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Gold Nanoparticle Mediated Photo-Chemotherapy

James Ramos[1], David Taylor[2] and Kaushal Rege[2]*

[1]School of Biological and Health Systems Engineering, Arizona State University, 501 E. Tyler Mall, ECG 301, Tempe, AZ 85287-6106, USA
[2]Chemical Engineering, Arizona State University, 501 E. Tyler Mall, ECG 301, Tempe, AZ 85287-6106, USA

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Surgery, radiation, and chemotherapy are the most common methods of combating cancer diseases. Despite several successes in treatment, it is necessary to develop better strategies that are capable of destroying cancer cells while limiting off-target damage of non-malignant cells. Nanotechnology offers exciting options for the site-selective delivery of current treatments to cancer cells [1]. Nanoparticle (NP)-based therapeutics involve the ability to engineer novel nanoscale platforms that can combine different treatment and in some cases, imaging modalities for a more aggressive, yet safer approach for cancer cell ablation. Whereas free chemotherapeutic drugs may diffuse non-specifically in tissues, NP-based delivery vehicles can localize into tumors due to the enhanced permeation and retention (EPR) effect. In addition, modification of NPs with appropriate ligands facilitates cancer cell targeting (i.e., molecules that bind to specific receptors overexpressed on cancer cells). Consequently, several classes of nanocarriers have been engineered for delivery of a wide range of cancer chemotherapeutics [2]. Of these systems, those based on gold NPs have received increasing attention for applications in drug delivery and imaging [3]. Gold particles exhibit unique optical properties when reduced to the nanoscale, and engineered to certain geometries. Surface plasmon resonance of gold nanoparticles allows them to strongly absorb and scatter incident light as well as convert resonant energy to heat. Several classes of gold nanoparticles have been engineered such that their plasmon resonance is tuned to near infrared (NIR) wavelengths, which allows them to absorb and convert this energy to heat leading to hyperthermic temperatures of surrounding media [4,5]. As a result, gold nanoparticles (GNPs) have received increased attention for localized administration of hyperthermia for cancer cells ablation, and this approach is currently in early clinical trials [6]. While hyperthermic treatments represent a promising approach for cancer therapy, they suffer from non-uniform heat distribution especially in areas located near large blood vessels, where heat can dissipate rapidly to circulating blood [7]. Additionally, hyperthermia is limited by cellular thermotolerance, whereby cells treated with low intensity repeated hyperthermic treatments are able to maintain viability due to an array of cell survival responses [8,9]. Combinatorial/synergistic treatments for cancer therapy can be developed by engineering NP-based systems that can be employed for simultaneously engendering hyperthermia and delivering chemotherapeutic drugs for enhanced ablation of cancer cells. In addition, hyperthermia increases tumor tissue perfusion, allowing easier absorption of chemotherapeutic drugs through cell membranes, leading to greater efficacies between the two treatments (i.e., hyperthermia and the delivered chemotherapeutic drug). Indeed, hyperthermia has been shown to reduce tumor resistance to various chemotherapeutic drugs including doxorubicin, cisplatin, bleomycin, nitrosoureas, and cyclophosphamide [10-12]. The ability to combine drug delivery and photothermal therapy on GNP-based delivery platforms has potential for higher efficacies of cancer cell ablation. This GNP-based photochemotherapy approach is a versatile strategy in which, drugs that kill cancer cells by diverse mechanisms can be employed in combination with photothermal ablation. Several studies have demonstrated the ability of different GNP-based platforms for the delivery of cancer cell-targeted chemotherapeutics, and the simultaneous NIR light-based induction of hyperthermia. For example, the antineoplastic drug doxorubicin, has been loaded into hollow gold nanospheres (HAuNS) [7,13], hollow gold nanoshells [14], and poly(ethylene glycol)-poly(lactic-co-glycolicacid)-Au half-shell nanoparticles (DOX-PLGA-Au H-S NPs) [15,16] for dual delivery of the drug and simultaneous application of NIR photothermal therapy. Similarly, gold nanoshells on silica nanorattles (GSNs) [17] have been investigated for delivery of the anti-cancer therapeutic docetaxel and simultaneous application of NIR photothermal therapy. Our group has investigated elastin-like polypeptide (ELP)-gold nanorod nanocomposites for dual delivery of the anti-cancer drug, 17-AAG simultaneously with NIR photothermal therapy [18]. Interestingly, the drugs used in these studies, ablate cancer cells via different mechanisms; doxorubicin is a DNA intercalating agent that inhibits DNA synthesis [19], docetaxel is a microtubule stabilizing agent that limits mitosis [20], and 17-AAG is an inhibitor of heat shock protein 90 (HSP90) which is a prosurvival protein that allows cells to resist hyperthermia [21]. In both, *in vitro* and *in vivo* studies, the combined chemotherapeutic drug and photothermal treatments using drug-loaded GNP platforms exhibited improved, and in some cases, complete cancer cell/tumor destruction, when compared to the GNP platform or drug alone. In addition, NIR treatment also aided controlled release of the loaded drug from the GNPs. Although GNP-induced hyperthermia is a promising approach for cancer cell ablation, one major limitation of administering this treatment is the depth of penetration of NIR light.

