytotoxicity and selectivity of the synthesized PEG-GNRs. Cells were incubated in the PEG-GNRs-containing medium for 24 h and irradiated by an 850 nm NIR laser in an incubator under constant temperature of 37 °C to simulate physiological conditions. The laser beam and power density was fixed at 0.4 W/cm^2, a value generally used for in vitro and in vivo GNR-based photothermal therapy.[24] The laser illumination was uniform (beam diameter about 4 cm), and illumination time was provisionally assigned to 20 min according to the pre-experiments. The PEG-GNRs were stable without any obvious change in shape or UV absorption under the experiment conditions. The concentration of PEG-GNRs was varied to determine the optimal condition to differentiate the cancerous cells and normal cells. Both the lung cancer cell line, A549, and normal lung cell line, HBE, were tested.

Cells which had been 24 h incubated with a gradient concentration of PEG-GNRs were irradiated for 20 min. Then the cells were transferred to the normal culture medium without PEG-GNRs and kept culturing. Two days later, the viability of the cells was examined by CCK-8 assay. A significant cytotoxicity was observed for the cancer cells and cell viability decreased with the increase of PEG-GNRs concentration. The IC_{50} of PEG-GNRs was 0.035 μM for A549 cells by calculation (Figure 1a). However, at this concentration, there was only a slight change in the viability of HBE cells (92.7% at 0.035 μM). The IC_{50} for HBE cells was 0.31 μM, which is 1 order of

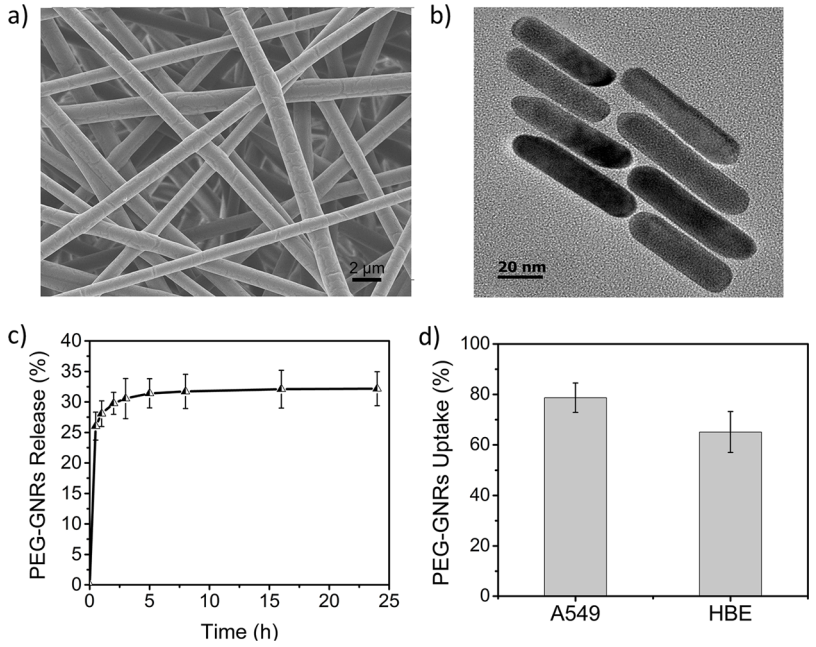


Figure 2. (a) Representative SEM image revealing the defined structures of PEG-GNR-loaded membrane (PLGA/PE = 85:15, PEG-GNRs 34.5 μg/mL). (b) Representative TEM image of PEG-GNRs released from the electrospun membrane. (c) Analysis of PEG-GNRs released at different times from the electrospun membrane in DMEM with 10% FBS. (d) Cellular uptake of PEG-GNRs in A549 and HBE cells.

magnitude higher than that of the cancerous cells (Figure 1b). As the in vitro quantitative assay comparing the cytotoxicity of PEG-GNRs with cancerous cells and normal cells has not been reported before, our result did indicate that NIR radiation of the PEG-GNRs can selectively induce cancer cell death without harming normal cells much under certain conditions. The high level selectivity ensures its low side-effects than radiotherapy and chemotherapy.

In addition, the photothermal effect of PEG-GNRs was verified with other cancer cell lines, such as cervical cancer HeLa (IC_{50} = 0.08 μM) and breast cancer MCF-7 (IC_{50} = 0.026 μM) (Figure S2, Supporting Information), which suggested that PEG-GNRs could be used as a general photothermal therapy converter for different cancerous cells. Moreover, the A549 cells without NIR irradiation showed much lower cytotoxicity with IC_{50} = 0.17 μM, demonstrating that the cytotoxicity of PEG-GNRs was relatively low and the NIR illumination promoted the therapy efficiency. Based on the results from Figure 1, we selected 0.1 μM as a proper concentration of PEG-GNRs which can remarkably inhibit the viability of cancer cells (17% for A549) but affect little for the normal HBE cells (81% viability) upon irradiation. According to the previous investigations on the toxicity of PEG-GNRs, 0.1 μM PEG-GNRs is a safe dosage for both in vitro and in vivo applications.[6,22]

