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NANOMEDICINE AND CANCER: A COMPERHENSIVE REVIEW

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PHARMACEUTICAL SCIENCES REVIEW ARTICLE

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ABSTRACT
Nanomedicine is an innovative and highly applicable tool in cancer.Nanomedicine is engineered nano scale 1-100nm structures and devices for diagnosis and therapy for cancer.Recently nanodevices capable of detecting cancer at its earliest stages, pinpointing it's location within the body and delivering anticancer drugs specifically to malignant cells.Nanotechnology is expected to have a dramatic impact on medicine. The application of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems is now often referred to as nanomedicine. Nanotubes, nanoshels, nanowires are different types of devices applicable in cancer diagnosis.The ultimate goal of nanomedicine is to develop well engineered nanotools for the prevention, diagnosis and treatment of many diseases. The extraordinary growth in nanotechnology has brought us closer to be able to vividly visualize molecular and cellular structures. This technology has ability to differentiate between normal and cancerous cells and to detect. With the use of nanomedicine, targeted drug delivery has been achieved.

KEYWORDS: *Nanomedicine, cancer, nanoparticles*

INTRODUCTION

Nanomedicine is nowadays an important tool in cancer.Nanomedicine broadly defined as the development of engineered nano scale 1-100nm structures and devices for better diagnostics and highly specific medical intervention in curing disease or repairing damaged tissues [1].

Currently, there is a lot of research going on to design novel nanodevices capable of detecting cancer at its earliest stages, pinpointing its location within the body and delivering anticancer drugs specifically to malignant cells.

Not too long ago diseases such as smallpox, polio, tuberculosis, and typhoid fever ran rampant. They consumed billions of lives within their prime, but the advent of new medical technologies such as antibiotics and immunizations stopped them in 2 their tracks. Nanoscale is generally considered to be at a size below 0.1 µm or 100 nm (a nanometer is one billionth of a metre, 10-9 m). Nanotechnology is expected to have a dramatic impact on medicine. The application of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems is now often referred to as nanomedicine. Among many possible applications of nanotechnology in medicine, the use of various nanomaterials as pharmaceutical delivery systems for drugs, DNA, and imaging agents has gained increasing attention. Many varieties of nanoparticles are available, Numerous nanoparticle-based drug delivery and drug targeting systems are currently developed or under development.[3,4]

The major areas in which nanomedicine is being developed in cancer include:

- *Prevention and control*. Developing nanoscale devices to deliver cancer prevention agents and designing multicomponent anticancer vaccines.
- *Early detection and proteomics.* Developing "smart" collection platforms for simultaneous mass analysis of cancer-associated markers.
- *Imaging diagnostics.* Designing targeted contrast agents that improve the resolution of cancer to a single cell.
- *Multifunctional Therapeutics.* Creating therapeutic devices that can control the release of cancer fighting drugs and optimally deliver medications.

APPLICATION OF NANOMEDICINE AS AN IMAGING AND DETECTION TOOL IN CANCER

Nanoparticle contrast agents are being developed for tumor detection purposes. Labeled nanoparticles and non-labeled particles are already being tested as imaging agents in diagnosis procedures such as computed tomography and nuclear magnetic resonance imaging.[8]

Super paramagnetic nanoparticles are used for magnetic resonance imaging (MRI).[9] They consist of an inorganic core of iron oxide coated or not with polymers like dextran.

There are two main groups of nanoparticles:

1) Super paramagnetic iron oxides whose diameter size is greater than 50nm,
2) Ultra small super paramagnetic iron oxides whose nanoparticles are smaller than 50 nm greater sensitivity as compared to conventional days 4.

NANOWIRES

Conductive wire, 10 to 20 nanometers thick, is strung across a channel through which a sample will pass. To detect proteins or DNA, probes made of complementary antibodies or DNA are attached to each wire. When a protein meets its matching antibody, it binds to the probe and changes the conductive properties of the wire, allowing the event to be detected electronically.

Nanowires can be coated with a probe such as an antibody that binds to a target protein. Proteins that bind to the antibody will change the nanowire's electrical conductance and this can be measured by a detector.[13], [14]. The DNA biosensors being developed are more efficient and more selective than current detection methods.

CANTILEVERS AND NANOCRYSTALS

Molecular probes, such as single-stranded DNA, can also be attached to beams just a few nanometers thick. When exposed to a DNA sample, complementary strands bind to the probes on the cantilever, causing the beams to bend slightly. [15]

DIFFERENT NANOCARRIERS

DENDRIMERS

Complex almost spherical macromolecules with diameter 1-10 nm, have improved physical, chemical, and biological properties compared to traditional polymers. Dendrimers have a tree-like structure with many branches where a variety of molecules, including drugs can be attached. Less than 5 nm in diameter. Dendrimer. On other branches, they attached fluorescent imaging agents and a vitamin called folic acid, [16,17]. In addition to these examples of individual nanoparticles,.

