Advances in Nano medicine

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Abstract: Application of nanotechnology in medicine has improvised diagnosis, treatment, and control of biological systems. Nano technological approach to particle design has made possible the availability of a wide spectrum of Nanoscale drugs and devices, which are now collectively referred as 'Nanomedicines'.
There has been tremendous amount of research going on in the field of Nanomedicine. This has resulted into several smart nanomaterials offering interesting applications in tissue engineering, nanorobotics for drug delivery, treatment and detection of cancer, theraupetic use in cardiovascular system, pain therapy, etc.

Nanomedicine has shown many promising prospects and thus has gained a huge global reception over the past decade. It has been proved to be the most potent tool to resolve almost all human health issues.

This review paper is intended to create awareness for the advances in the field of Nanomedicine and highlight few concerns regarding its applications.

Index Terms - Nano-robots, Nano materials, Nano particles, Nano-diagnosis, Quantum dots, Nano-shells, Nano cocoons, Nanotweezers, Nanosyringe, Nanopacemaker, Nanodevice, Nanosensor, Nano- drug delivery, Nano-pollution, Nano-toxicology, Nano-divide, Nanotech-age.

I. INTRODUCTION

Nanotechnology has influenced almost all industrial sectors in the present decade and medical sector is no exemption. The use of Nanotechnology in the field of medicine is now separately referred as “Nanomedicine”. It is a scientific study of biology chemistry and nanotechnology where engineered nanostructures act as biological mimetics for resolving complex health issues. Freitas has defined Nanomedicine as the science of diagnosing, treating, or preventing disease to preserve and improve human health, using molecular tools and molecular knowledge of the human body [1].

Every health issue is a result of some malfunctioning at cellular level. To cure this micro level issue the first line of treatment used is generally at macro level (Oral tablets/ visceral injections). This approach is not at all target specific, it not only results in wastage of healing drug but also gives side effects due to drug delivered to non specific organs as well while transportation. The advent of nanotechnology has enabled mankind to manipulate and control things at molecular level. Due to the usage of molecular level drugs/tools, Nanomedicine has showed the promise to offer effluent health solutions. These solutions are either in the form cell specific nanorobotic drug delivery which contains only desired amount of medicine, thereby curtailing the wastage and toxicity of the high doze of drug. On a higher scale, Nanomedicine has shown the possibility for early detection of incurable and deadly diseases, precision surgery and several other aspects in medicine which require molecular level editing.

All of this has resulted into a shift of focus in the field of medicine towards Nanomedicine. Various techniques that were only imagined a few years ago are making remarkable progress towards becoming realities, while many others are at various stages of testing, or actually being used today for diagnosis or treatment. Currently the ongoing research is more focused on the invention of cost effective nanoscale drugs and drug delivering technology so that it can suit the pockets of a common man.

The aim of this paper written in simple understandable language is to basically create a minimal awareness about the technological advances in the field of Nanomedicine. Hence complicated details have been avoided for a clear and lucid flow of information.

We begin with an introduction to Nanomedicine in section I, Further in section II we highlight the properties and importance of medically important nanomaterials. In section III we emphasize on several clinical prospects and developments in core areas of Nanomedicine reporting several nanotechnology tools and smart nanodevices used in medical research, experimental therapeutics, diagnostics and the future scope of the same. Further In section IV we discuss some important concerns for Nanomedicine followed by conclusion in section V.

II. NANOMATERIALS IN NANOMEDICINE

World Health Organization (WHO) highlighted in a report that, India is one of the leading nations with most cases of degenerative diseases such as Alzheimer’s disease, Parkinson’s disease, cardiovascular diseases, coronary disease, hypertension, and cerebrovascular accidents/strokes [2]. Specially Diabetes and cancer have tremendous impact on health and have been raising concerns particularly in India [3]. Extensive medical research right now is focused on early diagnosis and treatment of these deadly diseases. With the recent advances in the field of chemistry and material sciences several nanomaterials have been produced which are expected to improve the treatment of many diseases otherwise resistant to the traditional therapeutic approaches. Moreover, they represent novel drug delivery systems while decreasing the side effects of standard drugs. These Nanoparticles act as novel intravascular or cellular probes for both diagnostic (imaging) and therapeutic purposes (drug/gene delivery), which is expected to play a critical role in medicine [4]. So a thorough knowledge about Nanomaterials is a prerequisite to using them as and in Nanomedicine. Functionalities can be added to nanomaterials by interfacing them with biological molecules or structures. The size of nanomaterials is similar to that of most biological molecules and structures; therefore, nanomaterials can be useful for both in vivo and in vitro biomedical research and applications.

The nanomaterial landscape is vastly stretched from well characterized polymers, nanoemulsions, lipids, peptides, polymeric conjugates, Quantum dots, colloidal gold, proteins, Carbon Nanotubes, nanocrystals, liposomes, dendrimers, nanodiamonds, hybrid nanoparticles to sugars and surfactants that can be engineered into novel nanoformulations.

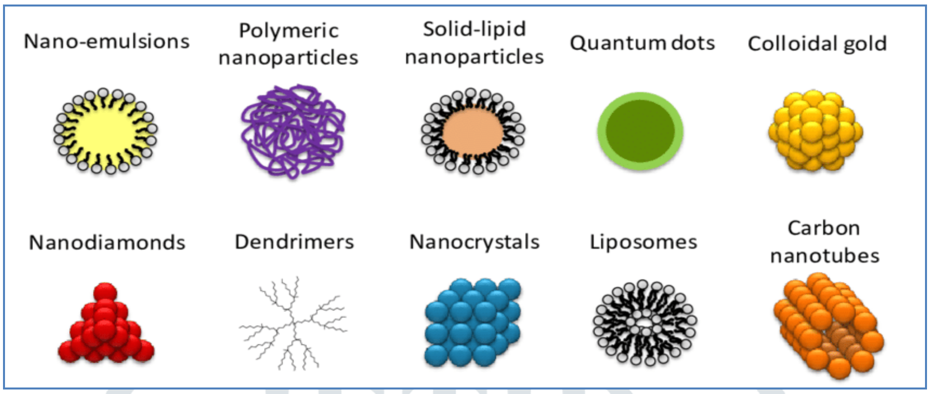

Fig.1. An overview of the nanomaterials currently being investigated in the clinic for treatments [5].