3.2. Preparation of PEG-GNRs Embedded Membrane and the Uptake of Released GNRs by Cells. After confirming the good photothermal property of PEG-GNRs, we prepared the membrane to load with the GNRs. Two biocompatible and biodegradable materials, poly(lactide-*co*-glycolide) (PLGA) and diblock copolymer poly(ethylene glycol)-*b*-poly(lactide) (PEG-*b*-PLA), were selected to prepare the membrane, since they are the widely used as in vivo implant materials approved by the Food and Drug Administration (FDA), and the PEG-GNRs-loaded fibrous membrane was easily formed by electrospinning with the mixture solution of the two polymers and PEG-GNRs.[25−27] The release profile of the membrane could be controlled according to the actual reagent dosage requirements by adjusting the proportion of the two polymers.[17] The ratio of PLGA and PEG-*b*-PLA was chosen as 85/15 for its optimal property of antiadhesion and controlled drug release.[17]

Figure 2a shows the morphology of PEG-GNRs-loaded electrospun fibrous membrane, which is the same as that of the blank membrane without PEG-GNRs. The mean diameter of the membrane fibers was 0.98 ± 0.13 μm, and the contents of GNRs in the membrane were measured as 1 g membrane contained 34.5 μg PEG-GNRs. We also investigated the physical properties of PEG-GNRs released from the membrane in DMEM solution with 10% FBS. TEM images of the released PEG-GNRs showed no obvious difference from the original ones, and their photophysical properties were all the same as the synthesized PEG-GNRs (Figure 2b).

After incubating the cells with the PEG-GNRs embedded membrane, the amount of PEG-GNRs that released from the electrospun fibrous membrane and taken up by cells in the culture medium was measured by ICP-MS (Figure 2c and d). As shown in Figure 2c, there was an initial burst release that reached about 30% of embedded PEG-GNRs in 2 h. The remaining PEG-GNRs (70%) were released steadily in 3 months with the membrane degradation (Figure S3, Supporting Information), and the total released PEG-GNRs in 3 months was almost equal to that of the PEG-GNRs embedded in the membrane.[17] Furthermore, we checked the Au content on the surface of the electrospun fibers (within the depth of 10 nm). The result showed that 23% PEG-GNRs was located on or nearby the surface layer of fibers, which was consistent to the data on the initial PEG-GNR release (Figure 2c). The 3 month release profile suggested the remaining GNRs were dispersed evenly in the electrospun fibers. The initial burst promises a suitable local concentration of PEG-GNRs for effective

photothermal therapy and the sustained release could maintain the concentration for long time anticancer recurrence.

Figure 2d illustrates the amount of PEG-GNRs taken by the A549 and HBE cells after 24 h incubation. More PEG-GNRs were detected in A549 cells than in HBE cells (78% vs 63%), which was possibly due to different cellular pathways of the nanorods in cancerous cells and normal cells.[7]

3.3. Photothermal Effect of PEG-GNRs-Embedded Membrane. Next, we investigated whether the PEG-GNRs released from the PEG-GNRs embedded membrane reserved the photothermal therapy ability. The electrospun fibrous membrane with a suitable dosage of PEG-GNRs (0.34 μM in the electrospun solution) which can release 0.1 μM PEG-GNRs in 2 h was used. With the released PEG-GNRs, the temperature of the solution could be heated to 42 °C under NIR 20 min irradiation (Figure S4, Supporting Information), which is a proper temperature for photothermal therapy of cancer.[5]

A549 cells and HBE cells were tested as models for cancerous cells and normal cells. Cells were incubated respectively with the PEG-GNRs-loaded membrane, PEG-GNRs solution, blank membrane, or normal medium as the control respectively for 24 h before irradiation at 850 nm for 20 min. After the irradiation treatment, cells were cultured for another 2 days, and the status of cells was quantified by flow cytometry with Annexin V-FITC and PI double staining. As Annexin V is a potent reagent to detect apoptotic cells and PI is used to label dead cells, the Annexin V- negative/PI-negative cells were live cells, Annexin V-positive/PI-negative cells were apoptotic cells, and Annexin V-positive/PI- positive cells were dead cells.[29] We analyzed the populations of these three cell types under different conditions. As shown in Figure 3a, A549 cells incubated with PEG-GNRs-loaded membrane exhibited a remarkable cytotoxicity (16% alive) which is consistent with those incubated in 0.1 μM PEG-GNRs solution (12% alive).