Quantum dots

nanometer sized semiconductor nanocrystals with superior fluorescent properties,possess remarkable optical and electronic properties that can be precisely tuned by changing their size and composition, due to their very small size (2-10 nm). Due to their relatively inexpensive and simple synthesis, quantum dots have already entered the market for experimental biomedical imaging applications.

Quantum dots are inorganic fluorescent semiconductor nanoparticels composed of 10-50 atoms with a diameter ranging from 2 to 10 nm [18,19]. Their sizes and shapes which determine their absorption and emission properties can be controlled precisely [20]. They are widely studied for optical image application in living systems and are stable for months without degradation and alteration [18]. Targeted ligands have been attached to QDs in order to achieve specific targeting for tumor cell labeling [19]. Thus, they are assured to be chosen as long-term, high-sensitivity and multicontrast imaging agents applied for the detection and diagnosis of cancer in vivo [20]. Now, many researchers focus on using quantum dots as carriers for genes delivery to overcome the obstacles of cell membranes. Klein and co-workers have developed functionalized silicon quantum dots (SiQD) to serve as self-tracking transfection tool for ABCB1 siRNA [21]. Li et al. investigated glutathione–mediated release of functional plasmid DNA from positively charged CdTe quantum dots, which suggested potential applications of these QDs in selective unpacking of payload in living cells in a visible manner [22]. The applicability of quantum dots for cancer therapies based on the mechanisms of photosensitization and radiosensitization has also been investigated. Possessing electronic energy levels in the range of 1-5eV, quantum dots can perform as photosentizers applied in photodynamic therapy (PDT) [23]

NANOPARTICALS

Particles composed of a variety of materials can be constructed to contain therapeutic molecules in their core and to release them at a desirable time and location. Some nanospheres are made of poly(isohexylcyanoacrylate), poly(methylcyanoacrylate) and biodegradable poly(ethylcyanoacrylate). Molecules like poly (ethylene glycol) reduces nonspecific attachment or uptake.[24] Fluorescent detection. A group of scientists have used nanoparticles to deliver a gene that forces blood vessels to selfdestruct.This prevents angiogenesis, or the formation of blood vessels in a tumor.[25]

NANOSHELLS

Solid silica nanospheres, sometimes encased in a thin layer of gold, will travel through the bloodstream without entering most healthy tissues, but they tend to accumulate in tumor tissue. Destruction of solid tumors using high heat has been in investigation for some time. Some thermal therapies include the use of laser light, focused ultrasound and microwaves.[26] Nanoshells have a core of silica coated with an ultra-thin metallic layer, normally gold.[27]

Due to their small size, nanoshells are preferentially concentrated in cancer cells by EPR or enhanced permeation retention.[28] In tissues that was treated with NIR light alone.[29] Thus using a NIR laser, cancer tissue can be destroyed by local thermal heating around the nanoshells.[29, 30]

MICELLES Polymeric micelles are usually formed into core-shell structures by spontaneous assembly when its concentration is above critical micelle concentration (CMC). They have a number of unique features, including nano-size, easy manipulation of surface chemistry, core functionalities, as well as ease of fabrication, making them suitable as carriers for encapsulation and delivery of water insoluble agents [31]. The micelles have a solid-like inner core, which serves as a potent nano-container of hydrophobic compounds for solubilization of chemotherapeutics, including docetaxel (DOC)[32], paclitaxel (PTX)[33], camptothecin[34], and dequalinium (DQA)[35], etc. While polyionic complex (PIC) micelles and cationic polymer micelles can incorporate and protect anionic gene or protein with low rate of cellular uptake and low physiological environment stability, such as vascular endothelial growth factor (VEGF), siRNA[36], luciferase reporter gene[37], and so forth. Thanks to their hydrophilic shell, polymer micelles play an important part in escaping the recognition of RES and prolonging the blood circulation of drugs. The small size (<100 nm) allows micelles for efficient accumulation in pathological tissues with permeabilized vasculature via the enhanced permeability and retention (EPR) effect [38]. However, the physiological factors, such as the density and heterogeneity of the vasculature at tumor sites, interstitial fluid pressure, and transport of macromolecules in the tumor interstitium, are responsible for the extent of micelles extravasations. Mikhail contributed a detailed review in this perspective [39]. Stimuli-responsive polymeric micelles are often designed for controlled release of drug into tumor tissue with external stimuli trigger, like temperature, pH, ultrasound and special enzymes [40, 41]. Combined the targeted delivery of therapeutics and pH-controlled drug release together, providing a tumor-selective nanocarrier for the efficient delivery of anti- cancer drugs [42].

