“NANOTECHNOLOGY ,NANODEVICES AND LABORATORY DIAGNOSIS”

Jyoti Priyadarshini Shrivastava
PROFESSOR
Department of Pathology
Gajra Raja Medical College,Gwalior(M.P.)
drpriyajyoti22@gmail.com

Nanotechnology(Nanotech) is a revolution of the twentieth century.The prefix “nano” is a Greek word which means “dwarf ”. Nanotechnology is the study of extremely small structures. Nature operates at the nanoscale, Cells in human body are 10 μm across. Cell organelles are even smaller . The dimensions of nanostructures are advantageous as they are in the range of the size of various biomolecules ex: nucleic acids, small proteins, and viruses,hence can be used in diagnostics .Understanding biological processes on the nanoscale level is a basis of development of nanotechnology.

By definition, Nanotechnology is an emerging branch of science for designing tools and devices of size 1 to 100 nm with specific function at the cellular, atomic and molecular levels. Nanotechnology employed in biomedical research and clinical practice is termed as nanomedicine. Nanomedicine can be defined as the application of nanotechnology in health care, diagnosis and treatment in order to maintain or increase the health status of population by using atomic/molecular knowledge and structures (nanometer = 1x10-9 meter) of the human body. Till date integration of nanoparticles and biology has led to the development of diagnostic devices, contrast agents, advanced therapy applications, drug delivery therapy, and imaging approaches.

Early disease detection even before symptoms appear, ease of diagnostic procedures with improved imaging of internal body structure have been developed with the help of a new branch of laboratory medicine termed nanodiagnostics. Use of microchips, biosensors, nanorobots, nano identification of single celled structures, and microelectromechanical systems are current techniques being developed for use in nanodiagnostics.Diagnosis is now being carried out on a nano-scale leading to a trend of utilising easy to use hand held devices.

American physicist Richard Feynman is considered to be the father of nanotechnology.(Fig.1)

Healthcare is concerned with the maintenance or restoration of the health of the body or mind by means of diagnosis, treatment(Management), and prevention of disease, illness, injury, and other physical and mental impairments including repair or regeneration.

Nanotechnology is guiding us to design nano devices(scientific instruments) with special and unique properties.Nanotechnology allows custom-designed materials on a molecular scale and enable the design of new and different devices.Nanotechnology with its unlimited diagnostic applications is currently bringing paradigm shift in the areas of biomarker research, cancer diagnosis and infectious microorganisms detection.

Properties of Nanoparticles:

1.Electrical conductance
2.Chemical reactivity
3.Protein adsorption
4.Magnetism
5.Optical effects
6.Physical strength
7.Increased Surface Area to Mass Ratio
8.Surface Enhanced Raman Spectroscopy
9.Fatigue resistance
10.Low percolation threshold
12.High reactivity due to increase surface area/surface energy

Types of Nanodevices in use are as follows:(Fig.2)

Nanoparticle (Diamond,salt,fullerene etc.)
Graphene.
Carbon Nanotubes.
Nanorods,Nanotubes,Nanowires.

Cantilevers
Dendrimers
Nanocrystalline Material.
Nanostructured Material

CLASSIFICATION OF NANOMATERIALS

A.Classification of Nanomaterials based on type of material:

•Carbon based Nanomaterial-Fullerenes,Graphene,Carbon black etc.
• Inorganic based Nanomaterial-Metal oxide,Lipid based,Ceramic etc.
•Organic based Nanomaterial-Ferritin,Micelles,Liposomes ,Dendrimers etc.
•Composite based Nanomaterial

B.Dimensionwise classification of Nanomaterials:

•Zero dimension (0D)-Spheres,Clusters
• One dimension(1D)- Nano rods, nano wires (dimension less than 100 nm)
• Two dimension(2D)-Nanofilms,Plates
• Three dimension(3D)-Nanoparticles

C. Classification based on Origin

A. Natural
B. Artificial

C.Classification based on pore dimensions

A. Microporous
B. Mesoporous
C. Macroporous

Phase composition:

• Single phase solids-Crystalline, amorphous particles etc.
• Multi-phase solids-Matrix composites, coated particles etc.
• Multi phase systems-Colloids,Aerogels,Ferro fluids etc.

Applications of nanodiagnostics

. Some important areas of clinically relevant applications are:
•Immunology/Immunohistochemistry.
•Genotyping.
•Early detection of cancer/Biomarker research.
•Detection of infectious microorganisms.