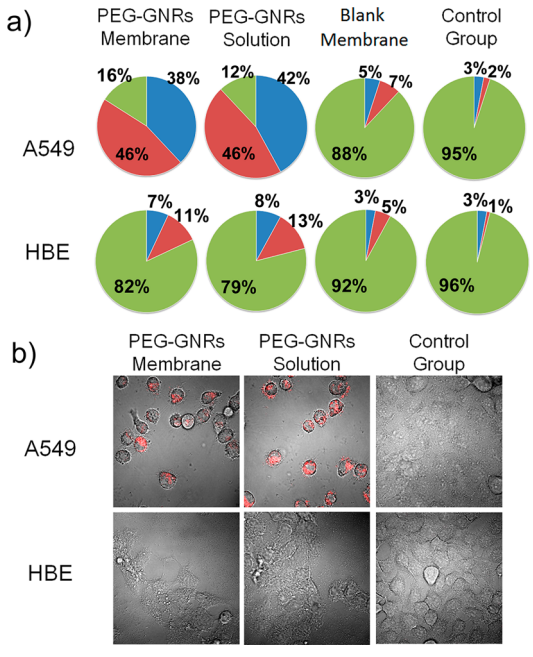


Figure 3. (a) Flow cytometry results of Annexin-V and PI double stained cells pretreated under different conditions. (b) Overlapped images of optical and fluorescence imaging of PI stained cells pretreated with or without the PEG-GNRs-embedded membrane.

The populations of the apoptotic cells in these two groups were also similar.

On the other hand, the majority of HBE cells which were incubated with either PEG-GNRs loaded membrane or PEG-GNRs solution were alive (82%, 79%). Most of A549 cells and HBE cells pretreated with blank membrane or the normal medium were also alive. This indicated neither the membrane nor PEG-GNRs had cytotoxicity in vitro. According to the in vivo characterization of toxicity and biodistribution of PEG-GNRs in previous studies, their toxicity and organ accumulation are relatively low.[22] Since 0.1 μM (3.45 μg/mL) of PEG-GNRs is much smaller than the concentration used in the previous reports (39−195 μg/mL), the safety of our PEG-GNRs embedded membrane can be expected for in vivo application.[28]

In addition, confocal microscopy images of cells with PI staining were carried out to verify the cell status (Figure 3b). All the HBE cells showed minor fluorescence signals. In contrast, A549 cells pretreated by PEG-GNRs-loaded membrane or PEG-GNRs-containing solution showed a positive PI incorporation. These results proved that the photothermal properties of PEG-GNRs were not affected in the process of either electrospinning or membrane loading, thus the PEG-GNRs embedded membrane can be applied for photothermal therapy.

To further investigate the experimental conditions which can kill cancerous cells while minimizing injury to normal cells for the PEG-GNRs-embedded membrane, we systematically varied the released PEG-GNRs concentration and irradiation time, and then quantified the population of dead cells under each condition by flow cytometry with PI staining. Although with the increasing PEG-GNRs concentration, more cells died for both A549 and HBE cells, and the effect of hyperthermia was much more serious for the A549 cells (e.g., 47% dead cells at 0.1 μM PEG-GNRs) than HBE cells (e.g., 10% dead cells at 0.1 μM PEG-GNRs). In contrast, the A549 cells without exposure to NIR laser had a low percentage of dead cells (12%). Moreover, the percentage of dead cells increased at longer exposure times (Figure 4b). It is a significant advantage in clinical application that the platform possesses the capability to control the therapy effect externally by adjusting irradiation time to satisfy the actual needs. As previous studies demonstrated, the efficacy of photothermal treatment is positive correlation to the exposition time and the power of laser irradiation.[30,31] The specific treatment condition should be adjusted according to the actual needs. Notably, the NIR irradiation showed no toxicity to the cells which were not incubated with PEG-GNRs-loaded membrane. According to our results (Figure 4), 20 min is a proper exposure time and 0.1 μM PEG-GNRs were the proper conditions for the largest A549/HBE killing ratio.

Cell proliferation is another reliable indicator for the evaluation of therapeutic effect.[32,33] After incubation with PEG-GNRs membranes or blank membranes for 24 h, we irradiated the A549 and HBE cells for 20 min and cultured them for another 48 h. Cells treated with irradiation but without any membrane were also examined as the control. The cell numbers were calculated by flow cytometry and normalized by the untreated cells (Figure 4c). The A549 cell proliferation was strongly arrested in the PEG-GNRs-loaded membrane treated group (38%) comparing to the blank membrane treated group (83%). HBE cells pretreated by PEG-GNRs-loaded membrane did not exhibit significant proliferation arrest (86%).

