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NANOTECHNOLOGY AND BIOCOMPUTATIONAL SCIENCE : A POSSIBLE ALTERNATIVE FOR THE TREATMENT OF CANCER

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ABSTRACT

Nanotechnology provides the field of medicine with promising hopes for assistance in diagnostic and treatment technologies as well as improving quality of life. Humans have the potential to live healthier lives in the near future due to the innovations of nanotechnology. In this review we consider each of these hurdles and examine how nanotechnology can help to address them. The role of biocomputation will be explored as a means to specify cancer drug therapy, with the goal of applying the results in the clinical setting, especially the modeling of drug delivery via nanoparticles. Biocomputation could save lives and enhance the quality of cancer treatment by making it possible to tailor therapy to the individual patient and reduce the time and costs involved. With these goals in mind, we will look in more detail at the system-level biocomputation of tumor growth and cancer therapy, and raise considerations for future research. We begin by briefly reviewing the advantages of nanotechnology, its application to cancer chemotherapy, and its challenges in a biological setting.

INTRODUCTION

Nanotechnology can be defined as the manipulation, precision-placement, modeling and manufacture of material at the nanometer scale (One meter consists of 1 billion nanometers) (Donaldson, Stone, 2004). It promises to provide many useful applications in many fields. There are many treatments today that take a lot of time and are also very expensive. Using nanotechnology, quicker and much cheaper treatments can be developed. By performing further research on this technology, cures can be found for diseases that have no cure today. We could make surgical instruments of such precision and deftness that they could operate on the cells and even molecules from which we are made - something well beyond today's medical technology. Therefore nanotechnology can help save the lives of many people. Although the clinical arsenal in treating cancer has been greatly extended in recent years with the application of new drugs and therapeutic modalities, the three basic approaches continue to be (in order of success) surgical resection, radiation, and chemotherapy. The latter treatment modality is primarily directed at metastatic cancer, which generally has a poor prognosis. A significant proportion of research investment is focused on improving the efficacy of chemotherapy, which is often the only hope in treating a cancer patient. Yet the challenges with chemotherapy are many. They include drug resistance by tumor cells, toxic effects on healthy tissue, inadequate targeting, and impaired transport to the tumor. Determination of proper drug dosage and scheduling, and optimal drug concentration can also be difficult. Finally, drug release kinetics at the tumor site is an important aspect of chemotherapy.

Advantages of using Nanotechnology in Cancer Treatment :

All manufactured products are made from molecules. The properties of these products depends on how molecules are arranged. For example if we arrange molecules in coal we get diamonds. Nanotechnology applied to cancer treatment may offer several promising advantages over conventional drugs. Nanoscale devices are two orders of magnitude smaller than tumor cells, making it possible for them to interact directly with intracellular organelles and proteins. Because of their molecule-like size, nanoscale “tools” may be capable of early disease detection using minimal amounts of tissue, even down to a single malignant cell [18]. These “tools” may not only prevent disease by monitoring genetic damage, but also treat cells *in vivo* while minimizing interference with healthy tissue. By combining different kinds of nanoscale “tools” on a

single device, it may be possible to run multiple diagnostic tests simultaneously [19]. In particular, it is hoped that cancer drug therapy involving nanotechnology will be more effective in targeting malignant cells and sparing healthy tissue. In this regard, the role of nanoparticles loaded with chemotherapeutic drugs has been receiving much attention. Research and development in this area is expected to dramatically increase in importance in the coming years.