1.Nanotechnology in immunology:

A.Gold Nanoparticles(AuNPs) show the expression of proinflammatory cytokines and with particular size significantly increase the immunostaining of IL-1β and IL-6. The inflammatory response was evident as early as day 1 following AuNPs exposure These findings suggest an important role of nanoparticles size on the acute phase immune response in experimental animals.

B.Immuno-Nanoparticles for Multiplex Protein Imaging in Cells and Tissues: Imaging-based molecular diagnosis using antibody-conjugated NPs (immuno-NPs)help in identification of various,numerous proteins in cells ansd tissues.

Successful applications of nanotechnology is enabling new generations of vaccines, adjuvants and immunomodulatory drugs with an aim to improve response to a range of infectious and non-infectious diseases.

C.Quantum dot immunohistochemistry (IHC) can detect the very low expressions of Human Epidermal Growth Factor Receptor 2 (HER2) as well as multichannel detection.

D.Biomarker detection:Many of them recognize receptors overexpressed on the surface of malignant cells, including the folate receptor, EGFR, HER2, GLUT, GRPR, and CCR5.Early detection at extremely low levels.

2.Nanotechnology in Genotyping:

Small size and improved surface area allows nanomaterials to be used as biosensors in the genotyping.They are highly sensitive in recognition of single-base mismatch in the presence of incomparable wild-type DNA fragments.
DNA microarray technology used in genotyping.(Microarray is collection of DNA spots). Oligonucleotides with specific DNA sequences, known as probes, bind to the target DNA to detect sequence variants.Microarrays can analyse a large number of variants simultaneously.
Nanomaterials have a role in Gene Therapy too.

3.Nanotechnology in cancer diagnosis /Biomarker Research:

Nanotechnology-based techniques accurately track living cells and monitor dynamic cellular events in tumors.

1. Nanotechnology used in cancer biomarker screening
   Cancer biomarkers are biological features proteins,fragments,glycans,antibodies or DNA. The expression of abnormally expressed biomarkers are used to study cellular processes, to identify cancer cells alterations. Also indicate the presence or state of a tumor guiding better understanding of tumors. Protein biomarkers for many cancers have been discovered.(Proteomics)
2. pH- response to fluorescent nanoprobes can help detect fibroblast activated protein-a on the cell membrane of tumor-associated fibroblast
3. Nanotechnology to make lab-on-chip microfluidics devices that can be used for immuno-screening or to study the properties of tumor cells.
4. Quantam Dots(QDs) can concentrate in a single internal organ .QDs, which combine with biomolecules, including peptides and antibodies, *in vivo*, can be used to target tumors for cancer imaging and treatment.
5. QDs used in Prostate and Ovarian cancers.
6. Circulating tumour cells(CTC's)are biomarkers,detection leads to early dianosis of cancer,metastasis and recurrence.Magnetic, fluorescent, plasmonic and conductive nanoparticles have been recently used to detect CTCs either directly/whole blood or with enrichment methods.

Nanotechnology is a new immuno-oncology weapon.It is better defined as "Small technology with a Big impact"
It is effective with a blend of diagnosis and treatment.Cancer nanotechnology is relatively novel interdisciplinary area with comprehensive research.Improvement in chemotherapeutic delivery through enhanced solubility and prolonged retention time has been the focus of research in nanomedicine,so as to minimise side effects and make treatment effective and friendly.

Enhanced solubility and prolonged retention leads to concentrated nanoparticle drugs in tumours due to the increased permeability of angiogenic blood vessels.Drug loaded carbon nanotubes 100nm long and a few nm wide enter angiogenic blood vessels but not normal blood vessels.

The submicroscopic size,flexibility of nanoparticles provides access to remote areas of human body and restrictive, selective tumor access avoiding killing normal/healthy cells.

Nanotechnology can be used for both in vivo and in vitro biomedical research and applications. Naño particles can be used in targeting tumor cells at an early stage by Particles like dendrimers, quantam dots and fullerene increasing cure rates and chances of survival.It can be used to develop "signature protein" to treat cancer.

