Nanotechnology applications in hematological malignancies

(Essay)

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By

Ahmed Samir Abd El-Hamid

M.B.B.Ch. Cairo University

Under supervision of

Prof.Dr.Hala Gabr Metwally

Professor of clinical and chemical pathology

Faculty of Medicine

Cairo University

Dr.Basma Mustafa El-Gamal

Assistant professor of clinical pathology

National Cancer Institute

Cairo University

Faculty of medicine

Cairo University

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بسم الله الرحمن الرحيم

"قالوا سبحانك لا علم لنا إلا ما
علمتنا انك أنت العليم
الحكيم"

البقرة :٣٢

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List of abbreviations

ADM : Adriamycin

AL : Acute leukemia

ALCL : Anaplastic large cell lymphoma

ALK : Anaplastic lymphoma kinase

ALL : Acute lymphoid leukemia

AML : Acute myeloid leukemia

APL : Acute promyelocytic leukemia

ATRA : All trans retinoic acid

AuNPs : Gold nanoparticles

B-CLL : B-Chronic lymphocytic leukemia

CML : Chronic myeloid leukemia

CNTs : Carbon nanotubes

CRI : Cancer related inflammation

DNA : Deoxyribonucleic acid

DNR : Daunorubicin

EGFR : Epidermal growth factor receptor

EPR : Enhanced permeation and retention

FCM : Flow cytometry

FDA : Food and drug administration agency

FISH : Fluorescent in situ hybridization

Flk-1 : Fetal liver kinase-1

Flt-1 : Fms-like tyrosine kinase-1

GMR : Giant magneto resistance

GNPs : Gold nanoparticles

GPI : Glycosylphosphatidylinositol

HIV : Human immune deficiency virus

HSCs : Hematopoietic stem cells

IR : Infra red

KDR : Kinase domain receptor

LHRH : Luteinizing hormone releasing hormone

LMWSC : Low molecular weight water-soluble chitosan

mABs : Monoclonal antibodies

MDR : Multidrug resistance

MNPs : Magnetic nanoparticles

MRD : Minimal residual disease

MRI : Magnetic resonance imaging

MWNT : Multiwalled carbon nanotubes

NIR : Near infra red

Nm : Nanometere

NT : Nanotechnology

PCR : Polymerase chain reaction

PE : Polyethelene glycol

QDs : Quantum dots

RNA : Ribonucleic acid

RSV : Respiratory syncytial virus

RT-PCR : Reverse transcriptase polymerase chain reaction

scFv :Single chain antibody fragments

siRNAs : Small interfering RNAs

SNPs : Single nucleotide polymorphism

SPIONs : Superparamagnetic iron oxide nanoparticles

SPR : Surface plasmon resonance

SQUID : Super conductor quantum interference devices

STM : scanning tunneling microscope

Tet : Tetrandrine

TK : Tyrosine kinase

VEGF : Vascular endothelial growth factor

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Abstract

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The biological picture of cancer is rapidly advancing from models built from phenomenological descriptions to network models derived from systems biology, which can capture the evolving pathophysiology of the disease at the molecular level. The translation of this (still academic) picture into a clinically relevant framework can be enabling for the war on cancer. Nanotechnology can play a pivotal role, providing the technological power and tools that will enable those developing new diagnostics, therapeutics, and preventives to keep pace with today's explosion in knowledge. There are many interesting nanodevices being developed that have a potential to improve cancer detection, diagnosis, and treatment. Hematological malignancies represent a specific class of cancer that attracted special attention in the field of nanodiagnsis and treatment.

Key Words :

Nanotechnology – Cancer - Hematological malignancies .

Introduction

Introduction

Nanotechnology is the creation of useful materials, devices, and systems through the manipulation of matter on a miniscule scale. A nanometer is a billionth of a meter. Nanotechnology is being applied to almost every field imaginable, including electronics, magnetics, optics, information technology, materials development, and biomedicine ***(U.S National Cancer Institute, 2011).***

Nanobiotechnology refers to materials and processes at the nanometer scale that are based on biological or biologically inspired molecules and nanotechnological devices used to monitor or control biological processes ***(Ramseden, 2005).***

Cancer is the third leading cause of death (after heart disease and stroke) in developed countries ***(Cai et al., 2008)***. During dealing with cancer, three major problems are encountered; the first problem is related to diagnosis: detection of cancer at early stages is a critical step in improving cancer treatment. Currently; conventional detection of cancer is done by observing the physical growth changes in the organ by X-rays and/or CT scans and is confirmed by biopsy. However, the limitation of these methods is that they are not very sensitive and the detection is possible only after substantial growth of the cancerous cells ***(Singh and Nehru, 2008).***

The second problem is related to therapy: conventional treatment options of cancer are surgery, radiation therapy and chemotherapy. However, all these methods have their own limitations (in surgery one loses the organ and cancer may appear again, in radiation therapy even the healthy cells get burnt, cancerous cells burning is not uniform and the

burnt part may become dead and non functional, in chemotherapy treatment is harmful to healthy cells, approach is gross and rarely successful if the cancer is in advanced stage ***(Singh and Nehru, 2008)***. The third problem is related to the follow up and detection of response after treatment.

Nanotechnology can find new solutions to all these problems, novel nanodevices are capable of one or more clinically important functions, including detecting cancer at its earliest stages, pinpointing its location within the body, delivering anticancer drugs specifically to malignant cells, and determining if these drugs are killing malignant cells ***(U.S. department of health and human services, NIH, NCI, 2004).***

Hematological malignancies are the types of cancer that affect blood, bone marrow and lymph nodes. Historically; hematological malignancies have been most commonly divided by whether the malignancy is mainly located in the blood (leukemia) or in lymph nodes (lymphomas).

Conventional laboratory diagnostic methods for leukemia and lymphoma apply combinations of bone marrow and peripheral blood morphological and cytochemical analyses including karyotyping, immunophenotyping by flow cytometry or microarray and amplification of malignant cell mutations by PCR, as well as lymph node biopsy especially in lymphoma ***(Arber and Cousar, 2009).***

However, all these methods have some limitations; PCR-based methods have proven to be highly sensitive diagnostic techniques for cellular recognition, but they are indirectly detecting cells by monitoring

RNA expression and require prolonged RNA isolation steps before analysis. In addition, the variable sensitivity of PCR can limit its effectiveness as a diagnostic technique and can lead to false-negative results, particularly with occult tumor cells where low-level signals are expected. Immunophenotypic analyses are also time-consuming and costly, and therefore, there is still a need to develop new technologies for rapid, economical cell recognition ***(Herr et al., 2006).***

Nanotechnology, either alone or in combination with traditional diagnostic methods, tries to provide new sensitive, specific, reproducible and cheap methods for diagnosis of hematological malignancies.

Regarding treatment, nanotechnology offers the best promise among the various approaches for targeted delivery of drugs and genes to the tumor site and alleviation of the side effects of chemotherapeutic agents ***(Robertson and Ferrari, 2007).***

Finally, current technologies used to examine bone marrow samples may fail to detect the presence of leukemia cells below 1% to 5% of total leukocytes after treatment, i.e., minimal residual disease. As a result, opportunities to intensify therapy may be overlooked, leading to relapsed disease, in these cases, the ability to reliably detect residual leukemia cells, when present below 5%, to monitor the efficacy of therapy is critical for improving care ***(Jaetao et al., 2009).***

Nanotechnology can also improve sensitivity for detection of minimal residual disease compared with the current standard of care.