Nanoparticle-Based Drug Delivery in Cancer Therapy

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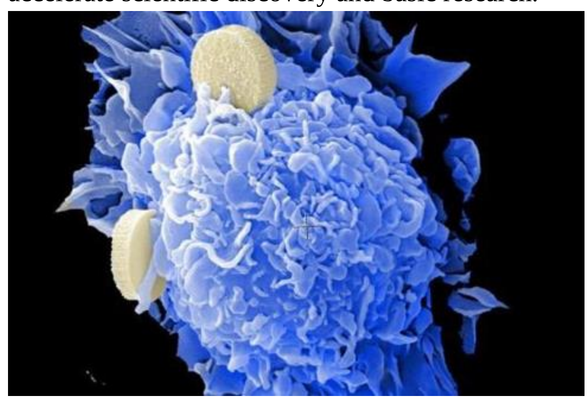
***Abstract* - The conquest of cancer continues to pose great challenges to medical science. The disease is notably complex, affecting nearly every tissue lineage in our bodies and arising from normal cells as a consequence of diverse mutations affecting many genes. Cancer nanotechnology is a branch concerned with the application of nanomaterials and nanoparticle-based theranostics to the diagnosis and treatment of cancer.**

INTRODUCTION

Scientists are using cells isolated from human tumors to tackle cancers, they are developing nanoparticles which acts as a mini delivery vehicle, this vehicle could be a drug or an antibody to reach the site of the tumor more efficiently like a (suicide genes) and attack the cancer cells. Researchers at John Hopkins School of Medicine are using nanoparticles to activate the immune system cells, this treatment is similar to how a vaccine works where immune cells only kill cancer cells. The Nanoparticles in Medicine thematic issue provides a comprehensive assessment of the state-of-the-art of biological and biomedical applications of nanomaterials. The issue encompasses the unique capabilities of nanoparticles for in vitro detection, in vivo diagnosis, multimodal imaging, chemo-, photo-, gene-, and immunotherapy, theranostics, and their clinical translation, and it is organized into sections covering inorganic (metallic and metal oxide) nanoparticles, liposomes, organic nanoparticles, and hybrid nanoparticles. .

The most common use of nanotechnology in medicine has been in the areas of

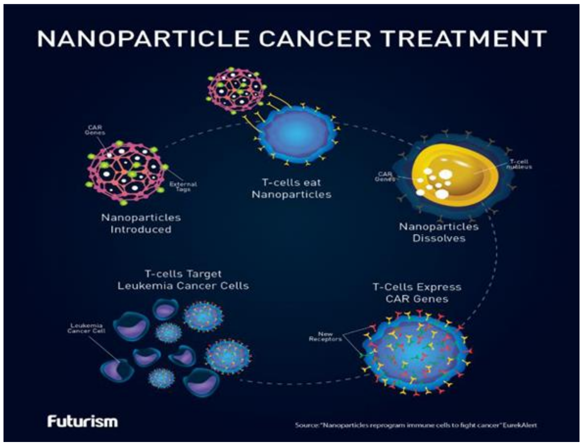
developing novel therapeutic and imaging modalities that have the potential to outperform the current state of the art in these areas. With the exponential introduction of novel nanotechnology platforms for life science applications, the potential application of nanotechnology in medicine extends significantly beyond these early uses. The National Cancer Institute in its 2004 commitment of $144 million toward the development of novel nanotechnologies for improving cancer mortality defined the path of opportunities in six areas including: (1) detection of molecular changes responsible for disease pathogenesis; (2) disease diagnosis and imaging; (3) drug delivery and therapy; (4) multifunctional systems for combined therapeutic and diagnostic applications; (5) vehicles to report the in vivo efficacy of a therapeutic agent; and (6) nanoscale enabling technologies, which will accelerate scientific discovery and basic research.



Dendritic cells with nanoparticles which are porous silicon particles loaded with immune stimulating mol. and tumor antigen, now activated injected back into host for anti-tumor action.

THE WORKING OF NANOTECHNOLOGY

The nanoparticles are modified as such that they get attached only to cancer cells and no other neighbouring healthy cells and get carried inside where they bind to the cancer cells, they are taken into the cell and cannot pass through the surface, instead part of the cell surface forms a pit and then it engulfs the nanoparticles .Cellular protein wraps around the vesicles and drive it inside the cell and then the vesicle containing the nanoparticle moves towards the centre of the cell farther and fuses with a compartment called the (ENDOCELL) this is particle digestive system of the cell, the inside is acidic and its' job is to digest the incoming material and the nanoparticles are degraded inside releasing drug into the cell, the drug then can kill the cancer cell.