4.Nanoparticles in infectious diseases:

Nanotechnology helps in rapid, accessible and is very effective due to its high sensitivity in pathogen detection.Nanomaterials with proven efficacy in detecting infections (viral and bacterial) include graphene-based materials, quantum dots (QDs) and gold or magnetic NPs .
In this era of zoonoses and pandemics,nanotechnology is so sensitive that even a single nanoparticle is capable of emitting a signal strong enough to be captured, thus enabling early identification of infections. Proper and effective treatment not only saves the patient, but also prevents the spread of the pathogens.Few examples are:Nanocrystalline silver kills the microbes from the wound.Nanoparticles with nitric oxide gas are used to treat infections as they kill bacteria.Nanoparticles can cross BBB and other natural barriers and combats drug resistance (Resistant T.B) and co-infection like TB-HIV deadly combo.

5.Nanotechnology in DNA Analysis

DNA (genetic material) is one of the most important and unique evidence that could identify the presence of a person at crime site.
Magnetic nanoparticles help extract DNA from skin, hair,saliva, blood and semen. By atomic force microscopy technique,Nanotechnology-based tools ex:carbon nanotube helps to analyze DNA sequences .

6.Stratified nanodevice vaccines

Stratified nanodevices have attracted great attention for the development of vaccination. Nanodevices are constructed layer by layer of a component which are being utilized to deliver vaccine/nanoparticle formulations in a specific, targeted, and controlled manner. Nowadays, nanodevices are combined to the particulate-based system to improve the efficacy of vaccination.

7.Fabrication of folic acid magnetic nanotheranostics:

Nanodevices based on magnetite functionalized with folic acid (FA) with enhanced properties to be employed as theranostics in various types of cancer.

8.Nanotechnology and Stem cells:

a.Magnetic nanoparticles (MNP)s help isolate and group stem cells. Quantum dots guides molecular imaging and tracing of stem cells

b.Gene or drugs delivery into stem cellsmediated by carbon nano tubes, fluorescent CNTs and fluorescent MNPs

c.All these advances speed up the development of stem cells toward the application in regenerative medicine along with Stem cell-based therapeutics for the prevention, diagnosis and treatment of degenerative human diseases.

Unique nanostructures are being designed for controllable regulation of proliferation and differentiation of stem cells

9.Nanotechnology and emerging threats:

New diseases continue to be a threat especially emerging primitive bacterial diseases and zoonoses. Nanotechnology will enable diagnosis at presymptomatic stage and create a cure in a matter of days. With complete genomes and proteomes analysis for humans and for all known pathogens with highly parallel DNA and protein analysis and sufficient computer resources, it will be possible to spot any new pathogen almost immediately.This can check emergence of Pandemics.

10. Miscellaneous:

Nanotechnology is under study for the diagnosis and treatment of atherosclerosis ehere there is the buildup of plaque in arteries on the intimal layer. A nanoparticle is under development which mimics the body's "good" cholesterol, known as HDL (high-density lipoprotein), a heart friendly cholesterol which helps to shrink plaque.

Using Nanotechnology,we can activate and achieve stimulation of the body's own mechanisms to successfully repair diseased or damaged tissues.Graphene nanoribbons are being developed to help repair spinal cord injuries; preliminary research reveals that neurons grow well on the conductive graphene surface. Novel materials engineered to mimic the crystal mineral structure of bone or a restorative resin for dental applications .The aim is to replace the need for transplants and artificial organs.In the foreseeable future,advancement in remote monitoring and care, an economical option is in pipeline.

Nanotechnologies will enable personalised or customised medicine through point-of-care diagnostics through nanotech based rapid diagnostic tests and integration of diagnostics with therapeutics alongside affordability and Quality life.With increase in life span,average life expectancy being 72 years,Quality of Life is a major issue.

Although the potential diagnostic applications are unlimited, the most important current applications are foreseen in the areas of biomarker discovery, cancer diagnosis, and detection of infectious microorganisms.

Direct analysis of DNA and protein will enhance speed, accuracy, and sensitivity over conventional molecular diagnostic methods.Nanotech brought to light how biological information can be acquired easily, quickly and inexpensively, analyzed, thereby enormously increasing the possibilities of achieving preventive medicine.The recent COVID-19 pandemic has reemphasized the importance and value of prevention.

The use of nanostructures in in vitro laboratory diagnostics offers augmentation of the sensitivity and specificity required in clinical practice,reducing expenses and test time of the assays, and permits portable microfluidic platforms suitable for resource-constrained settings.

Nanotech has shown a promising approach in the field of immunology with the production of nano vaccines,nanoemulsions, adjuvants, anticancer drugs, and immuno-modulatory cytokines to combat infectious,chronic and autoimmune diseases. It helps precise drug delivery.Its role in imaging techniques is remarkable.It has a role in regenerative therapy and Gene therapy too.

