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Review Article

Nanophotonics for Molecular Diagnostics and Therapy Applications

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Light has always fascinated mankind and since the beginning of recorded history it has been both a subject of research and a tool for investigation of other phenomena. Today, with the advent of nanotechnology, the use of light has reached its own dimension where light-matter interactions take place at wavelength and subwavelength scales and where the physical/chemical nature of nanostructures controls the interactions. This is the field of nanophotonics which allows for the exploration and manipulation of light in and around nanostructures, single molecules, and molecular complexes. What is more is the use of nanophotonics in biomolecular interactions—nanobiophotonics—has prompt for a plethora of molecular diagnostics and therapeutics making use of the remarkable nanoscale properties. In this paper, we shall focus on the uses of nanobiophotonics for molecular diagnostics involving specific sequence characterization of nucleic acids and for gene delivery systems of relevance for therapy strategies. The use of nanobiophotonics for the combined diagnostics/therapeutics (theranostics) will also be addressed, with particular focus on those systems enabling the development of safer, more efficient, and specific platforms. Finally, the translation of nanophotonics for theranostics into the clinical setting will be discussed.

1. Introduction

Nanophotonics deals with the interaction of light with matter at a nanometer scale, providing challenges for fundamental research and opportunities for new technologies, encompassing the study of new optical interactions, materials, fabrication techniques, and architectures, including the exploration of natural and synthetic, or artificially engineered, structures such as photonic crystals, holey fibers, quantum dots, subwavelength structures, and plasmonics [1, 2]. The use of photonic nanotechnologies in medicine is a rapidly emerging and potentially powerful approach for disease protection, detection, and treatment. The high speed of light manipulation and the remote nature of optical methods suggest that light may successfully connect diagnostics, treatment, and even the guidance of the treatment in one theranostic procedure combination of therapeutics with diagnostics (including patient prescreening and therapy monitoring).

Limitations in medical practice are closely associated with the fact that diagnostics, therapy, and therapy guidance are three discrete and isolated stages. In order to overcome some of the sensitivity and specificity of current medicines, theranostics unites the three above stages in one single process, supporting early-stage diagnosis and treatment [3, 4]. Nowadays, there is an ever increasing need to enhance the capability of theranostics procedures where nanophotonics-based sensors may provide for the simultaneous detection of several gene-associated conditions and nanodevices utilizing light-guided and light-activated therapy with the ability to monitor real-time drug action (see Figure 1).

