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Editorial

Nanotechnology on Demand to Cancer Therapy

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Editorial

Nanotechnology, the study and application of extremely small things and that can be used across several science fields, such as chemistry, biology, physics, materials science, and engineering, has a huge potential for the development of new and successful therapeutic approaches in the field of medicine. The possibility of engineering and manipulate the physicochemical properties of materials at nanoscale, allows the possibility of establishing interactions with biological structures at molecular level. These very close interactions have brought to the reality the possibility of development of new therapeutic formulations with high efficiency and low toxicity. The first attempts to use nanotechnology in cancer therapy consisted on the development of new nanoplatforms that offered the possibility to assemble chemotherapeutic drugs. These new nanoplatforms were manipulated at nanoscale level to enable the usage of drugs that could not been used previously at the macroscale due to high levels of toxicity and low solubility. Furthermore, these nanoplatforms offered the possibility to be engineered in order to adjust their biocompatibility according to the clinical requirements and/or promote the controlled release of the drugs over time according to the evolution of the disease. Controlled drug release could be induced by internal (local pH, biodegradation) or external stimulus (Near infrared radiation or Magnetic field). These types of nanoparticles are defined as the first generation or non-target and are characterized by taking advantage of a biological factor associated with the abnormal growth of tumour tissues, called Enhanced Permeability and Retention (EPR) effect [1]. This particularity of the tumours facilitates the diffusion of nanoparticles through the endothelial cells of small blood vessels and their accumulation within the tumour due to the disability of the lymphatic system. The first generation nanoplatforms can be already found in clinical and pre-clinical uses and consist mainly in liposomes, polymers and dendrimers [2]. However, these nanoplatforms show some limitations on their performance on cancer treatment under *in vivo* conditions. The main problem is related to the diffusion of these nanoparticles in a random way in the human body, allowing their biodistribution and accumulation in healthy organs and tissues causing toxic side effects. It was reported that less than 5% of the nanoparticles administrated can reach the tumour cells being the remaining ones eliminated by the immunity system (opsonization, uptake by Reticuloendothelial System (RES)) and extravasated through the healthy tissues [3].

The continuously research on the mechanisms and signaling pathways involved in the development and progression of cancer allowed the identification of specific biological structures overexpressed on the surface of cancerous cells (transferrin, folic acid and somatostatin). These new discover about molecular and cellular biology of solid tumours was the basis for the development of a new generation of nanoparticles, usually designated as targeted nanoparticles. These nanoplatforms are able to direct the treatment to specific sites due to the assembly of ligands (antibodies, engineered antibody fragments, proteins, peptides, small molecules and aptamers) that are complementary of the structures overexpressed at surface of the cancerous cells [4]. The establishment of interactions between ligand and receptor facilitates the cellular internalization of the nanoplatform via receptor-mediator endocytosis. Through the development of these smart targeted nanoparticles, it is expected to increase the efficacy and decrease the toxicity of these entities during therapeutic phase. These new nanoplatforms proved to be efficient *in vitro* conditions, however the success conditions has been very limited due to the drastic physiological conditions observed *in vivo*, that difficult the targeting of the nanoparticles to the cancerous cells. The number of target nanoparticles that reaches the cancer cells in humans is lower than 0.01% of the total administered. Despite this, some target nanoplatforms are already approved for clinical applications or under pre-clinical studies [2].

A recent approach in cancer treatment consists on the development of nanoplatforms that can carry out several functions at the same time, from diagnosis to therapy, being usually designated as theranostics. Nanotechnology offers many methodologies to assemble different molecular structures and nanoparticles, precise for a specific function during each phase of the cancer treatment, into a multifunctional platform. This new concept, from the theoretical point of view looks very promising, however the complexity evidenced by theranostic nanoparticles under biological conditions, limits drastically its application [5]. In fact, pharmacokinetics and pharmacodynamic requirements for bioimaging and drug delivery are very different, which greatly restrict the use of the same nonoplatform to perform both functions. So far these studies have not yet passed the prototype stage.

Another methodology was developed in order to overcome these limitations. Instead of develop multifunctional platforms able to perform several functions at the same time, the new strategy combines different types of specialized nanoparticles that can be triggered sequentially by different phases of cancer therapy (usually designated as collective behaviour of nanoparticles) [6]. These studies are in a very early stage; however so far seem very prominent for the development of one new therapeutic solution for cancer therapy. Recently nanotechnology started to perform an important role in cancer immunotherapy. Cancer immunotherapy consist on variety of approaches that mobilize the immune system to recognize and kill cancer cells, has been shown to be a very promising treatment for cancer in the last few years http://www.nature.com/reviews/

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multimedia/tumourimmunotherapy/index.htm. Nanotechnology can be the bases of this new approach through the design of nanovacines capable of triggering effective antitumor immunity [7]. Despite immunotherapy studies being at an initial stage, preliminary results demonstrate that contains great potential, however for clinical translation of the most effective approaches will required the optimization of the corresponding nanoplatform.

In summary, nanotechnology has been increasingly incorporated on cancer therapy treatments by the development of new nanoplatforms for therapeutics, bioimaging and biodetection or additionally by the engineering of new nanosensors able to detect biological signatures of cancer at early stages of disease. Despite the great potential of nanotechnology in the search for new solutions for cancer therapy, the critical issue is always transfer nano-based cancer therapy from the laboratory to clinical applications.

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