Nanoscience in cancer treatment

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Ashvin Varadharajan
Armed Forces Medical College

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Review Article

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Ashvin Varadharajan [a], *Prarabdh Kothari* [a], *Deepanshu Gupta* [a]

[a] Medical Student, Armed Forces Medical College, Pune

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ABSTRACT

Nanomedicine is a unique interdisciplinary branch that integrates nanoscience and medicine to improve diagnostic abilities and treatment measures. The ability of nanoscience to synthesize a vast array of materials presents new avenues for developing diagnostic and therapeutic technologies. An important implication of this is in the field of cancer diagnosis and treatment. With the development of nanovectors, cancer chemotherapy now has advanced liposomal drug delivery systems at its disposal. Some nanovectors are, by themselves, used in chemotherapy. The field of cancer diagnostics has also benefitted greatly, since the targeted delivery of contrast agents using nanovectors has resulted in improved imaging modalities. The 'nanoarray', a version of the microarray having a millionfold increase in the information density, can simultaneously detect a large number of molecular species when used in cancer diagnostic technologies. The advent of newer nanomedicine-based platforms such as quantum dots, nanoshells, bio-barcodes, and implantable sensors is sure to revolutionise the field of diagnostics and therapeutics of cancer in the future.

Email: ashvinv2510@gmail.com (Ashvin Varadharajan)

Introduction

In the current era, interdisciplinarity is becoming increasingly common in the field of medical research. Different disciplines have varied perspectives and approaches to the same object of inquiry. Thus, an interdisciplinary venture enables researchers to develop a more holistic solution to a problem, by integrating methods and tools of one discipline with the knowledge of another.[1] One such attempt is to integrate nanoscience and medicine for more effective diagnosis and treatment of diseases, leading to the rise of the field of 'nanomedicine'. Nanomedicine has diverse applications, ranging from drug delivery systems[2] and implants[3], to diagnostic and imaging tools.[4] This review article shall attempt to briefly describe the applications of nanomedicine in cancer.

About Nanoscience as A Field

Nanoscience refers to the study of the properties of matter at the 'nanoscale' level, with sizes in the range of 1-100 nanometres. It principally focuses on the unique, 'size-dependent' properties of solid-state materials. In other words, it is the study of structures and materials at an ultra-small level, i.e., on a scale of few nanometres, and the unique properties which these materials demonstrate. The physical and chemical properties of matter are very different at the 'nano' scale as compared to the 'macro' scale. It is an interdisciplinary field that incorporates knowledge and inputs from a variety of different fields such as chemistry, physics, biology, medicine, and engineering. Nanotechnology, also known as molecular manufacturing, is an extension of the knowledge of nanoscience used in the design and production of devices and systems at the 'nano' scale. In the words of Norio Taniguchi, the first person to use the term, "nanotechnology mainly consists of the processing of separation, consolidation, and deformation of materials by one atom or one molecule".[5]

The early 2000s saw a growing public awareness about the field of nanotechnology. In the years that followed, nanotechnology has been applied to human health with promising results, especially for treating cancers.

Technology in Nanoscience

The first progress in nanotechnology was made by the invention of STM (Scanning Tunnelling Microscope) which is used even today. This invention also led to the development of AFM (Atomic Force Microscope) and SPM (Scanning Probe Microscope) which are currently the instruments of choice for nanotechnology-related research.[5]
Other widely used techniques include-

• Nanoparticle synthesis- nanoparticles are synthesised by using either a bottom-up approach, which involves nucleating atomic-sized materials into the eventual nanoparticles, or a top-down approach, where bulk materials are broken down into smaller fragments which are then converted into nanoscale structures.[6]

• Electrospinning- a voltage-driven manufacturing process for creating electro-spun fibres and particles whose size ranges between a few nanometers to micrometers.[7]

• Cathodoluminescence (CL)- used for characterizing optical properties at the nanoscale which can then be used to explore many fundamental properties of the nanomaterial.[8]

• Nanoindentation- for measuring mechanical properties such as modulus and hardness of materials.[9]

• Langmuir Films- thin organic films with the thickness of one molecule. These serve as useful components in many practical and commercial applications such as sensors, detectors, displays, and electronic circuit components.

• Tensiometry- for measuring surface tension, contact angles, density, and other properties. This can be used to study the interactions between gas, liquid, and solid phases.