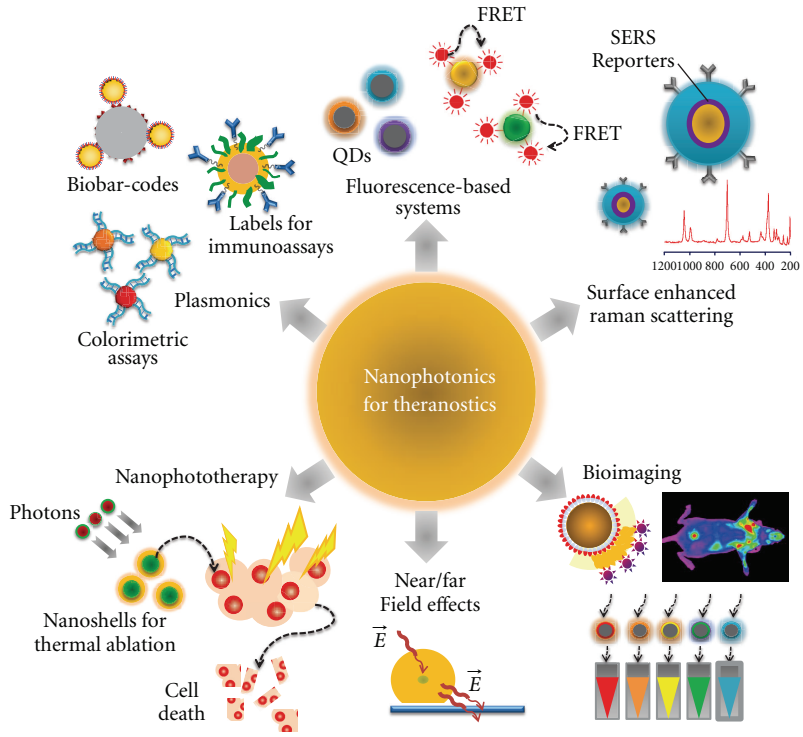

FIGURE 1: *Nanophotonics for theranostics*. Nanoparticles-based strategies can be used for biosensing using *plasmonic nanosensors*, such as metal nanoparticles functionalized with nucleic acid strand for colorimetric assays and biobar codes for protein detection or intense labels for immunoassays. Some nanoparticle systems can also be used for sensing by exploring a typical *FRET system* or can be surrounded with *Raman reporters* in order to provide *in vivo* detection and tumour targeting. In fact, NPs symbolize an important class of materials with unique features suitable for *biomedical imaging* applications such as increased sensitivity in detection and high quantum yields for fluorescence. Alternatively, NPs can survey *near/far field* enhancing qualities that hold promise for a bounty of novel applications in optics and photonics. Engineered NPs can also act as *phototherapeutic agents* that can be attached to specific targets for selective damage to cancer cells.

2. Nanophotonics For Diagnostics

2.1. Surface Plasmons on Nanoparticles and Surfaces. Surface plasmons are collective charge oscillations that occur at the interface between conductors and dielectrics. They can take various forms, ranging from freely propagating electron density waves along metal surfaces to localized electron oscillations on metal nanoparticles (NPs) [5, 6]. When light passes through a metal nanoparticle, it induces dipole moments that oscillate at the respective frequency of the incident wave, consequently dispersing secondary radiation in all directions. This collective oscillation of the free conduction electrons is called localized surface plasmon resonance (LSPR). Light on NP induces the conduction electrons to oscillate collectively with a resonant frequency that depends on the nanoparticles' size, shape, composition, interparticle distance, and environment (dielectric properties) [7–10]. As a result of these SPR modes, the nanoparticles absorb and scatter light so intensely that single NPs are easily observed by eye using dark-field (optical scattering) microscopy. Plasmonic NPs provide a nearly unlimited photon resource for observing molecular binding for longer periods of time, once they do not blink or bleach like fluorophores [11].

Nanoparticle-based colorimetric assays for diagnostics have been a subject of intensive research, where LSPR can be used to detect DNA or proteins by the changes in the local index of refraction upon adsorption of the target molecule to the metal surface. Due to the intense SPR in the visible yielding extremely bright colors, gold nanoparticle colloids have been widely used of molecular diagnostics. In fact, gold nanoparticles (AuNPs) functionalized with ssDNA capable of specifically hybridizing to a complementary target for the detection of specific nucleic acid sequences in biological samples have been extensively used [12–27]. Other approaches use the AuNPs' plasmonic as a core/seed that can be tailored with a wide variety of surface functionalities to provide highly selective nanoprobes for diagnostics [28] or the SPR scattering imaging or SPR absorption spectroscopy generated from antibody-conjugated AuNPs in molecular biosensor techniques for the diagnosis of oral epithelial living cancer cells *in vivo* and *in vitro* [29] and the use of multifunctional AuNPs which incorporate both cytosolic delivery and targeting moieties on the same particle functioning as intracellular sensors to monitor actin rearrangement in live fibroblasts [30].

Plasmonic NPs have also been used as extremely intense labels for immunoassays [31–34] and biochemical sensors [19, 35–37]. Also, the use of colloidal silver plasmon resonant particles (PRPs) coated with standard ligands as target-specific labels has been reported for *in situ* hybridization and

immunocytology assays [34]. Most notably, a nanoparticle-based Biobar code has been developed for the detection of proteins that relies on magnetic microparticle probes with antibodies that specifically bind a target of interest and nanoparticle probes that are encoded with DNA that is unique to the protein target of interest and antibodies that can sandwich the target captured by the microparticle probes [33]. Haes and coworkers have reported on an optical biosensor based on localized surface plasmon resonance spectroscopy developed to monitor the interaction between the antigen, amyloid-β-derived diffusible ligands (ADDLs), and specific anti-ADDL antibodies, used in the detection of a biomarker for Alzheimer's Disease [35].