Over the years inorganic nanoparticles have fascinated considerable interest due to their intriguing physicochemical properties and surface plasmon behavior [6]. Inorganic nanoparticles such as magnetic nanoparticles (iron oxide), gold, platinum, chromium, manganese, zinc, selenium, titanium, molybdenum, palladium, silica, copper, cerium oxide, and silver nanoparticles, nanoshells, and nanocages have been continuously used and modified to enable their use as a therapeutic and diagnostic agent. Most of the nanoparticles are engineered or functionalized in such a way that they are able to trick the body's immune response.

Nanoparticles discussed above can assist in efficient treatment of ailments due to the possession of some of the following novel properties,

- Easy implantation inside body,
- Shorter biochemical reaction time,
- Smaller faster and more sensitive delivery devices,
- Least invasive techniques,
- High degree of functional specificity,
- Possibility of fluorescent biological marking,
- Possibility of obtaining magnetic structures,
- Possibility of temperature manipulation etc.

III. PROMISING PROSPECTS OF NANOMEDICINE

Nanomedicine finds application in four broad categories diagnosis via imaging, drug delivery, implants /cell repair (tissue engineering), innovative nanotools/devices and techniques.

A. Nanodiagnosis via imaging:

The small size and size dependent properties make nanoparticles the most appropriate candidates for imaging. Fluorescent Quantum dots are the most promising nanostructures for diagnostic applications. They are semiconductor nanocrystals having size tuneable light emission characteristics. These emissions are much brighter than conventional organic dyes. They not only produce high contrast images at a lower cost but also are more stable and long lasting and can detect multiple signals simultaneously [7]. A biological sample showing good contrast due to green quantum dots is shown in Fig. 2.

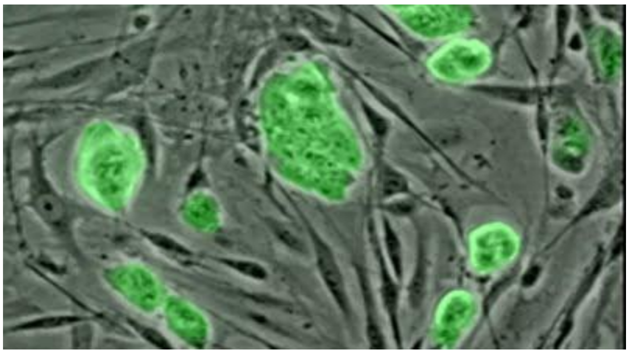

Fig.2. Green Quantum dots adhere to stem cells and thus produce good contrast for their imaging. [8]

The ability to make quantum dots water soluble and target them to specific bio-molecules has lead to promising applications in cellular labeling, deep-tissue imaging, assay labeling and as efficient fluorescence resonance energy transfer donors[8],[9].

CdSe quantum dots glow when U.V light is incident on them. If they are attached to tumour they can guide surgeons for accurate tumour removal with minimal invasion [10].

Gold nanoparticles with attached antibodies can locate and cluster flu virus. When light is incident on a sample containing flu virus particles the amount of light reflected back increases due to the nanoparticles, allowing easy diagnosis for flu virus’s presence [11].

Magnetic Nanoparticles are known for application in medicine as MRI agents. They are also extensively used in protein and cell manipulation due to their strong ability to respond to external magnetic fields. In particular, superparamagnetic iron oxide Nanoparticles (SPIONs) have attracted a lot of attention for drug delivery applications in theranostics (i.e., combined therapy and diagnosis). Iron oxide and magnetic nanoparticles when coated with peptide are able to bind to the tumor. The magnetic properties of iron oxide were observed to enhance the MRI image contrast of the tumor to a great extent [12]. Sample magnetic nanoparticle with compatible coating and ligand is shown in Fig. 3.

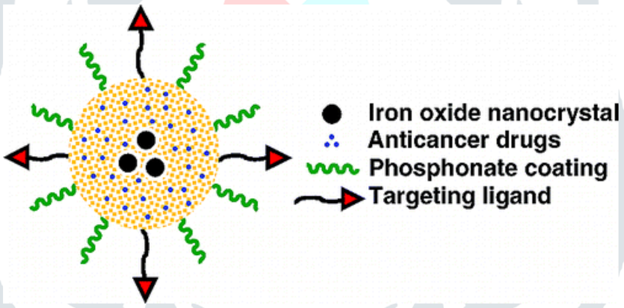

Fig.3.Iron oxide nanocrystals that help MRI imaging for delivery of anticancerdrugs [13]

Nanopore sequencing is an ultra-rapid method of DNA sequencing based on pore Nano engineering. A small electric potential draws a charged strand of DNA through a nanopore in a protein complex, which is inserted into a lipid bilayer separating two conductive compartments. The current and time profile is recorded and these are translated into electronic signatures to identify each base. This method can sequence more than 1000 bases per second and have great potential for the detection of genetic disorders, and for gene diagnosis of pathogens [14].

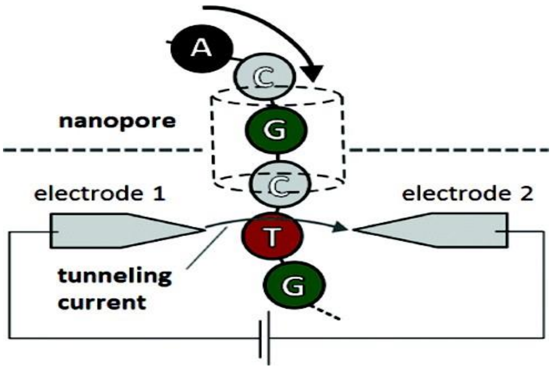

Fig.4.Shows the schematic of nanopore DNA sequencing [15]

Nanoscale cantilevers, microscopic, excitable beams resembling a row of diving boards, are built using semiconductor lithographic techniques. These can be coated with molecules capable of binding specific substrates—DNA complementary to a specific gene sequence. Such micron-sized devices, comprising many nanometer-sized cantilevers, can detect single molecules of

DNA or protein. Atomic force microscope cantilevers tips can be functionalised to probe a molecular structure of interest and measure biochemical interactions therein [16].

DNA-labeled magnetic nanobeads have the potential to serve as a versatile foundation for detecting virtually any protein or nucleic acid with far more sensitivity than is possible with conventional methods now in use [17]. Scientists recently have also designed a nanorobotics system that may be used to study the properties of cancer, and help improve diagnosis and treatment of the deadly disease. The nanobot, described in the journal Science Robotics, is a set of magnetic tweezers that can position a nanoscale bead inside a human cell in three dimensions with unprecedented precision [18]. The nanobead can be controlled inside the cell using real time feedback from confocal microscopy imaging. With this technique early-stage and later-stage cancer cells can be detected and cell nuclei properties can be effectively studied.