CARBON NANOTUBES (diameter of 1-20 nm)

Carbon nanotubes, and magnetic iron oxide nanoparticles, gold-coated silica nanoshells, can transform electro-magnetic energy into heat, causing a temperature increase lethal to cancer cells merely by increasing the magnetic field or by irradiation with an external laser source of near infra red light at the very location where these nanoparticles are bound to or internalized within tumour cells.[43].single-walled carbon nanotubes (SWCNT) with a single cylindrical carbon wall and multi-walled carbon nanotubes (MWCNT) with multiple walls—cylinders nested within other cylinders [44]. Thanks to their unique electronic, thermal, and structural characteristics, they can offer a promising approach for gene and drug delivery for cancer therapy [44, 45]. Heating of organs and tissues by placing multifunctional nanomaterials at tumor sites is emerging as an art of tumor treatment by "nanothermal therapy" [46].

Translocated into cell nucleus by nanotubes and cause cell death with continuous near-infrared radiation (NIR) because of excessive local heating of SWCNT in vitro[47]. It can afford carbon nanotubes an opportunity to be uptaken only by cancerous cells via functionalization of them with tumor-specific ligands and antibody, like folic acid and monoclonal antibody which can act as targeting agents for many tumors [48]. Accordingly, a highly effective drug delivery system triggered by pH change has been developed via firstly coated with a polysaccharide material and then modified with folic acid [48].

NANOTECHNOLOGY TOOLS IN MEDICINE

Different methods for the synthesis of nanoengineered materials and devices can accommodate precursors from solid, liquid or gas phases and encompass a tremendously varied set of experimental techniques. Detailed presentations of these are beyond the scope of this review.

microcontact printing) techniques begin with a macroscopic material or group of materials and incorporate smaller-scale details into them, whereas "*bottom-up*" (organic- synthesis, self-assembly) approaches, begin by designing and synthesizing custom-made molecules that have the ability to self-assemble or self-organize into higher order mesoscale and macroscale structures[49] A myriad of studies is available for applications of micro- and nanotechnologies in chips for medical molecular diagnostics. For the subsequent readout detection either fluorescence- or radionuclide-based markers, or surface plasmon resonance spectroscopy can be applied [50]

scanning probe microscopy (STM, AFM) that allow three dimensional-type topographical atomic and molecular views or optical responses (SNOM) of nanoscale structures ; in situ monitoring techniques that allow the monitoring and evaluation of building block assembly and growth[51] ellipsometry, an optical method, with the capability of measuring in liquid environment (e.g, protein solution) to study protein and cells adsorption on solid surfaces6, it has been employed to discriminate and identify bacteria at the species level, and is very promising for analytical purposes in biochemistry and in medicine[52,53]

Not only to image surfaces of molecules or sub-cellular compartments, but also to measure molecular forces between molecules. This is substantially increasing our knowledge of molecular interactions[54] Figures a and b, show the SNOM and AFM microscopes, respectively. Figure c is an AFM topography image of a cluster of fibrinogen molecules adsorbed on amorphous carbon thin film, after incubation of 5min. The adsorbed cluster has preserved the morphological characteristics of the protein molecule[55]

FUTURE IMPLICATIONS

Nanotechnology will radically change the way we diagnose, treat and prevent cancer to help meet the goal of eliminating suffering and death from cancer. Nanotechnology can provide the technical power and tools that will enable those developing new diagnostics, therapeutics, and preventives to keep pace with today's explosion in knowledge. With nanomedicine, we might be able to stop cancer even before it develops. With such technology, nanomedicine has the potential to increase the life span of human beings.

In future there are some techniques like nanobotes and nanohumvees aare going to introduced. Which having very specific functions like they are very target specific to destroy the cancerous cellsl and have no effect on host cells.

It will create populations with a large proportion of elderly people – an aging society. The elderly are going to require more health attention and consequently more health expenditures. One scenario that we have to imagine is whether the savings from more efficient cancer nanomedicine will counterbalance the expense of an increased aged population.21 In addition, as nanotechnology improves cancer treatment in terms of efficiency and quality.

DISCUSSION & CONCLUSION

Nanotechnology in modern medicine and nanomedicine is in infancy, having the potential to change medical research dramatically in the 21st century. Nanomedical devices can be applied for analytical, imaging, detection, diagnostic and therapeutic purposes and procedures, such as targeting cancer, drug delivery, improving cell-material interactions, scaffolds for tissue engineering, and gene delivery systems, and provide innovative opportunities in the fight against incurable diseases. Thanks to nanotechnology tools and techniques, there has been a huge progress on understanding the function of biological structures and their interaction and integration with several non-living systems, but there are still open issues to be answered, mainly related to biocompatibility of the materials and devices which are introduced into the body. Many novel nanoparticles and nanodevices are expected to be used, with an enormous positive impact on human health. The vision is to improve health by enhancing the efficacy and safety of nanosystems and nanodevices. In addition, early diagnosis, implants with improved properties, cancer treatment and minimum invasive treatments for heart disease, diabetes and other diseases are anticipated. In the coming years, nanotechnology will play a key role in the medicine of tomorrow providing revolutionary opportunities for early disease detection, diagnostic and therapeutic procedures to improving health and enhancing human physical abilities, and enabling precise and effective therapy tailored to the patient.

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