2.2. Raman-Spectroscopy-Based Systems. When light interacts with a substance, it can be absorbed, transmitted, or scattered. Scattered radiation can result from an elastic collision (Rayleigh scattering) or inelastic (Raman scattering). Raman spectroscopy is based on a change of frequency when light is inelastically scattered by molecules or atoms resulting in a molecular fingerprint information on molecular structure or intermolecular interaction of a specific process or molecule. The potential of Raman spectroscopy as biomedical diagnostics tool is rather low due to its low cross-section ($\sim 10^{-30}\,\mathrm{cm}^2$) that results in low sensitivity [38]. However, in 1977, two groups independently described the use of noble metal surfaces to enhance the Raman scattering signal of target molecules [39, 40]—Surface enhancement raman spectroscopy (SERS). Jeanmaire and Van Duyne proposed a twofold electromagnetic field enhancement that was later associated with the interaction between the incident and scattered photons with the nanostructure's LSPR [41]. Simultaneously, Albrecht and Creighton suggested the source of the enhancement to be caused by a specific interaction between an adsorbate and the nanoparticle surface, briefly, a charge transfer from the adsorbate into the empty energetic levels on the metal surface or from the occupied levels of the nanoparticle's surface to the adsorbate [42–44].

Generally, SERS requires that the biological analyte reaches a suitable surface where the substrates are treated as two-dimensional macroscopic surfaces onto which adsorbed molecules suffer a local-field enhancement. Despite direct adsorption not being a good solution because of its dependence on the affinity between substrate and analyte, a method to identify and distinguish different strains of virus based on signal differences generated by the surface amino-acids using silver nanorods has been successfully developed [45]. Using a similar approach of direct adsorption, Pînzary et al. used naked silver nanoparticles to differentiate *in situ* healthy colon from carcinoma colon tissue [46]. Nanotags have been widely employed to address the lack of specificity [47, 48]. These nanotags usually possess a metallic colloidal core functionalized with a Raman reporting molecule and the specific molecule used to capture the analyte and have been used to directly detect DNA sequences [49, 50] and amplified DNA products of epizootic pathogens using complementary DNA strands so that only the complementary target hybridizes with the probes [51]. Using a similar system, but exploring the distance-dependent enhancement of the electromagnetic field with a hairpin probe molecule, Wabuyele has also been used to distinguish single nucleotide polymorphisms in cancer-related genes [52]. Combining nanotags with other nanoparticles or binding surfaces that target the same analyte in a sandwich conformation proved useful to detect antibodies in serum [53]. A similar approach using a flat substrate instead of NPs had already been proposed to detect DNA, RNA, and proteins [54, 55]. However, in this approach, the substrate is used only to immobilize the analyte; a gold-nanoparticle-based nanotag is used to identify the analyte and the surface enhancement is obtained by silver coating of the nanotag. miRNA profiling has also been pursued via a slightly different approach based on the hybridization of the target molecules with a thiolated oligonucleotide and subsequent functionalization on a silver substrate [56]. SERS have also been explored to identify changes in the analyzed system such as interaction between DNA and xenobiotic molecules like cisplatin [57] or DNA-binding proteins [58, 59]. The combination of magnetic iron/gold core-shell nanoparticles with gold nanorods has also been used to specifically enumerate *E. coli* in water samples in a rapid and sensitive test [60]. In this case, the magnetic nanoparticles are used to concentrate the bacteria, improving the Raman signal by concentration and the posteriorly added gold nanorods serve as Raman signal enhancers.

SERS can also be used in conjunction with colloidal gold to detect and target tumors *in vivo*, where the AuNPs are surrounded with Raman reporters that provide light emission 200 times brighter than quantum dots [61, 62]. It was also found that the Raman reporters became more stable and yielded larger optical enhancements when NPs were encapsulated with a thiol-modified polyethylene glycol coat, which also allows for increased biocompatibility and circulation times *in vivo*. When conjugated to tumor-targeting ligands, these conjugated SERS-NPs were able to target tumor markers at surface of malignant cells, such as epidermal growth factor receptor (EGFR) that is sometimes overexpressed in cells of certain cancer types [29] and used to locate the tumor in xenograft tumor models [50].