In the field of theranostics, CNTs are excellent candidates, as they possess relatively strong NIR absorption, which can be used for both high-resolution imaging (e.g., photoacoustic modality) and photothermal therapy [19].

Mahmoudi and an international collaboration of researchers recently reported early cancer detection with sensory protein corona 'fingerprints' [20]. When nanoparticles enter the blood stream or other biological fluids, they are quickly surrounded by a layer of proteins that gets adsorbed to the surfaces of nanoparticles (NPs), thus, forming a protein layer around the particles called as the protein corona. Subsequent interactions between the NP and biological entities are mediated by the presence and nature of this corona. Different individuals may have a personalized protein corona owing to their distinct type, severity and period of disease, heterogeneity, individual genetic variations and environmental factors. Mahmoudi et al revealed that by combining the concepts of disease-specific protein corona and sensor array technology, a label-free platform for the early detection and identification of diseases can be created [20].

B. Nanodrug delivery:

In present day success of drug delivery is based upon three facts: a) efficient encapsulation of the drugs, b) successful delivery of said drugs to the targeted region of the body, and c) successful release of that drug there.

Nanodrug delivery systems are nanometric carriers employed to deliver drugs, heat, light, biomolecules, polypeptides, proteins, vaccines, nucleic acids, genes etc. to the target organs. The delivery in the organs is ensured with cell precision [21], [22]. This technique prevents damage to healthy cells in the same organ.

Generally, nanometeric carriers comprise of particles with size below 1000 nm and with various morphologies including nanospheres, nanocapsules, nanococoons, nanoghosts, nanobubbles, nano- micelles, nanoliposomes, and, nanoshells etc. [23], [24]. These nanocarriers help in solubilizing the lipophilic drugs, protecting fragile drugs from enzymatic degradation, pH conditions, etc., and targeting specific sites with systematic release of drug contents. Over the years, nanoparticle drug delivery systems have shown huge potential in biological, medical and pharmaceutical applications [25].

Nanoshells can be used for effective drug delivery. Fig.5 shows a sample nanoshell that can be used for the purpose. Nanoshells may also be used to concentrate heat from infrared light to destroy cancer cells with minimal damage to surrounding healthy cells as shown in Fig.6.

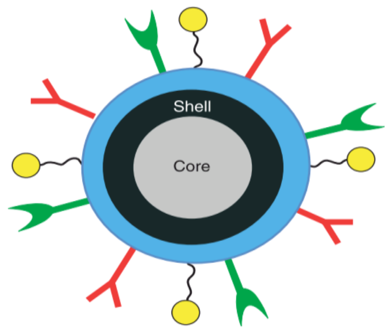

Fig.5.Core-shell nanoparticle with two phases containing different drugs they may respond to different stimuli. It is coated with polyethylene glycol PEG (blue) to prolong circulation half life and functionalized with two targeting ligands (red and green) as well as ferromagnetic nanoparticles (yellow) to enhance MRI images. [26]

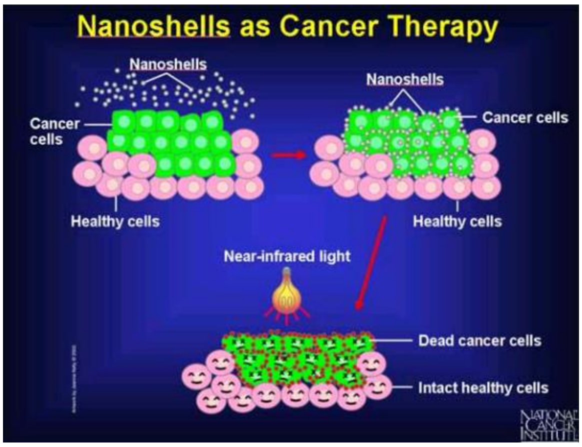

Fig.6. Nanoshells used for cancer therapy @national cancer institute [27].

Microchips on nanocarriers can be used for drug delivery by allowing the flow of single or multiple demands. They can be specially used in conditions that require pulsating drug release post implantation [28].

Polymeric micelles can be used to form hydrophobic cores to accommodate water-insoluble drugs shielded from water by a layer of hydrophilic group. Thus they can be efficiently used as delivery van for such drugs [29].

Although there is a large library of drugs that can be used in cancer treatment, the problem is selectively killing all the cancer cells while reducing collateral toxicity to healthy cells. Biomedical engineering researchers also developed a drug delivery system consisting of nanococcons made of DNA that target cancer cells and trick the cells into absorbing the cocoon before unleashing anticancer drugs [30]

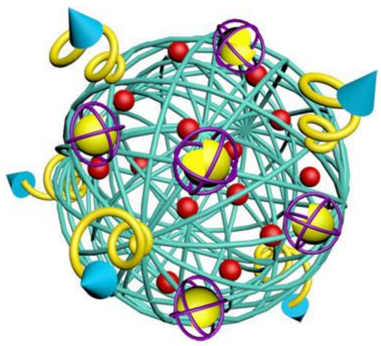

Fig. 7. The nano-cocoon has ligands on its surface that bind to receptors on the surface of cancer cells. (Image: Zhen Gu, University of North Carolina at Chapel Hill)

Infection with human immunodeficiency virus (HIV), if not addressed can lead to acquired immune deficiency syndrome (AIDS), a devastating disease where an individual's immune system is almost destroyed [31]. The medicines that treat HIV are called antiretroviral drugs. Combination antiretroviral therapy has to be taken for a lifetime, has major side effects and is ineffective in patients in whom the virus develops resistance. Nanotechnology has played a pivotal role in delivering the antiretroviral drugs and improving compliance [32]. One such method is by creating polymeric nanoparticles that deliver antiretroviral (ARV) drugs at intra cellular level as well as to the brain [33]. .

Nanospheres are hollow nanoscale structures made of polymers which can be loaded with special molecules like anticancer drugs. Injectable nanospheres have important potential applications such as site-specific delivery and medical imaging [34].

Nanoghost technology is one of the latest approaches developed for smart drug/gene delivery. Nanoghosts are a type of nanovesicles derived from naturally functionalized mammalian cell surface membranes of whole biological cells such as mesenchymal stem cells (MSCs) that are devoid of cytoplasm and organelles. These naturally derived carriers overcome drug loading issues, evade tumor specific immune responses, provide greater nanoparticle stability and improve drug release profiles [35].

