

# On How Could Light and Nanostructures Lead the Way to a Safer Anticancer Therapy

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Destroying biological pathogens is easy. The point is how to destroy them while sparing the host. This is especially obvious when dealing with cancer. History shows that anticancer therapies have always been aggressive to patients. For instance, in the 19th century, arsenides and arsenic salts were commonly prescribed as anticancer drugs [1]. The use of arsenic derivatives for treating cancer was an art – hard to master, properly applied only by a few. Although arsenic was considered to be effective against cancer, it was difficult to deal with its narrow therapeutic window. In the early 20th century, improved therapies supplanted arsenic derivatives in anticancer treatment – actually, the use of arsenic compounds for therapeutic purposes is far from being left aside as it continues to be investigated and encouraged [1]. But important side effects persist. The problem is that anticancer drugs act without the precious help given by phylogenetic differences between the host and the biological pathogen. They should destroy abnormal eukaryotic cells, derived from host's own cells. This is the main reason behind the harmful, sometimes lethal, side effects of conventional anticancer therapies. Over the last few decades, despite the efforts in developing and improving anticancer therapies, no major progress has been achieved.

The question of how to specifically address cancerous cells is pivotal for improving conventional anticancer therapies. One promising solution is to activate the immune system, the expert in differentiating self from non-self, against cancer-specific antigens. Although such a strategy brings exciting prospects, such as the possibility of destroying metastatic tumors at once, it still lacks a wide and robust effectiveness. On the other hand, recent researches have brought to light some interesting approaches that potentially reduce the side effects of conventional anticancer drugs. Particularly, some nanostructured drug delivery systems have been shown to increase the ratio of drug concentration in tumor to normal tissue [2]. However, even nanostructured drug delivery systems are far from being the only solution to the issue of specificity. They do increase drug concentration in tumor tissue in comparison to the free drug, but most of the drug dose is still distributed through normal tissues.

Combined approaches are more likely to increase tumor specificity. A good example of such a combination is the Photodynamic Therapy (PDT) based on photosensitizers associated to nanocarriers. PDT is based on three key agents: photosensitizer, light (600-800 nm for single-photon) and oxygen. Once activated by light, the photosensitizer converts triplet-state oxygen into singlet-state oxygen, a more potent oxidizing species. These events lead to tumor death and often to immune system activation or boosting against tumor antigens [2]. Several works show that PDT is effective against a wide variety of cancers [3]. In some clinical studies, long-lasting complete remission was achieved in almost 90% of patients after application of anticancer PDT [4]. Currently, PDT is already approved for the treatment of several cancer types and numerous clinical studies are being performed that will expand the clinical application of this therapy [5].

Importantly, anticancer PDT is a powerful tool for destroying cancer while sparing normal tissues. It is much less aggressive to

normal tissues in comparison to conventional chemotherapy and preserves the architecture and functionality of the body site where the treated tumor is located [4]. Moreover, as the photosensitizer does not exert any important toxicity in the dark, the PDT-related cytotoxicity can be restricted to the tumor area by simply adjusting the focus of the applied light.

An increased accumulation of the photosensitizer in tumor tissue could further enhance the safety of anticancer PDT. This is why many researchers are associating nanotechnology to PDT. Nanocarriers are known to present good accumulation in tumor tissue and may increase PDT safety. Currently, PDT based on photosensitizers associated to nanocarriers is approved for the treatment of macular degeneration (Visudyne) [3], for example, and several studies on its potential for treating cancer are being conducted. In a recent study, [6] showed that the photosensitizer aluminum-phthalocyanine chloride associated to nanosized liposomes was effective in PDT against a model of chemically-induced tongue tumor. Several alterations were observed in treated tumors, such as infiltration of polymorphonuclear cells, vasculature collapse and necrosis. These results suggest that this liposome-associated photosensitizer can be used in anticancer PDT. Associating light and nanostructures, two tumor specificity-conferring agents, in one single anticancer treatment can lead to a safer anticancer therapy.

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