Currently, the most advanced NIR laser systems are limited to a penetration depth in soft tissue of up to approximately 2 cm [22]. This limits the application of hyperthermia treatments, including those based on GNPs, to topical or near-surface applications. However, due to this depth limitation, alternative techniques have been pursed in order to reach increased depths. Using minimally invasive interventional techniques, fibres inserted directly into tumors/tissues have been investigated for administration of laser-based hyperthermic treatment for primary and metastatic liver cancer [23-25] as well as in lung metastases [26]. In addition, delivery of NP-based therapies for combination photo-chemotherapy can also be applied to inoperable, advanced diseases, as well as in combination with surgery [7]. As studies continue to emerge for the use of GNP platforms for combined drug delivery and photothermal therapy, their potential for increased

***Corresponding author:** Kaushal Rege, Chemical Engineering, Arizona State University, 501 E. Tyler Mall, ECG 301, Tempe, AZ 85287-6106, USA, Tel: 480-727-8616; Fax: 480-727-3292; E-mail: kaushal.rege@asu.edu

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efficacies of cancer cell eradication will continue to be highlighted. It will also become increasingly important to design and investigate mechanism-based combination treatments that overcome cancer cell resistance. The integration of emerging imaging techniques that allow for *in vitro* and *in vivo* imaging of GNPs including NIR-induced two-photon luminescence [27,28], photoacoustic imaging [29] and dark field imaging [30] can allow for image-guided combination treatments to tumors. It is increasingly evident that multifunctional GNPs have tremendous potential as emerging theranostic platforms for simultaneous administration of hyperthermia and chemotherapeutic drugs, together with imaging, for applications in cancer treatment.