Nanobubbles are gas-filled spherical nano-sized structures often stabilized by polymeric/lipid shells. These nanocarriers in combination with thermal, ultrasound, acoustic or magnetic sensitivities are used as more efficient imaging and drug delivery agents in various therapeutic treatments. For instance researchers have shown that dynamically tuned intracellular plasmonic nanobubbles are well suited for cell theranostics since they combine diagnosis (through optical scattering), therapy (through mechanical, nonthermal and selective damage of target cells) and optical guidance of the therapy into one fast process [36].

Injectable Nanoparticle Generator is the first of its kind new drug delivery strategy developed by the scientists at Houston Methodist Research Institute in Texas. It consists of a Doxorubicin (chemotherapy drug) loaded polymer made up of multiple strands enwrapped in a biodegradable nanoporous silicon material. When injected intravenously, due to natural response, they accumulate at the tumors, where the silicon material degrades slowly releasing the drug polymeric strands. These strands spontaneously form nanoparticles that are then taken up by the cancer cells. The acidic environment inside the cancer cells triggers the polymeric strands to release the drug. This kind of novel approach helps the drug to cross multiple biological barriers in order to achieve targeted therapy [37].

C. Nano cell repair (Tissue Engineering)

With the advent of nanotechnology, regenerative medicine has evolved tremendously in recent years and appears to be a promising approach in restoring function and regeneration of diseased tissues and organs. Since the cell–cell and cell-matrix interaction in biological systems takes place at the nanoscale level, the application of nanotechnology gives an edge in modifying the cellular function and/or matrix function in a more desired way to mimic the native tissue/organ [38]. The branch of Nanotechnology that involves reproduce or repair of damaged tissues is called Tissue engineering. It makes use of artificially stimulated cell proliferation by using suitable nanomaterial-based scaffolds and growth factors. Tissue engineering might replace conventional treatments, e.g. transplantation of organs or artificial implants which would further lead to life extension in humans and other animals.

Nanofibers stimulate stem cells present in bone marrow to produce natural cartilage that repairs the damaged joint. Researchers at the Moscow Institute of Physics and Technology (MIPT) created a 3-D model of synthetic nanofibers to learn how to engineer more efficient scaffolds for biomedical applications shown in fig 8. [39]

Nanofibre films can be used for artificial skin, blood vessel repair and wound dressing as well if linked with a suitable linking agent [40-42].

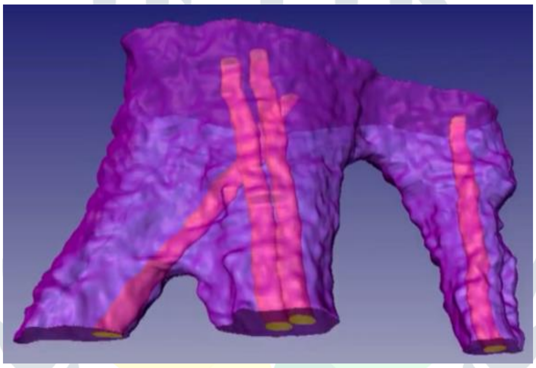

Fig. 8.Cardiac muscle cells (purple) envelop a 3-D model of nanofibers (pink)[39].

Gold nanoparticles and titanium dioxide (TiO_2) nanoparticles, have been used to enhance cell proliferation rates for bone and cardiac tissue regeneration, respectively. Nanoparticle-embedded nanocomposite polymers both in the form of hydrogels and electrospun fibers have exhibited superior mechanical properties for Tissue engineering applications [43].

Nanopores in proteins can also help split DNA strands and record the basic genetic information of any organism which can be used for tissue regeneration. [44-46]. Stem cells in mesenchyma can be genetically modified for bone regeneration [47]. Researchers are looking for ways to grow complex tissues with the goal of one day growing human organs for transplant in future.

Owing to growing interest in the future of dental application of nanotechnology, branch of nanodentistry has emerged. The development of nanodentistry will allow nearly perfect oral health by the use of nanomaterials, nanorobots, tissue engineering and biotechnology [48]. The new treatment opportunities in dentistry include local anesthesia, permanent cure of hypersensitivity, complete orthodontic realignment, covalently bonded diamondized enamel and continuous oral health maintenance with the help of mechanical dentirobots that destroy caries-causing bacteria and even repair blemishes on the teeth where decay has set in [49]. Nanotechnology is set to revolutionize clinical dental practice. In near future, oral health care services will become less stressful for the dental surgeons, more acceptable to patients and the outcome will significantly become more favorable with nanodentistry.

It is important to mention that wound healing using nanotechnology remains a major area of research interest worldwide. The research efforts concerned with skin regeneration are briefly outlined in the following sub-sections: (i) nanostructured scaffolds (ii) nanoparticles as delivery systems (iii) hydrogels and (iv) stem cells for skin regeneration. A schematic representation of skin regeneration by nanotechnological approaches is shown in Figure 9.

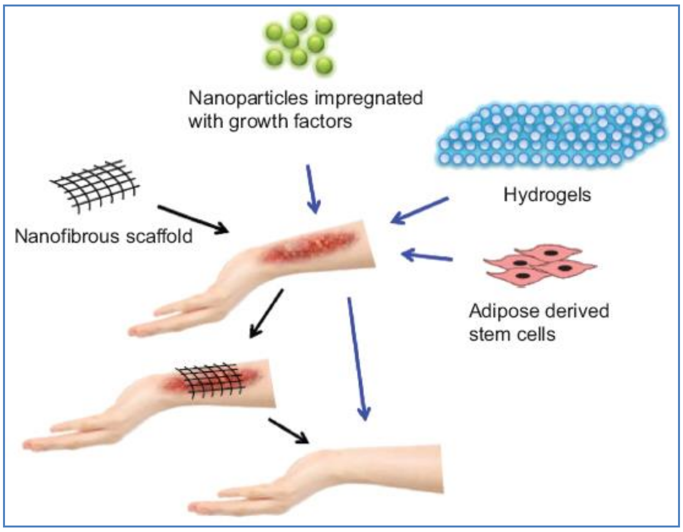

Fig.9. Nanotechnology methods for skin regeneration. [50]

D. Smart Nanotools & Devices

Nanodevices are nanoparticles that are created for the purpose of interacting with cells and tissues and carrying out very specific tasks. The most famous nanodevices are the imaging tools. Oral pills can be taken that contain miniature cameras. These Nano cameras can reach deep parts of the body and provide high-resolution pictures of very small cells which makes them very useful for diagnosis and also during surgeries on tissue, genes and cells as shown in fig. 10. [51].