2.3. Fluorescence-Based Systems. Quantum dots (QDs) are semiconductor nanoparticles with narrow, tunable, symmetrical emission spectra, and high quantum yields [63–65], and together with compatibility with DNA and proteins, make QDs exceptional substitutes as fluorescence labels. The use of QDs for nucleic acid characterization has long been proposed, for example, CdSe/ZnS QDs for SNP identification on human TP53 gene, multiallele detection of hepatitis B and C viruses [66], and *in situ* detection of chromosome abnormalities and mutations [67]. QDs have also been used as chemical sensors by exploring a typical FRET system where a dark quencher is placed at a protein-binding site attached to a QD surface. The quantum dots emission is quenched in presence of the analyte and upon analyte displacement the emission is restored [68]. A simpler approach was used to detect adenine using fluorescent ZnS nanoparticles at pH7, making use of capability of

adenine itself to quench emission of the quantum-dot-like nanoparticles [69].

Several studies report on the modulation of fluorophores at the vicinity of nanoparticles (e.g., gold, silver, and quantum dots) [70, 71], an interaction that has found application in a variety of systems to detect biologically relevant targets with particular focus upon AuNPs due to their ease in functionalization with biomolecules [72–75]. Several methods based on the quenching of fluorescence have been proposed for DNA detection consisting of fluorophore-labeled ssDNA electrostatically adsorbed onto gold nanoparticles [76], carbon nanotubes [77], and carbon nanoclots [78], where the presence of a complementary target triggers desadsorption of the newly formed dsDNA from the nanostructures due to the electrostatic variation between ssDNA and dsDNA, and fluorescence emission is restored. Also, fluorescence quenching of fluorophores close to metal nanoparticles functionalized with thiol-modified oligonucleotides has been explored in different conformations. Tang and co-workers proposed a method to probe hydroxyl radicals using an AuNP-oligonucleotide-FAM system where the hydroxyl radical promotes strand breakage and consequent release of FAM, restoring the previously quenched fluorescence [79]. The same quenching mechanism was used to detect specific DNA strands using two probes (one with an AuNP label and another labeled with TAMRA) that hybridize to two DNA sequences near each other [80], bringing the fluorophore and AuNP close enough to quench fluorescence emission.

Proteins have also been probed through nanoparticle-fluorescence-mediated systems, for example, human blood proteins have been let to interact with fluorescent AuNPs and detected through quenching [81]. In another example, a sandwich immunoassay using AuNPs quenching has been proposed for the detection of the protein cardiac troponin T by its interaction with two different antibodies, one attached to AuNPs and the other labeled with fluorescent dyes [82]. By means of an opposite modulation, infrared fluorescent nanoparticles showed enhanced fluorescence when interacting with protein [83].

A popular application of fluorescence modulation by nanoparticles has been specific ion sensing. Su and co-workers developed a copper sensor by covering fluorescent DNA-Cu/Ag nanoclusters with mercaptopropionic acid which quenches the intrinsic fluorescence of the nanoparticle; in the presence of Cu^{2+}, the capping agent is oxidized to form a disulfide compound resulting in release of the nanoparticle and restoration of emission suitable for quantification between 5 and 200 nM [84]. A very specific colorimetric and fluorimetric method to detect Hg^{2+} ions was developed with porphyrin-modified $Au@SiO_2$ nanoparticles, where the intensively fluorescent red complex turns green and weakly fluorescent in presence of Hg^{2+} [85]. Another examples include sensing of Pb^{2+} and adenosine by combining an adenosine aptamer and a DNAzyme with an abasic site where 2-amino-5,6,7-trimethyl-1,8-naphthyridine is trapped to quench its fluorescence [86]. When in solution, Pb^{2+} enables the DNAzyme to cleave its substrate thus removing the fluorescent compound from the abasic site restoring its fluorescence. Similarly, the presence of adenosine induces structural change of the aptamer, resulting in the release of the fluorescent molecule from the DNA duplex and a subsequent fluorescence enhancement.