Challenges of Nanotechnology

The difficulties facing nanotechnology in the service of clinical medicine are numerous. These difficulties should be kept in mind when considering chemotherapeutic treatment involving nanotechnology and the potential role of biocomputation. First, there are basic physical issues with matter at such a small scale. Since matter behaves differently on the nano than it does at micro and macro levels, most of the science at the nanoscale has been devoted to basic research, designed to expand understanding of how matter behaves on this scale [19]. Because nanomaterials have large surface areas relative to their volumes, phenomena such as friction are more critical than they are in larger systems. The small size of nanoparticles may result in significant delay or speed-up in their intended actions. They may accumulate at unintended sites in the body. They may provoke unexpected immune system reactions. Cells may adapt to the nanoparticles, modifying the body's behavior in unforeseen ways [19]. The efficacy of nanoparticles may be adversely affected by their interaction with the cellular environment. For instance, the reticuloendothelial system (RES) may clear nanoscale devices, even "stealth" versions, too rapidly for them to be effective because of the tendency of the RES to phagocytose nanoparticles. Nanoparticles can be taken up by dendritic cells [16] and by macrophages [14]. RES accumulation of nanoparticles could potentially lead to a compromise of the immune system. On the other hand, larger nanoparticles may accumulate in larger organs, leading to toxicity [19]. Perhaps the biggest issue of all is that the physically compromised tumor vasculature may prevent most of the nanodevices from reaching the target cells by vascular transport or diffusion. Alterations in the tumor vasculature may adversely affect the convection of the nanodevices in the blood stream. Local cell density and other stromal features may hamper drug or nanodevice diffusion through tumoral tissue. This topic will be examined in more detail when we consider the issue of chemotherapeutic drug transport, system-level biocomputation of cancer therapy.

Chemotherapy via Nanoparticles

In general, nanoscale drug delivery systems for chemotherapy can be divided into two categories: polymer- and lipid-based. Polymers, which are usually larger than lipid molecules, form a solid phase, such as polymeric nanoparticles, films, and pellets, while lipids form a liquid (or liquid crystalline phase), such as liposomes, cubersomes, micelles and other emulsions [17]. While polymer-based systems are considered biologically more stable than lipid-based systems, the latter are generally more biocompatible. Polymer-based systems might possess good drug targeting ability because their uptake may be different for cells in different tissues . In fact, Feng and Chien [17] have suggested that a combination of polymer- and lipid-based systems could integrate their advantages while avoiding their respective disadvantages. An example of such a nanoparticle would be a liposomes-in-microspheres (LIM) system, where drugs are first loaded into liposomes, and then encapsulated into polymeric microspheres. This way both hydrophobic and hydrophilic drugs can be delivered in one nanoparticle. The bioactivity of peptides and proteins would be preserved in the liposomes, whose stability is protected by the polymeric matrix [17]. Chemotherapy using nanoparticles has been studied in clinical trials for several years and numerous studies have been published in this regard. Two liposomally delivered drugs are currently on the market: daunorubicin and doxorubicin. These encapsulated drugs can be formulated to maximize their half-life in the circulation.

Biocomputation in Cancer Treatment :

The challenges of nanotechnology may be better evaluated through the use of biocomputational methods that examine the fundamental physical principles that affect delivery and degradation of nanoparticles in cancer treatment. Biocomputation, in general, provides a means of mathematically modeling these physical principles so that basic truths about the interaction of nanotechnology and living tissue may be better understood. This knowledge could save time and resources by providing guidance to the experimentalist and the clinician, support a coherent framework for further research, and offer the potential to predict experimental outcomes. The main challenge of biocomputation is to be able to incorporate these physical principles into a biologically relevant model while retaining the capability to numerically solve for concrete results. It is difficult to model from the nanoparticle (10−9 m) to the tumor (10−3 m) scale, not only because matter behaves very differently in each, but because