References

1. Jelveh S, Chitrani DB (2011) Gold Nanostructures as a Platform for Combinational Therapy in Future Cancer Therapeutics. Cancers 3: 1081-1110.
2. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, et al. (2007) Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol 2: 751-760.
3. Chithrani B, Devika (2010) Nanoparticles for improved therapeutics and imaging in cancer therapy. Recent Pat Nanotechnol 4: 171-180.
4. Chatterjee DK, Diagaradjane P, Krishnan S (2011) Nanoparticle-mediated hyperthermia in cancer therapy. Therapeutic Delivery 2: 1001-1014.
5. Kennedy LC, Bickford LR, Lewinski NA, Coughlin AJ, Hu Y, et al (2011) A New Era for Cancer Treatment: Gold-Nanoparticle Mediated Thermal Therapies. Small **7**: 169-183.
6. Pilot Study of AuroLase (tm) (2012) Therapy in Refractory and/or Recurrent Tumors of the Head and Neck. cited October.
7. You J, Zhang R, Xiong C, Zhong M, Melancon M, et al (2012) Effective Photothermal Chemotherapy Using Doxorubicin-Loaded Gold Nanospheres that Target EphB4 Receptors in Tumors. Cancer Res 72: 4777-4786.
8. Cherukuri P, Glazer ES, Curley SA (2010) Targeted Hyperthermia Using Metal Nanoparticles. Adv Drug Deliv Rev 62: 339-345.
9. Hildebrandt B, Wust P, Ahlers O, Dieing A, Sreenivasa G, et al. (2002) The cellular and molecular basis of hyperthermia. Critical Reviews in Oncology/ Hematology 43: 33-56.
10. Martirosyan KS (2012) Thermosensitive Magnetic Nanoparticles for Self-Controlled Hyperthermia Cancer Treatment. J Nanomed Nanotechnol 3.
11. Kampinga HH (2006) Cell biological effects of hyperthermia alone or combined with radiation or drugs: a short introduction to newcomers in the field. Int J Hyperthermia 22: 191-196.
12. Dayanc BE, Beachy HS, Ostberg JR, Repasky AE, et al. (2008) Dissecting the role of hyperthermia in natural killer cell mediated anti-tumor responses. Int J Hyperthermia 24: 41-56.
13. You J (2012) Photothermal chemotherapy with doxorubicin-loaded hollow gold nanospheres: A platform for near-infrared light-triggered drug release. Journal of Controlled Release 158: 319-328.
14. Wu C, Yu C, Chu M (2011) A gold nanoshell with a silica inner chell synthesized using liposome templates for doxorubicin loading and near-infrared photothermal therapy. International Journal of Nanomedicine 6: 807-813.
15. Lee SM, Park H, Choi JW, Park YN, Yun CO, et al. (2011) Multifunctional Nanoparticles for Targeted Chemophotothermal Treatment of Cancer Cells. Angew Chem Int Ed 50: 7581-7586.
16. Park H, Yang J, Lee J, Haam S, Choi IH, et al. (2009) Multifunctional Nanoparticles for Combined Doxorubicin and Photothermal Treatments. ACS Nano 3: 2919-2926.
17. Liu H, Chen D, Li L, Liu T, Tan L, et al. (2011) Multifunctional Gold Nanoshells on Silica Nanorattles: A Platform for Combination of Photothermal Therapy and Chemotherapy with Low Systemis Toxicity. Angew Chem Int Ed 50: 891-895.
18. Huang HC, Yang Y, Nanda A, Koria P, Rege K (2011) Synergistic administration of photothermal therapy and chemotherapy to cancer cells using polypeptide-based degradable plasmonic matrices. Nanomedicine 6: 459-473.
19. Taylor DJ, Parsons CE, Han H, Jayaraman A, Rege K (2011) Parallel screening of FDA-approved antineoplastic drugs for identifying sensitizers of TRAIL-induced apoptosis in cancer cells. BMC Cancer 11: 18.
20. Clarke SJ, Rivory LP (1999) Clinical pharmacokinetics of docetaxel. Clinical Pharmacokinetics 36**:** 99-114.
21. Zhang H, Burrows F (2004) Targeting multiple signal transduction pathways through inhibition of Hsp90. Journal of Molecular Medicine 82: 488-499.
22. Gu Y, Chen WR, Xia M, Jeong SW, Liu H, et al. (2005) Effect of photothermal therapy on breast tumor vascular contents: noninvasive monitoring by near-infrared spectroscopy. Photochem Photobiol 81**:** 1002-1009.
23. Gough-Palmer AL, Gedroyc WMW (2008) Laser Ablation of hepatocellular carcinoma-A review. World J Gastroenterol 14: 7170-7174.
24. Vogl THJ, Straub R, Zangos S, Mack MG, Eichler K (2004) MR-guided laser-induced thermotherapy (LITT) of liver tumours: experimental and clinical data. Int J Hyperthermia 20: 713-724.
25. Vogl TJ, Straub R, Eichler K, Söllner O, Mack MG (2004) Colorectal carcinoma metastases in liver: laser-induced interstitial thermotherapy local tumour control rate and survival data. Radiology 230: 450-458.
26. Rosenberg C, Puls R, Hegenscheid K, Jens Kuehn J, Bollman T, et al. (2009) Laser ablation of metastatic lesions of the lung: long-term outcome. AJR Am J Roentgenol 192: 785-792.
27. Li JL, Gu M (2010) Surface plasmonic gold nanorods for enhanced two-photon microscopic imaging and apoptosis induction of cancer cells. Biomaterials 31: 9492-9498.
28. Vu L (2012) Generation of a Focused Poly (amino ether) Library: Polymer-mediated Trangene Delivery and Gold-Nanorod based Theranostic System. Theranostics.
29. Li PC, Wang CRC, Shieh DB, Wei CW, Liao CK (2008) *In vivo* Photoacoustic Molecular Imaging with Simultaneous Multiple Selective Targeting Using Antibody-Conjugated Gold Nanorods. Optics Express 16: 18605-18615.
30. Huang K, Ma H, Liu J, Huo S, Kumar A, et al. (2012) Size-Dependent Localization and Penetration of Ultrasmall Gold Nanoparticles in Cancer Cells, Multicellular Spheriods, and Tumors *in Vivo*. ACS Nano 6: 4483-4493.