2.4. Nanophotonics Bioimaging. Nanoparticles show unique features suitable for biomedical imaging applications, such as an increased sensitivity in detection through amplification of signal changes (e.g., magnetic resonance imaging); high fluorescence quantum yields and large magnetic moments; properties that induce phagocytosis and selective uptake by macrophages (e.g., liposomes); physicochemical manipulations of energy (i.e., quantum dots); among others [87]. Because light absorption from biologic tissue components is minimized at near infrared (NIR) wavelengths, most nanoparticles (e.g., noble metal and magnetic NPs, nanoshells, nanoclusters, nanocages, nanorods and quantum dots) for *in vivo* imaging and therapy have been designed to strongly absorb in the NIR and used for *in vivo* diagnostics [83, 88, 89]. Ex vivo and *in vivo* imaging applications of nanoparticles have included their use as contrast agents for magnetic resonance imaging (MRI) [90], optical coherence tomography (OCT) [91–93], photoacoustic imaging (PAI) [94], and two-photon luminescence (TPL) spectroscopy [95].

2.4.1. Magnetic Resonance Imaging. Magnetic resonance imaging (MRI) is based heavily on nuclear magnetic resonance (NMR), first described by R. Damadian. Magnetic resonance measurements cause no obvious deleterious effects on biological tissue, and the incident radiation consists of common radio frequencies at right angles to a static magnetic field [96]. Iron oxide nanoparticles show superparamagnetism, allowing for the facile alignment of the magnetic moments to an applied magnetic field, thus of great interest as contrast agents for MRI [97]. Presently, magnetic iron oxide nanoparticles are routinely used as contrast agents to enhance an MRI image, providing sharper contrast between soft and hard tissue in the body (e.g. liver and spleen or lymph nodes) [98]. Jun et al. presented a synthetically controlled magnetic nanocrystal model system that led to the improvement of high-performance nanocrystal—antibody probe systems for the diagnosis of breast cancer cells via magnetic resonance imaging [99]. Also, $MnFe_2O_4$ nanocrystals *functionalized* with an antibody conjugate (herceptin) capable of specific targeting of cancerous cells was successfully used for *in vivo* MRI in mice [88]. Driehuysb et al. developed an imaging method to detect submillimeter-sized metastases with molecular specificity by targeting cancer cells with iron oxide nanoparticles functionalized with cancer-binding ligands, demonstrating *in vivo* detection of pulmonary micrometastases in mice injected with breast adenocarcinoma cells [100]. Hybrid NPs with a superparamagnetic iron oxide/silica core and a gold nanoshell, with significant absorbance and scattering in the NIR region, have been used *in vivo* as contrast agents for MRI presenting a good MR signal in hepatoma, each moiety providing for a distinct signal that enhanced detection [101].

2.4.2. Optical Coherence Tomography. Optical Coherence Tomography (OCT) is an imaging modality that provides cross-sectional subsurface imaging of biological tissue with micrometer scale resolution which is based on a broadband light source and a fiber-optic interferometer. It captures three-dimensional images from within optical scattering media, typically employing near-infrared light. The use of relatively long wavelength light allows it to penetrate into the scattering medium [102–104]. The extra scattering provided by Au-nanoshells enhances optical contrast and brightness for improved diagnostic imaging of tumors in mice due to the preferential accumulation of the nanoshells in the tumor [105]. Tseng et al. developed nanorings with a localized surface plasmon resonance covering a spectral range of 1300 nm that produced both photothermal and image contrast enhancement effects in OCT when delivered into pig adipose samples [106]. Additionally, the image contrast enhancement effect could be isolated by continuously scanning the sample with a lower scan frequency, allowing to effectively control the therapeutic modality. In the same way, gold capped nanoroses have been used in photothermal OCT to detect macrophages in *ex vivo* rabbit arteries [107].