of the enormous computational cost associated with having to span six orders of magnitude of length scales over a significant period of biological time. In fact, simulation may require integration of multiple hierarchies of models, each differing in several orders of magnitude in terms of scale and qualitative properties . Modeling of drug delivery encompasses the formulation of quantitative descriptions for drug transport in biological systems to evaluate feasibility of new drug delivery methods, to estimate dose response and toxicity, and to speed experimental and clinical evaluation . Modeling principles apply to both procedures and technologies. For example, local drug administration, targeted drug delivery, and controlled drug release polymers should all be considered. In the treatment of cancer, it is hoped that biocomputation will facilitate formulation of optimal treatment models that enable administration strategies for chemotherapy that maximize benefit while minimizing side effects [17]. Biocomputation based generation of theoretical results could potentially be validated by correlation of numerical predictions with *in vitro* and *in vivo* data of a particular patient's cancer response to chemotherapy. In turn, these experimentally and clinically validated biocomputation results may be used to design personalized therapy protocols *in silico* using computer simulations. Biocomputation of targeted and controlled drug delivery via nanoparticles is not only expected to offer insight into *in vivo* drug delivery, but also simulate the therapeutic effects of the delivery device and stipulate its preparation specifications in order to better address the challenges of nanotechnology. This approach may offer a means to optimize existing products and enhance new product development for cancer chemotherapy and disease treatment. The types of drug, excipient, and composition of the device could be essential components of a model [17]. Since there are no encompassing mathematical models that can apply to all conceivable physical and chemical processes in product development, it is important to develop an adequate theory grounded in physical considerations for specific systems. For instance, physical considerations that apply to polymer devices include drug delivery and diffusion, polymer swelling and degradation/erosion. It may also be necessary to consider osmotic, steric, magnetic, and charge effects [17].

DISCUSSION

Recently, nanotechnology has been proven to be a highly effective method of cancer treatment or diagnosis, due to numerous successful studies undertaken in the past few years, some of which were mentioned in the introduction. However, is there any real

possibility of nanotechnology ever becoming the established, finite cure for cancer, and replacing the 'traditional' treatments such as chemotherapy and radiotherapy? The incredibly rapid rate at which nanotechnology has been developing suggests that this speculation could become reality quite soon. On 3rd March 2009, the journal Cancer Research published the findings of an investigation into *'Cancer-Specific Transgene Expression Mediated by Systemic Injection of Nanoparticles'* [4], and although this study had been solely executed in mice, the researchers said that they were endeavouring to continue this study with human trials in 2011, thus providing a cure for metastatic tumours. These findings would have been seen as 'Star Trek' science and it would have been considered impossible to execute such an experiment just a few years ago. In order for the nanoparticles to be effective against the cancer, the ideal anti-tumoral agent had to be able to target malignant cells throughout the body whilst sparing normal tissues, and so far cancer gene therapy has been restricted due to the lack of systemically active, cancer-specific delivery vectors, especially in the field of non-viral, synthetic gene delivery vectors. The nanoparticles were composed of polypropylenimine dendrimers of third generation (PPIG3), so when combined with DNA, they were truly capable of efficient gene transfer to tumour deposits, upon systemic injection. Significantly, when a therapeutic transgene was used, marked anti-tumour activity was observed, leading, in some experiments, to the "cure" of all the mice that were treated.

CONCLUSION

Conclusively, my investigation has demonstrated that nanotechnology definitely has the potential to be the future and sole cure for cancer, as it has already proved itself through various instances to be the most effective and optimum form of future treatment and diagnosis of cancer. Not only have nanowires and cantilevers been proven for their capability to provide an efficient method of recognising cancer biomarkers in the blood for different cancers, nanoparticle composites have also been developed with opposing properties allowing for more accurate diagnosis and location of cancer (and nanoshells been proven to be more effective cancer gene therapy vectors than the conventional viral vectors.) Furthermore, nanoshells most definitely have the impressive potential to treat malignant brain tumours, due to their effectiveness at delivering the drugs across the blood-brain-barrier, which was previously one of the most challenging aspects of cancer treatment. There are of course relatively successful

methods of cancer treatment already available, such as radiotherapy and chemotherapy; according to the NHS, radiotherapy *'is used to treat about 40% of people with cancer'*[7]**.** Nonetheless, both alternative treatments have their own significant risks. For radiotherapy, the proper dosage needed to cure all malignant brain tumours is approximately 12,000 Rads, but such a high dosage is also extremely neurotoxic and deadly, and chemotherapy has an imposing number of risks from alopecia to severe fatigue to ototoxicity to neutropenia (this can leave the patient highly susceptible to infections) to thrombocytopenia (which can result in blood clotting problems).

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