• Ion milling- it is a process of removing the top amorphous layer on a material to reveal the ideal surfaces for high-resolution imaging and post-processing.[10]

• Profilometry- a technique used to extract topographical data from a surface. It includes Optical, Confocal, and Stylus profilometry.[11]

• Quartz Crystal Microbalance- a highly sensitive balance that can measure mass changes in the range of nanograms.[12]

Materials such as carbon nanotubes, carbon dots, solid drug nanoparticle (SDN) formulations, biodegradable, and biocompatible comb-like polymers (CLBs), porphysomes, Peptide nanofibers (PNFs), Epigallocatechin gallate (EGCG) can be designed using techniques of nanotechnology.

The ability of nanotechnology to synthesise such a vast array of materials, makes it a promising avenue in the search for new methods of cancer diagnosis and treatment.

Nanoscience in Cancer Diagnosis and Treatment

Nanotechnology has evolved a class of molecules referred to as 'nanovectors'. These nanovectors are of interest for use in drug-delivery systems, improved imaging techniques, and visualisation of early molecular markers of disease, to name a few.

Nanovectors are generally classified into three 'generations'. The first generation comprises mainly liposomal delivery systems, which localise within the cancer lesions passively. The Liposomal Daunorubicin delivery system is one such example. Second generation nanovectors incorporated the concept of PEGylation, and the Enhanced Permeation and Retention (EPR) effect, to enhance the circulation time, stability, entrapment, and retention of the desired substance, resulting in products such as liposomal Doxorubicin (Doxil® - the first FDA approved nano-drug (1995)).[13] These can target their action by using antibodies, remote activation, or response to the environment. The third generation nanovectors are specifically designed to overcome different biological barriers and act on different subcellular targets, to perform functions in a time-sequenced manner with coordination between multiple, simultaneously released payloads of nanoparticles.[14]

With these these added 'tools' in the inventory of nanovectors, delivering more drug per biorecognition event as compared to immunotargeted drugs has become more efficient. Nanovectors also have a reduced clearance time, and hence decrease the toxic side effects caused by the persistence of drugs in the system. They also protect the drug against enzymatic degradation. By virtue of their properties, nanovectors can even allow drugs to cross barriers which earlier hindered their penetration, such as the blood-brain barrier, and vascular endothelium.[15] Since nanovectors can also carry imaging contrasts, they can be effectively used in targeted imaging modalities such as MRIs. Some nanoparticles themselves have image-enhancing properties.[16]

Nanovectors may directly be used in cancer chemotherapy. Nanoshells, which are metal-coated nanovectors, can reach highly specific sites of tumours, and be selectively activated by tissue irradiation. This would lead to thermal ablation, and the destruction of malignant tissue.[15]

Nanotechnology has been making headway in the domain of microarrays. 'Nanoarrays' allow a millionfold increase in the information density that can be packed in them, because the molecular depositions may now be controlled in the nanometre range. This has scope for detecting a large number of molecular species at the same time.[17,18]

The Future Ahead

Nanotechnology has a large potential for human use in the future, and a variety of platforms are under development. Quantum dots and nanoshells are being developed to improve MRI and CT scans in the imaging of cancer. Experiments have shown that some ligands can bind to apoptotic cells and hence, by monitoring apoptosis, the response to cancer therapy can also be monitored; for instance, the C2 domain of synaptotagmin and annexin 5 conjugated with iron oxide nanoparticles.[19] Similarly, research is also going on to improve implantable drug delivery systems to minimize peak plasma levels and reduce the frequency of re-dosing.[20]

Nanotechnology is also being tested to increase the growth and regeneration of nerve cells.[21] In-vivo early detection of cancer can occur using nanovector-delivered contrast agents involved in antibody targeting or signal amplification. For instance, Gadolinium carriers may replace sentinel lymph node biopsy. Implantable sensors may be designed, which prevent the non-specific absorption of serum protein ('biofouling'). Nanochips implanted with thousands of sensors made using nanowire, nanotube, and nanocantilever technology can be used to read the entire proteome and detect multiple diagnostic biomarkers. 'Bio-barcodes' are double-stranded DNA, with one end connected to a gold nanoparticle (AuNP), and the other to the analyte. These have a higher sensitivity and specificity than ELISA, and can be used in the rapid detection of trace analyte related to clinical medicine, food toxins, etc.[22]

In conclusion, the application of nanotechnology can revolutionise the field of cancer diagnostics and therapeutics. With rapid advancements in nanoscience, the interdisciplinary field of nanomedicine offers great potential for further research and development.

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