2.4.3. Photoacoustic Imaging. In photoacoustic imaging (PAI) and photoacoustic tomography (PAT), a pulse of NIR laser light, typically 757 nm, is used in resonance with the surface plasmon instead of a continuous NIR source. With this technique causing rapid thermal expansion of the surrounding media, the generated sound wave can be detected on the surface of the subject. NIR reduces the amount of absorption that occurs, but absorption of light by various other organs is unavoidable [108, 109]. Yang et al. demonstrated the feasibility of using poly(ethylene glycol)-coated Au nanocages as a new *in vivo* NIR contrast-enhancing agent for photoacoustic tomography and image their distribution in the vasculature of rat brain. These Au-nanocages enhanced the contrast between blood and the surrounding tissues by up to 81%, achieving a more detailed image of vascular structures at greater depths. Additionally, they were shown to present slight advantages over Au-nanoshells, being better suited for *in vivo* applications, specially due to their more compact size (<50 nm compared to >100 nm for Au-nanoshells) and larger optical absorption cross-sections [110]. Due to the ability of gold-nanorods to have the maximum of the plasmon resonance tuned further into the NIR, Motamedi et al. reported a contrast agent for a laser optoacoustic imaging system for *in vivo* detection of gold nanorods and to enhance the diagnostic power of optoacoustic imaging [111]. Song et al. proposed a noninvasive *in vivo* spectroscopic photoacoustic sentinel lymph node mapping in a rat model using gold nanorods as lymph node tracers [112].

2.4.4. Two-Photon Luminescence. In two-photon luminescence (TPL) spectroscopy, an electron is excited from the conductance band to the valence band of the metal nanoparticles using two photons. As the electron relaxes to the conductance band, light is released and amplified due to a resonant coupling with localized surface plasmons, enhancing a variety of linear and nonlinear optical properties [113, 114]. TPL was first described by Boyd et al. that found that roughened metal surfaces exhibited much higher induced luminescence efficiency than smooth surfaces [115]. In fact, TPL is a potentially powerful technique for noninvasive imaging at the micron scale hundreds of microns deep into scattering tissue. This way, it ought to be possible to discriminate cancerous and healthy tissue based on two-photon imaging from endogenous fluorophores. For enhanced imaging, two-photon contrast agents have been developed showing the ability to increase signal-to-noise ratio and targeted to molecular signatures of interest that are not fluorescent. Because imaging of intrinsic fluorophores is often difficult due to their relatively weak signals, the use of such a bright contrast agent holds the promise to enable *in vivo* applications of two photon imaging in a clinical setting [113, 116, 117]. Wang et al. collected images of single gold nanorods flowing in the mouse ear blood vessels with luminescence three times stronger than background [114]. It is worth mentioning that the TPL signal from a single nanorod is 58 times that of the two-photon fluorescence signal from a single rhodamine molecule.

2.4.5. QDs for In Vivo Imaging. In the last decade, water soluble bioconjugated QDs have been increasingly applied for imaging [63, 64, 118] However, QD probes for imaging show poor stability once inside cytosolic environment and reduced biocompatibility in living organisms [119], which constitutes a serious drawback for widespread *in vivo* application.

Despite the serious concerns related to the *in vivo* use of QDs, these nanocrystals show remarkable imaging properties that may be judged of value for improved diagnostics. In fact, QDs have proven of great value when imaging vascular networks of mammals such as lymphatic and cardiovascular systems [120–124]. Also, Kim et al. demonstrated that quantum dots allowed a major cancer surgery to be performed in large animals (mice and pigs) under complete image guidance, by locating the position of sentinel lymph nodes [125]. With similar potential to that observed when imaging the lymph system, the imaging of cardiovascular systems has also been achieved using QDs [126, 127]. Larson et al. demonstrated that QDs retained their fluorescence after injection and could be detected in the capillaries of skin and adipose tissue of a mouse [128]. The fluorescent emission and multiplexing capabilities of QDs are being exploited to improve the sensitivity and selectivity in the early detection of tumors [61, 129, 130]. Åkerman et al. described for the first time the application of targeted cancer imaging by using ZnS-capped CdSe QDs coated with a lung-targeting peptide that accumulate in the lungs of mice, whereas two other peptides specifically direct QDs to blood vessels or lymphatic vessels in tumors [131]. Later, Gao et al. described the development of multifunctional nanoparticle probes based on QDs with a copolymer linked to tumor-targeting ligands and drug-delivery functionalities for cancer targeting and imaging in living animals [132]. Once the toxicological aspects associated with QDs have been clarified, such studies

demonstrate the potential of QDs for ultrasensitive and multiplexed imaging of molecular targets *in vivo*.