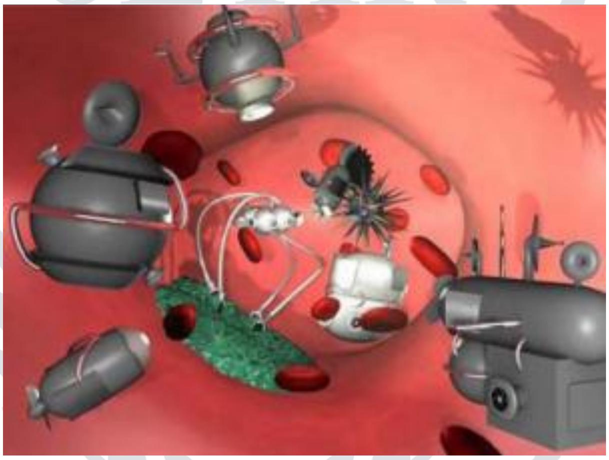

Figure 10. Miniature cameras inside blood vessels. [51]

Nanotweezer is one of the manipulation techniques used which could enable long term analysis of what's going on inside individual cells to better understand how healthy cells work and where diseased cells go wrong. This technique can be used in the differential diagnosis of tissue growths, calculi, cysts, abscess etc. [52]. Optical tweezers can also be used to trap, manipulate and probe nanomaterials under optical illumination. A new set of nanotweezers can remove single molecules or organelles from individual cells — such as mitochondria from nerve cells and can extract DNA and other single molecules from a living cell without killing it as shown in fig.11 [53].

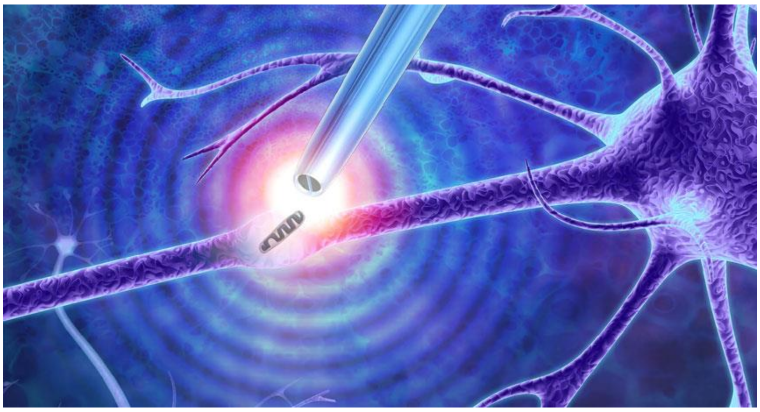

Fig. 11. Nano tweezers performing biopsies on living cells [53]

Nanowires are the artificial materials that consist of ultrafine wires or linear array of dots. Boron doped silicon nanowires were used to create highly sensitive, real-time electrically based sensors for biological and chemical species. Direct, real-time electrical detection of single virus particles can be achieved with high selectivity by using nanowire field effect transistors. When a virus particle binds to the antibody receptor on a nanowire device, the conductance of the device changes from the baseline value, and when the virus unbinds, the conductance returns to the baseline value. [54]

Special sensor nanobots can be inserted into the blood under the skin where they can check blood contents and warn of any possible diseases. They can also be used to monitor the sugar level in the blood. Advantages of using such nanobots are that they are very cheap and portable. Medical “nanorobots” may also be able to intervene at the cellular level, performing in-vivo cytosurgery. In one simple cytosurgical procedure called “chromosome replacement therapy”, a “nanorobot” controlled by a physician would extract existing chromosomes from a particular diseased cell and insert new ones in their place, in that same cell [55]. If the patient chooses, inherited defective genes could be replaced with non defective base-pair sequences, permanently curing a genetic disease.

Fig.12. Nanomedicine researchers have successfully programmed nanorobots to find tumors and cut off their blood supply while leaving healthy tissue unharmed [56]

In the future programmable nanobots could be developed to repair specific diseased cells functioning similar to antibodies [57]

Engineered bacterial “biobots” (synthetic microbes) may be designed to produce useful vitamins, hormones, enzymes or cytokines in which a patient’s body was deficient or to selectively absorb and metabolize harmful substances such as poisons toxins etc into harmless end products [58]. Scientists have created flesh-like mini-robots that can move when they detect light. The fleet of walking “biobots” are powered using muscle cells and controlled using electrical and optical pulses. The sinewy robots are less than half an inch long and are made from 3D-printed hydrogens and living cells [59].

Researchers from University of California Los Angeles and the University of Connecticut have designed a new biofriendly energy storage system called a biological nanosupercapacitor, which operates using charged particles, or ions, from fluids in the human body. The device is harmless to the body's biological systems, and it could lead to longer-lasting cardiac pacemakers and other implantable medical devices. The new biosupercapacitor comprises a carbon nanomaterial called graphene layered with modified human proteins as an electrode, a conductor through which electricity from the energy harvester can enter or leave. The new platform could eventually also be used to develop next-generation implantable devices to speed up bone growth, promote healing or stimulate the brain [60].

Fig.13. Nanopacemaker [60]

Nanopipettes are electrical devices that can measure the differences in ionic current at a nanopore. Their small sizes enables direct, real-time in vitro measurements with high spatial resolution and reduced invasiveness, allowing the monitoring of intracellular changes of an individual cell over the course of drug treatment. Recently, nanopipettes have gained importance as novel sensing tools and have been investigated for the detection of proteins [61,62], metal cations [63], DNA [64] and carbohydrates [65].

Nanosomes used as nanoscale vehicles are efficient transporters of active ingredients that penetrate into deep layers of skin to deliver vitamin E. Protein and hydrophobic drugs can be encapsulated within these nanosomes for their effective delivery [66].

Currently researchers in Switzerland have successfully removed heavy metal ions, overdozed steroid drugs and proteins from human blood by using nanomagnets [67].

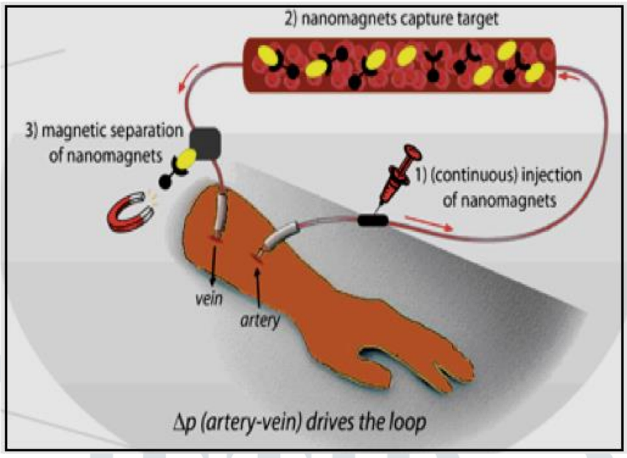

Fig. 14. Schematic depiction of the blood purification process using nanomagnets. (Image: Functional Materials Laboratory, ETH Zurich)

Nanoneedles: Suture needles incorporating nano-sized stainless steel crystals have also been developed (trade name: SandrikBioline, RK91 needles, AB Sandrik Sweden).