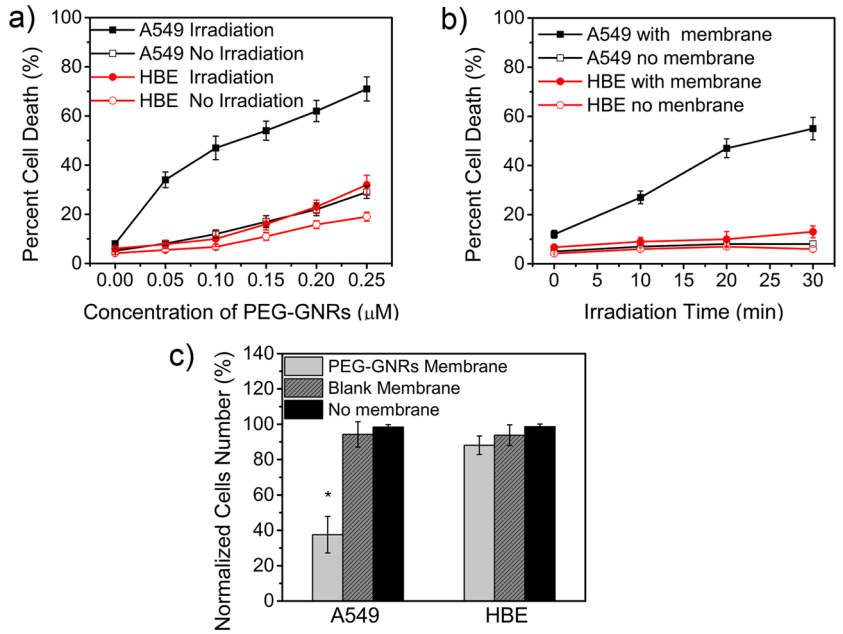


Figure 4. (a, b) Photothermal-mediated cytotoxicity of A549 and HBE cells after incubating cells with the PEG-GNR-embedded membrane under different conditions. (a) Incubation of the cells with different concentrations of PEG-GNRs released from the membrane. (b) Irradiation of the cells with different times. (c) Inhibition of cell proliferation after incubating the cells with the PEG-GNR-embedded membrane for 2 days. The cell numbers were calculated by flow cytometry and normalized by the untreated cells.

The results all confirmed that illumination of the PEG-GNRs-loaded membrane destroyed the cancer cells and inhibited cancer cell proliferation inhibition with high specificity.

In the current strategies of photothermal therapy, the photothermal converters are administrated by intravenous injection or direct injection, and the accumulation of the reagents in liver and spleen is inevitable after the high concentration of converters enter into the systematic circulation.[8,10] Although gold nanoparticles are biocompatible, their stable accumulation raises concern of potential hazards in the long term.[5] In this work, we proposed a new design of the photothermal converter administration, where the reagents can be sustained released from membranes. Our new method of using nanomaterial embedded membrane has several advantages. For example, local release of PEG-GNRs ensures their easy accumulation around cancer cells for effective hyperthermia. It also facilities the photothermal converters targeting to the tumors which are inaccessible by intravenous injection, such as brain tumor due to the blood-brain barrier. The sustained release profile of PEG-GNRs benefits a long-time prevention of cancer recurrence. Moreover, PEG-GNRs could be easily conjugated with chemotherapy agents to further improve the therapy effect or positron emission tomography (PET) imaging reagent to have dual functions.[34] Recently, an electrospun polysterene fiber loaded with iron oxide nanoparticles (IONPs) has been developed to keep the IONPs inside fibers without leaking and enhance magnetic hyperthermia through repeated heating of cancer cells.[35] In our approach, we make use of the nanoparticles leaking from the biodegradable fiber, which is easier to achieve. Moreover, as the biodegradable membranes are widely used in the surgical lesion, no extra effort is needed to introduce the membranes to the tumors. Therefore, the GNRs embedded biodegradable membrane developed in this study holds a great potential in clinical application.

4. CONCLUSIONS

In summary, we have designed a new platform for cancer therapy, an electrospun PLGA/PEG-b-PLA fibrous membrane loaded with PEG-GNRs. In this platform, the polymer membrane served as both the carrier for PEG-GNRs and the physical barrier on the surgical lesion, providing excellent biocompatibility, controllability of PEG-GNRs in situ release, antiadhesion properties, and prevention of tumor spreading. We have demonstrated that the use of PEG-GNRs embedded membrane could selectively kill the cancerous cells and inhibit their proliferation upon 850 nm irradiation though in vitro experiments. It is expected to be a promising platform for cancer therapy.

■ ASSOCIATED CONTENT

Supporting Information

TEM images of PEGylated GNRs, UV−visible absorbance spectrum of the GNRs before and after PEG conjugation, effects of PEG-GNRs concentration on the viability of HeLa cells and MCF-7 cells, release profile of PEG-GNRs from electrospun membrane for three months, release profile of PEG-GNRs from membrane with or without NIR irradiation, temperature change of the cell medium containing PEG-GNRs after the NIR irradiation. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

[§]M.C. and H.W. contributed equally. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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