

Editorial

# Nanophotonics and Theranostics: Will Light Do the Magic?

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When speaking about optical approaches for theranostics, that is method that unites diagnosis, treatment and preferably treatment guidance in one procedure, it is good to recall what light already did in medicine as well as to consider the most pressing unresolved medical challenges that will benefit from new approaches including theranostics.

Light by itself is a universal form of energy (Figure 1) that can be rapidly delivered and converted into various medically-relevant forms such as heat, chemical and mechanical processes, sound and light, all of which are used for diagnosis and various therapies. The historic examples of light doing magic in medicine are the invention of the microscope in XVI century [1] and of "bloodless" laser surgery in XX century [2].

Present medical practices including surgery, and chemo- and radiation-therapies often suffer from an inability to remove or kill pathological cells when the latter are intertwined with functionally important organs and develop resistance to drugs and radiation. This forces clinicians to balance the risks of residual and recurrent disease with damaging important cells and organs, thus further complicating the disease by compromising the patient's quality of life and physiological health. The ultimate solution is to transform current macro-treatment into cell level theranostic tools which will rapidly and selectively detect and destroy only pathological cells while sparing nearby normal cells. Unfortunately, such a tool does not yet exist, and it is precisely here that the combination of light and nanotechnology is most promising.



**Figure 1.** Range of light: from Mega - to nano-scale.

The recently advances in chemistry allowed to employ a phenomenon of plasmon resonance [3] for the conversion of light into medically-relevant processes at nanoscale via metal (plasmonic) nanoparticles that show a million times higher optical absorbance than any natural molecules. Among them, gold nanoparticles have both the highest optical absorbance and the lowest toxicity. Interestingly, gold nanoparticles are not new. In fact, they were invented by Michael Faraday in the XIX century [4] and have been used in clinics for more than fifty years [5]. On the other hand, recent advances in laser technologies allowed the use of near-infrared continuous and pulsed light with the maximal tissue penetration depth (up to 10 mm [6]) and safety. Fiber optical technologies allowed the delivery of light even deeper, up to 300-400 mm, thus enabling laser micro-surgery [7]. Finally, advances in conjugation chemistry made possible the precise delivery of gold nanoparticles to specific pathological cells, where these nanoparticles can be remotely and instantaneously activated with visible or near-infrared laser light. All the above created a unique interdisciplinary platform for the development and clinical translation of bio-nano-photonics. The current issue presents several research and review papers that report both the fundamentals and applications of light-activated nanoparticles in biology and medicine.

Diagnostic methods employ optical scattering [8-11], luminescence [11, 12] and fluorescence [9, 10] by nanoparticles and optical scattering and acoustic signals by plasmonic nanobubbles [13]. Cell-specific targeting and the internalization of nanoparticles provided high sensitivity and specificity of the diagnosis. Optical detection methods are mostly appropriate for *in vitro* and extra-corporeal applications with unlimited optical transparency. Photoacoustic methods [14] are better suited to *in vivo* applications, with poor optical transparency of opaque tissues. It is worth mentioning one specific animal model, zebrafish [15], that combines the physiology of a vertebrate animal with the high optical transparency of *in vitro* samples.

The therapeutic methods discussed in this issue include several groups. Most established laser- and gold nanoparticle- therapy employs the photothermal effect and delivers cell level hyperthermia [9-11]. This drug-free approach employs continuous lasers and gold colloids or specifically engineered near-infrared gold nanoparticles such as nanorods, nanoshells and others. The limitation of such an approach is in low cell specificity due to the unavoidable non-specific uptake of nanoparticles by healthy cells and due to thermal diffusion during relatively long exposure

times. Another drug-free approach employs very short laser pulses to prevent thermal diffusion and instead of heat employs the purely mechanical impact of the nanoparticle-generated expanding and collapsing vapor nanobubbles (plasmonic nanobubbles) [13, 14]. The threshold nature of plasmonic nanobubbles allowed an improvement in their cellular specificity compared to nanoparticle therapies [8, 13, 14]. The next group of therapeutic methods employs light-activated nanoparticles for the on-demand release of encapsulated drugs [10-12, 16, 17]. Nanoparticle-generated heat melts the membrane of a complex nanocarrier within minutes or less, and releases its therapeutic payload [16, 17]. Even faster release occurs via the plasmonic nanobubble-induced explosive mechanical disruption of the nanocarrier. In this case, instead of relatively slow diffusion, the payload is ejected from a nanocarrier in mere nanoseconds [14].

The possibility of combining several agents with different functions in one nanocarrier created a new class of theranostic nanoparticles [9-10, 16, 17]. For example, liposome or microcapsule may carry an encapsulated drug and attached antibodies for targeted therapy, gold nanoparticles for heating and fluorescent molecules or quantum dots for optical imaging or magnetic nanoparticles for magnetic resonance imaging. This all-in-one concept is intriguing, although the complexity of such theranostic nanoparticles will have to deal with the challenges of toxicity and stability.

Most of the papers presented in this issue consider cancer as the main target. The aggressive and resistant nature of cancer cells often leads to the failure of standard practices. This is where the new approaches discussed below can be considered as adjuvant therapies for improving patients' survival rates and quality of life as well as for making the treatment both shorter and less stressful.

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