3. Nanophotonics for Therapy

Nanophototerapy uses pulsed lasers and absorbing nanoparticles attached to specific targets for selective damage to cancer cells. Plasmonic photothermal therapy (PPTT) and photodynamic therapy (PDT) are two of the main techniques that take advantage of the selective absorbance of the surface plasmon resonance and the fact that the nanoparticles relax by liberating heat into their surrounding environment.

3.1. Plasmonic Photothermal Therapy. Plasmonic photothermal therapy is a less invasive experimental technique that holds great promise for the treatment of cell malignancies and, in particular, of cancer. It combines two key components: (i) light source, specifically lasers with a spectral range of 650–900 nm for deep tissue penetration and (ii) optical absorption of AuNPs which release the optical irradiation as heat in the picoseconds time scale, thereby inducing photothermal ablation [133–135]. Kirui et al. reported the use of gold and iron oxide hybrid nanoparticles in targeting, imaging, and selective thermal killing of colorectal cancer cells [136]. Huang and colleagues have demonstrated that gold nanorods have a longitudinal absorption band in the NIR on account of SPR oscillations and are effective as photothermal agents [137]. Gold nanorods aspect ratios allow tuning the SPR band from the visible to the NIR (transmits readily through human skin and tissue), making them suitable for photothermal converters of near infrared light for in vivo applications [138, 139]. Effective photothermal destruction of cancer cells and tissue have been demonstrated for other gold nanostructures, such as branched gold nanoparticles [140], gold nanoshells [141–143], gold nanocages [134], and gold nanospheres [144].

3.2. Photodynamic Therapy. Photodynamic therapy employs chemical photosensitizers that generate reactive oxygen species (ROS), such as a singlet oxygen ($^1O_2$), capable of tumor destruction [145, 146]. This technique is noninvasive and can be applied locally or systemically without noticeable cumulative toxicity effects without high costs. To attain maximal killing efficiency of tumor cells, the photosensitizer must be in close proximity to the tumor cells, thus requiring specific targeting when administered systemically. One of the major limitations is the poor tissue penetration of high-energy light and the systemic dispersal of the photosensitizer [147, 148].

Aiming at circumventing some of the limitations of photodynamic therapy, Zhang et al. reported a new type of photosensitizers based on photon upconverting nanoparticles (a process where low energy light, usually near-infrared (NIR) or infrared (IR), is converted to higher energies, ultraviolet (UV), or visible, via multiple absorptions or energy transfer steps) [149, 150]. One year later, Yong et al. reported the use of NPs modified with zinc phthalocyanin photosensitizer that produce green/red emission on near-infrared (NIR) excitation and is capable of singlet oxygen sensitization; upon targeted binding to cancer cells, significant cell destruction was induced [151]. Recently, Qian et al. published similar results with the use of zinc phthalocyanine nanocrystals coated with a uniform layer of mesoporous silica [152].

4. Conclusions

Light is an amazing intermediate with a gargantuan capacity for carrying multiple information and functions. Instinctively, we view light as rays, which propagate in a single direction, either being absorbed or reflected to some extent by any object on which it impinges. However, the propagation of light through a material is itself a quantum effect, involving the excitation and relaxation of electrons in the material. It is well known that light has the facility to act through biological, chemical, mechanical, and thermal pathways at molecular/cellular levels in diagnostic and therapeutic applications.

Currently, we are in the dawn of a new age in therapy driven by nanotechnology vehicles. Although there are technical challenges associated with the therapeutic application of nanodevices, the integration of therapy with diagnostic profiling has accelerated the pace of discovery of new nanotechnology methods. In addition to continuing to push forward on the above challenges, nanotechnology together with photonics can be used both for identifying useful target candidates and for validating their importance in disease states. Nanophotonics may present new opportunities for personalized medicine in which diagnosis and treatment are based on each individual's molecular profile. Further research into the fundamental mechanisms that efficiently control light using nanodevices could unveil new dimensions of nanoparticle-mediated theranostic systems.

Here, we have attempted to give the reader a limited overview of some aspects of the current state of research into the fascinating aspects and control over nanophotonics in molecular diagnostics and therapy applications.

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