A big question remais.Is Nanotechnology a Friend or a Foe.We still lack proper and complete knowledge about the effect of nanoparticles on biochemical pathways and processes of human body. Scientists are primarily concerned about the toxicity, characterization and exposure pathways associated with Nano medicine that might pose a serious threat to the human beings and environment. The society's ethical use of Nano medicine beyond the concerned safety issues is a matter of concern, to the researchers.Safety studies are needed for in vivo use.

Every new technology comes with pros and cons .Nanoparticles are the most versatile material with unique inherent properties for developing diagnostics, since they can be conjugated with various agents ..Because of its close interrelationships with other technologies, nanobiotechnology will play an important role in clinical diagnosis and development of nanomedicine in the future.Time will reveal the true picture.

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Fig.1 Richard Philips Feynman

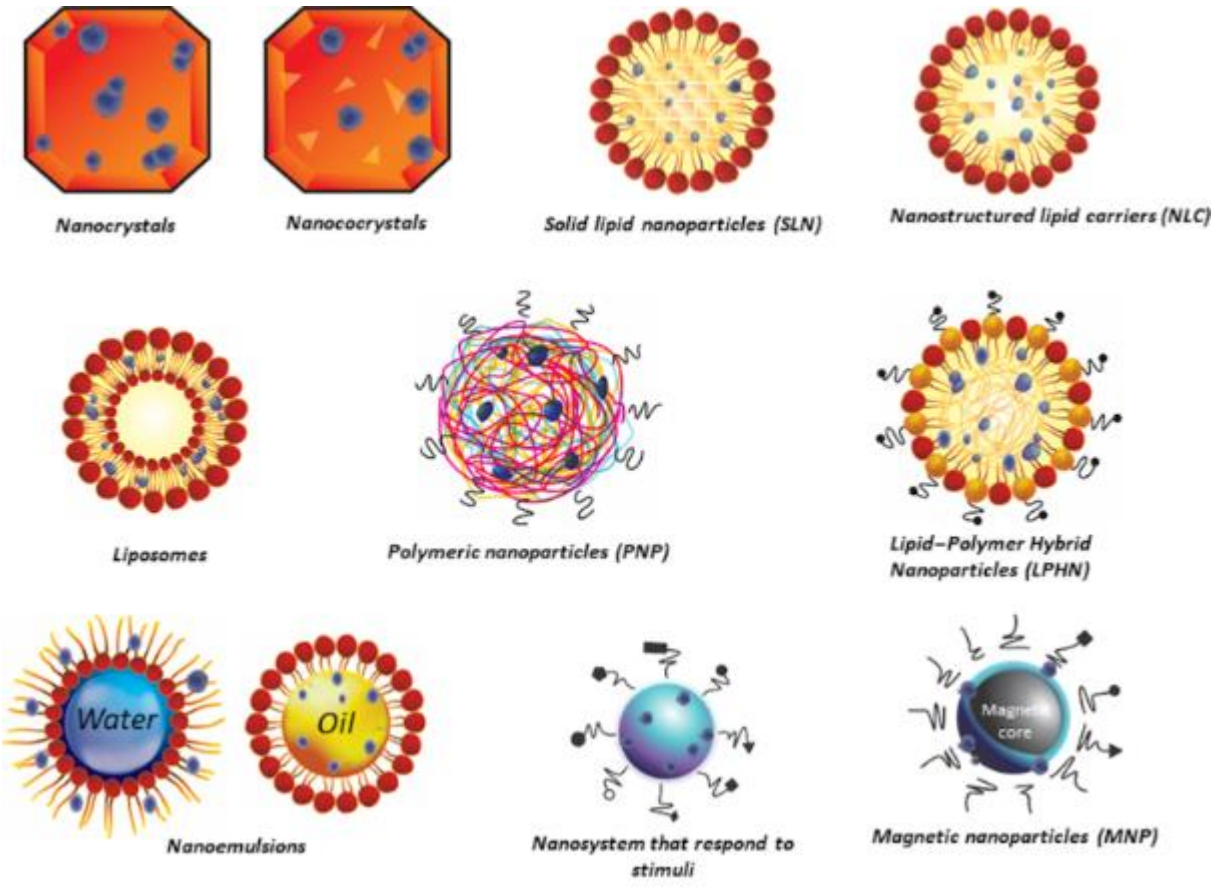

Fig.2 Various types of Nanoparticles