ETH Zurich researchers have developed a method using a nanosyringe whose tiny needle is able to penetrate single living cells and extract their content. The technology can be used for cell cultures, for example, in order to investigate the interior of the cells. This allows scientists to identify the differences between individual cells at the molecular level, as well as to identify and analyse rare cell types [68].

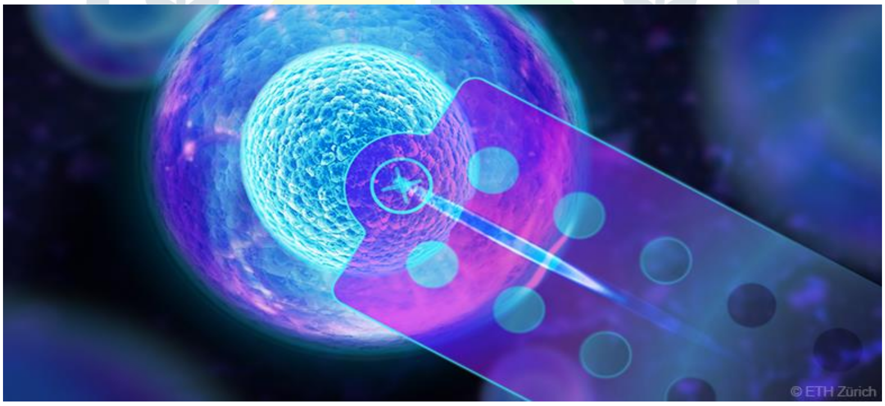

Fig.15. Nanosyringe to extract the content of single living cells for molecular analyses. (Visualisations: ETH Zurich)

Over the next ten to twenty years nanotechnology may fundamentally transform science, technology, and society offering a significant opportunity to enhance human health in novel ways, especially by enabling early disease detection and diagnosis, as well as precise and effective therapy tailored to the patient. There is currently lot of research undergoing in Nanorobotics and there is a further scope of building programmable Nanorobots which could be capable of destroying cancers, fixing genetic errors in cells and assist the immune system in combating infections. We further hope that Nanomedicine reaches to the less explored areas of radiotherapy, radio diagnosis etc. In fact use of Nanomedicine for age reversal mechanisms and cure of birth defect diseases using gene therapy may attract researchers. It will also be a great breakthrough to explore if some Nanomedicine could be designed as preventive measures for existing ailments like cancer, hereditary diseases etc. that only have a cure till date.

IV. POTENTIAL CONCERNS FOR NANOMEDICINE

It is clearly evident that the entry of nanotechnology has resulted into a total phase shift in the way we deal with ailments. In spite of these evidences of attractive applications, the large scale marketing of Nanomedicine is still not a command reality due to following concerns.

A. Complicated and costly design:

The first and most important challenge faced by Nanomedicine similar to any other medicine is surviving body response. Every organisms body has a tendency to reject any foreign material, this rejection happens to be done by engulfing the substance by phagocytes and subsequent destruction or ejection via excretion or dumping it into some vestigial organ like spleen [69], or depositing it on the kidneys or liver in human body. This human body response adds to the misery of the in vivo Nano device design that already is complicated due to size 'nano'.

To cope with this condition researchers cap inorganic nanoparticles using biocompatible molecules (ethylene glycol, red blood cell membranes or liposomes [70] to stop white blood cells from recognizing the nanoparticles as foreign materials and allowing them to circulate in the blood stream long enough to perform the assigned task. This capping along with nanosize design make the medicine out of common pocket's reach.

B. Lack of complete knowledge

It is a well-established fact now that nanoparticles of a particular material may have size dependent physicochemical properties that may be entirely different from the parent material [71]. So, it is very necessary to study nanoparticles of a material with different sizes separately [72]. In spite of the huge focus on Nano technological research very little is known about the nature and behaviour of currently synthesized nanoparticles in biological environment. Moreover, the projected acceleration in progress of nanotechnology would result into synthesis of many more nanoparticles of different materials and sizes and make it tedious to categorise them on the basis of their properties. Thus understanding, predicting, and managing the health risks associated with occupational, environmental, and consumer exposures to nanomaterial by knowing their properties is an essential, research focus area.

Owing to the small size of nanoparticles they are readily taken up by the human body. As most of the nanoparticles are non-biodegradable they tend to get accumulated into the body if the exposure to nanoparticles rises, which is the nearest future possibility. What would be the effects of such accumulation is a big question mark still.

C. Toxicity of nanoparticles

The basic expectation from Nanomedicine is to cure body ailments to the highest satisfaction levels with minimal invasion. As we are not fully aware of the properties of nanoparticles forming the Nanomedicine, we can't determine how they would affect biological processes inside the body. For various Nanomedicine available in the market, tests on lab animals have proved them to cure the concerned ailment they are meant for and also nontoxic. There were concerns about the toxicity of cadmium [73] the content of majority of quantum dots. Currently focus is on using silicon or calcium phosphate based composite in place of cadmium [74]. Infact the study of appropriate nanoparticles used as medicine which is completely nontoxic is the current field of exploration.

D. Impact on the environment

While using nanoparticles it's important to find their biodistribution and effect on the ecosystem. Nanopollution is the name given to all nanowaste created due to nanomaterial manufacturing process. Nanowaste doesn't appear in nature, whether living organisms can deal with this waste is again not known. To precisely find the effect that nanowaste would have on living organisms, it's imperative to evaluate the whole life cycle of these particles right from their fabrication, storage and distribution, application and potential abuse, and disposal. [75-77].

Green Nanoscience is viewed to be the next generation solution to our Nanowaste problem**.** The environment friendly development of Nanomedicine techniques and nanoconjugates through adoption of non-hazardous chemicals is advancing actively and being reported in different journals [78]. There is plethora of research undergoing in synthesis of metal nanoparticles using plant extracts and agricultural wastes. The need of hour is the size and quantity control of nanoparticles in green synthesis, and more importantly reproducibility of it.