EARLY DETECTION AND DIAGNOSIS

For cancer, nanodevices are being investigated for the capture of blood borne biomarkers, shed exosomes. Nano-enabled sensors are capable of high sensitivity, specificity and multiplexed measurements. Next generation devices couple capture with genetic analysis to further elucidate a patient's cancer and potential treatments and disease course. Already clinically established as contrast agents for anatomical structure, nanoparticles are being developed to act as molecular imaging agents, reporting on the presence of cancer-relevant genetic mutations or the functional characteristics of tumor cells. This information can be used to choose a treatment course or alter a therapeutic plan. Bioactivatable nanoparticles that change properties in response to factors or processes within the body act as dynamic reporters of in vivo states and can provide both spatial and temporal information on disease progression and therapeutic response

TREATMENT AND THERAPY

Research on nanotechnology cancer therapy extends beyond drug delivery into the creation of new therapeutics available only through use of nanomaterial properties. Although small compared to cells, nanoparticles are large enough to encapsulate many small molecule compounds, which can be of multiple types. At the same time, the relatively large surface area of nanoparticle can be functionalized with ligands, including small molecules, DNA or RNA strands, peptides, aptamers or antibodies. These ligands can be used for therapeutic effect or to direct nanoparticle fate in vivo. These properties enable combination drug delivery, multi-modality treatment and combined therapeutic and diagnostic, known as "theranostic," action. The physical properties of nanoparticles, such as energy absorption and re-radiation, can also be used to disrupt diseased tissue, as in laser ablation and hyperthermia applications.

CURRENT NANOTECHNOLOGY TREATMENTS

The use of nanotechnology for diagnosis and treatment of cancer is largely still in the development phase. The application of nanotechnology to medicine includes the use of precisely engineered materials to develop novel therapies and devices that may reduce toxicity as well as enhance the efficacy and delivery of treatments. As a result, the application of nanotechnology to cancer can lead to many advances in the prevention, detection, and treatment of cancer. The first nanotechnology-based cancer drugs have passed regulatory scrutiny and are already on the market including Doxil® and Abraxane®.

In recent years, the U.S. Food and Drug Administration (FDA) has approved numerous Investigational New Drug (IND) applications for nano-formulations, enabling clinical trials for breast, gynecological, solid tumor, lung, mesenchymal tissue, lymphoma, central nervous system and genito-urinary cancer treatments.

APPROVED CANCER DRUG THERAPIES BASED ON NANOTECHNOLOGY

Trade name	Compound	Nanocarrier
Abraxane	Paclitaxel	Albumin bound paclitaxel
DaunoXome	daunorubicin	Pegylated Liposome
Doxil	doxorubicin	Pegylated Liposome
Bexxar	anti-CD20 conjugated to idodine131	Radioimmunoconjugate
Zevalin	anti CD 20 conjugated to yittrium-90	Radioimmunoconjugate
Zeladex	goserelin acetate	Polymer rods
Myoset	doxorubicin	Non-pegylated liposome
Oncasper	PEG-L-asparaginase	Polymer-protein conjugate
Ontak	IL-2 fused to diphtheria toxin	Immuno toxin fusion protein
SMANCS	Zinostatin	polymer protein conjugate

CHALLENGES IN NANO DRUG DELIVERY

The use of diverse nanomaterials with desired properties and recent progress in the drug delivery arena have revealed outstanding challenges in cancer therapy and management. It is anticipated that the nanomaterials will revolutionize the entire health care system based on the dramatic developments made in drug delivery sector over the past few decades. However, the design of effective cancer nanotherapeutics remains a great challenge, and only a few nanoformulations have entered clinical trials. A schematic representation of the major challenges in the delivery of cancer nanotherapeutics. The physicochemical properties of nanomaterials play a significant role in the biocompatibility, and toxicity in the biological systems. Therefore, synthesis and characterization of the nanomaterials for drug delivery need to be carefully performed to avoid the potential.

Applications of Nanotechnology in cancer treatment:

1. Nanotechnology aids in tumor imaging
   Different anti-tumor drugs and biomolecules including peptides, antibodies or other chemicals, can be used with nanoparticles to label highly specific tumors, which are useful for early detection and screening of cancer cells.
2. Nanotechnology Tools Used in Cancer Diagnosis
   Nanotechnology can validate cancer imaging at the tissue, cell, and molecular levels. This is achieved through the capacity of nanotechnology applications to explore the tumor's environment, For instance, pH- response to fluorescent nanoprobes can help detect fibroblast activated protein-a on the cell membrane of tumor-associated fibroblasts.
3. Nanotechnology used in cancer biomarker screening
   Cancer biomarkers are biological features whose expression indicates the presence or state of a tumor. Such markers are used to study cellular processes, to monitor or identify changes in cancer cells, and these results could ultimately lead to a better understanding of tumors. Biomarkers can be proteins, protein fragments or DNA. Among them, tumor biomarkers, which are indicators of a tumor, can be tested to verify the presence of specific tumors.

CONCLUSION

As successful as researchers have been in using nanotechnology to address and solve many important questions, the ultimate measure of the field's success lies in the translation of research discoveries to the clinic and the target is to eliminate many of the off-target side effects with current treatments and provide a long lasting immunity.

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