E. Ethical aspects

Along with the practical challenges nanotechnology is thought to bring about some ethical challenges as well. The huge cost of Nanomedicine no doubt offers new solutions to dread ailments in the form of Nanomedical implants, drugs and treatments, but it is raising the question of justice and fairness in the health care system as well as between rich and poor societies creating a nanodivide. Major economies like US and china have had a stimulated global revolution in getting people trained for jobs related to the modern era of reign of nanotechnology. But still there is a concern that world's educational systems have lagged behind in preparing students for the "Nanotech Age" [79].

V. Conclusion

Introduction of nanotechnology in medicine has greatly enhanced our understanding of health care by introducing novel approaches to bio-analysis and imaging. The use of nanotechnology in medicine offers great potential for improving our lives at present and what scientists will be able to achieve in the future is beyond current imagination [80]. The time when we have self-assembled biocompatible Nanodevices that will detect, evaluate, treat and report to the clinical doctor automatically seems to be nearing [81]. To reach up to this expectation a lot of interdisciplinary research is to be carried out integrating synthetic materials with biological building blocks for designing upcoming Nanomedicine.

Thus we conclude that we have indeed travelled ahead in nanotechnology and Nanomedicine but there is still wide opportunity of research in Nanotechnology in general and its use in Nanomedicine in particular.

It is immensely significant to create awareness thereby making the masses ready for the Nanomedicine in the coming Nanoage so that gradually mankind would be benefitted with it and even harness its remarkable potential without fear and with trust and confidence.

References

[1] R. A. Freitas Jr., “Nanomedicine”, Vol. I: Basic Capabilities, Landes Bioscience, 1999, “Nanomedicine”, Vol. IIA: Biocompatibility, Landes Bioscience, 2003, http://www.Nanomedicine.com.
[2] Murray, C.J., Lopez, A.D.: Global and regional cause-of-death patterns in 1990. Bull. World Health Organ. 72(3), 447 (1994).
[3] Lancet 2006; 367: 1747–1757 [PubMed] [Google Scholar].
[4] Singh S., Hicham F., Singh B. Nanotechnology, Nanotechnology based drug delivery systems. J. Occupat. Med. Toxcol. 2007;2:16.[Google Scholar]
[5] https://www.researchgate.net/figure/Schematic-representation-of-the-most-commonly-used-Nanomedicine-types-composed-of_fig2_313022151
[6] Current Drug Metabolism, 2013, 14, 518-530
[7] nature methods | VOL.5 NO.9 | SEPTEMBER 2008, Quantum dots versus organic dyes as fluorescent labels
[8] http://nanoall.blogspot.in/2011/05/nanoparticle-for-labeling-stem-cells.html
[9] Quantum dot bioconjugates for imaging,labelling and sensing, nature materials | VOL 4 | JUNE 2005 | www.nature.com/naturematerials
[10] Jaiswal, J. K., Mattoussi, H., Mauro, J. M., and Simon, S. M. (2003) Long-term multiple color imaging of live cells using quantum dot bioconjugates. Nat. Biotechnology. 21, 47–51
[11] www.invitrogen.com/, www.jpk.com
[12] Schellenberger, E. A., Reynolds, F., Weissleder, R., and Josephson, L. (2004) Surface-functionalized nanoparticle library yields probes for apoptotic cells. ChemBioChem5, 275–279.
[13] http://pubs.acs.org/doi/abs/10.1021/nn800072t
[14] Chen, C. M., and Peng, E. H. (2003) Nanopore sequencing of polynucleotides assisted by a rotating electric field. Appl. Phys. Lett. 82, 1308–1310.
[15] http://www.engadget.com/2010/12/24/nanopore-dna-sequencing-technique-promises-entire-genome-in-minu/
[16] http://dspace.mit.edu/bitstream/handle/1721.1/34205/71300807.pdf
[17] Journal of Applied Physics 103, 07A306 (2008)
[18] https://www.gadgetsnow.com/tech-news/nanobots-may-help-diagnose-treat-cancer/articleshow/68413708.cms
[19] Adv Drug Deliv Rev. 2013 Dec;65(15):1951-6
[20] https://www.nanowerk.com/spotlight/spotid=52991.php
[21] LaVan DA, McGuire T, Langer R. (2003). "Small-scale systems for in vivo drug delivery". Nat Biotechnology.21 (10): 1184–1191. http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed&uid=14520404&cmd=showdetailview.
[22] Cavalcanti A, Shirinzadeh B, Freitas RA Jr, Hogg T. (2008). "Nanorobot architecture for medical target identification". Nanotechnology19 (1): 015103(15pp). Bibcode2008Nanot..19a5103C. doi:10.1088/0957-4484/19/01/015103. http://www.iop.org/EJ/abstract/0957-4484/19/1/015103
[23] T. Jung,W. Kamm, A. Breitenbach, E. Kaiserling, J.X. Xiao, T. Kissel, (2000). Biodegradable nanoparticles for oral delivery of peptides: is there a role for polymers to affect mucosal uptake? Eur. J. Pharm. Biopharm. 50 147–160
[24] C. Pinto Reis, R.J. Neufeld, A.J. Ribeiro, F. Veiga, (2006). Nanoencapsulation I. Methods for preparation of drug-loaded polymeric nanoparticles, Nanomedicine 2 8–21.
[25] L. Illum, (2007). Nanoparticulate systems for nasal delivery of drugs: a real improvement over simple systems? J. Pharm. Sci. 96 473–483.
[26] 2011 John Wiley& Sons, Inc. WIREs NanomedNanobiotechnol2011 3, 223–228 DOI: 10.1002/wnan.128
[27] Nanotechnology pathology project: future developments ,tarika vadgama ,pathology lectures at medlink 2010 or medisix 2011
[28] Grayson, A. C. R., Choi, I. S., Tyler, B. M., Wang, P. P., Brem, H., Cima, M. J., and Langer, R. (2003) Multi-pulse drug delivery from aresorable polymeric microchip device. Nat. Mat. 2, 767–772
[29] Gao, Z. G., Lukyanov, A. N., Singhal, A., and Torchilin, V. P.(2002) Diacyllipid-polymer micelles as nanocarriers for poorly soluble anticancer drugs. Nano Lett. 2, 979–982.
[30] www.nanowerk.com/spotlight/spotid=51090.php
[31] Moss, J.A., 2013. HIV/AIDS review. Radiol. Technol. 84(3), 247–267. [PubMed]

[32] Jayant R., Nair M. Nanotechnology for the treatment of NeuroAIDS. J. Nanomed. Res. 2016;3(1):00047. [Google Scholar]
[33] Mamo T., Moseman E.A. Emerging nanotechnology approaches for HIV/AIDS treatment and prevention. Nanomedicine. 2010;5(2):269–285. [PMC free article] [PubMed] [Google Scholar]
[34] International Journal of Pharmaceutical Sciences Review and Research Volume 5, Issue 3, November – December 2010; Article-015
[35] https://www.nanowerk.com/spotlight/spotid=51090.php
[36] https://www.nanowerk.com/spotlight/spotid=14603.php
[37] https://www.nanowerk.com/nanotechnology-news/newsid=43567.php.
[38] International journal of Nanomedicine:Volume 2014:9(1) Pages 4153—4167.
[39] ActaBiomater. 2018 Mar 1;68:214-222. doi: 10.1016/j.actbio.2017.12.031. Epub 2017 Dec 27
[40] Gu, Z., Feng, Z., Wang, T., He, N.: CN101011597 (2007).
[41] Takeda, M., Hasui, T., Matsumoto, N.: WO07023887 (2007).
[42] Tran, P. A., L. Zhang, et al. (2010). "Corrigendum to "Carbon nanofibers and carbon nanotubes in regenerative medicine"[Advanced Drug Delivery Review 61(2009) 1097-1114]." Advanced Drug Delivery Reviews 62(6): 667-667.
[43] Liu A, Hong Z, Zhuang X, Chen X, Cui Y, Liu Y, Jing X Acta Biomater. 2008 Jul; 4(4):1005-15
[44] http://nanopore.bme.ucsc.edu/html/about.html
[45] http://www.sciencedaily.com/releases/2010/11/101129111826.htm
[46] Zhang, L. and T. J. Webster (2009). "Nanotechnology and nanomaterials: Promises for improved tissue regeneration." Nano Today 4(1): 66-80.
[47] Nanobiomechanics of Repair Bone Regenerated by Genetically Modified Mesenchymal Stem Cells, TISSUE ENGINEERING: Part A ,Volume 14, Number 10, 2008,DOI: 10.1089/ten.tea.2007.0241
[48] Freitas RA.,JrNanodentistry. J Am Dent Assoc. 2000;131:1559–65. [PubMed] [Google Scholar]
[49] Rybachuk AV, Chema IS, Nebesna TY. Nanotechnology and nanoparticles in dentistry. J Pharmacol Pharm. 2008;1:18–20. [Google Scholar]
[50] Regenerative Nanomedicine: current perspectives and future directions https://doi.org/10.2147/IJN.S45332}
[51] Blender Battles (M.J. Perkel, The ups and downs of nanobiotech, The Scientist (2004) 1–8. http://www.the-scientist.com/2004/08/30/14/1, 12 November 2006).
[52] Saravana KR, Vijayalakshmi R. Nanotechnology in dentistry. Indian J Dent Res. 2006;17:62–5.[PubMed] [Google Scholar]
[53] https://www.sciencenews.org/article/new-nanotweezers-let-scientists-do-biopsies-living-cells
[54] Proc Natl Acad Sci U S A. 2004 Sep 28; 101(39): 14017–14022
[55] Journal of Evolution and Technology - Vol. 16 Issue 1 - June 2007 - pgs 1-97 http://jetpress.org/volume16/freitas.html
[56] Nature Biotechnology volume36, pages258–264 (2018)
[57] M. J. Perkel, The ups and downs of nanobiotech. The Scientist (2004) 1-8
[58] JIMSA July-September 2012 Vol. 25 No. 3
[59] News.com.au reported by "The Sun"
[60] https://phys.org/news/2017-05-battery-free-implantable-medical-device-energy.html
[61] Actis P, Mak A, Pourmand N. Bioanal Rev. 2010;1:177–185. [PMC free article] [PubMed] [Google Scholar]
[62] Umehara S, Karhanek M, Davis RW, Pourmand N. Proc. Natl. Acad. Sci. U. S. A. 2009;106:4611–4616. [PMC free article] [PubMed] [Google Scholar]
[63] Vilozny B, Actis P, Seger RA, Vallmajo-Martin Q, Pourmand N. Anal. Chem. 2011;83:6121–6126.[PMC free article] [PubMed] [Google Scholar]
[64] Karhanek M, Kemp JT, Pourmand N, Davis RW, Webb CD. Nano Lett. 2005;5:403–407. [PubMed] [Google Scholar]
[65] Vilozny B, Wollenberg AL, Actis P, Hwang D, Singaram B, Pourmand N. Nanoscale. 2013;5:9214–9221. [PMC free article] [PubMed] [Google Scholar]
[66] July 2017 Artificial Cells 46(1):1-11
[67] https://www.nanowerk.com/spotlight/spotid=17353.php
[68] https://reliawire.com/nanosyringe-living-cells/
[69] Advances in Nanoparticles, 2017, 6, 93-102
[70] http://www.benthamdirect.org/pages/content.php?PNM/2011/00000001/00000001/0001PNM.SGM
[71] http://www.nanospectra.com/clinicians/spublications.html) ^Mozafari, M.R.(ed), (2006) Nanocarrier Technologies: Frontiers of Nanotherapy (Chapters 1 and 2) pages10-11, 25-34
[72] Challenges in assessingnanomaterial toxicology:a personal perspective, Charles L. Geraci1 and Vincent Castranova2∗2010 John Wiley & Sons, Inc. WIREs Nanomed ,Nanobiotechnol2010 2 569–577
[73] QSAR modeling of nanomaterials ,EnricoBurello∗and Andrew P. Worth, 2011 John Wiley& Sons, Inc. WIREs NanomedNanobiotechnol2011 3 298–306 DOI: 10.1002/wnan.137
[74] Derfus, A. M., Chan, W. C. W., and Bhatia, S. N. (2004), Probing the cytotoxicity of semiconductor quantum dots. Nano Lett. 4, 11–18.
[75] Calcium phosphate-based composite nanoparticles in bioimaging and therapeutic delivery applications, Amra Tabaković,1 Mark Kester2 and James H. Adair1∗WIREs NanomedNanobiotechnol2012, 4:96–112. doi: 10.1002/wnan.163

[76] Health and safety implications of occupational exposure to engineered nanomaterials, Larissa V. Stebounova,1Hallie Morgan,2 Vicki H. Grassian1,3∗and Sara Brenner2∗WIREs NanomedNanobiotechnol2011. doi: 10.1002/wnan.174

[77] Toward toxicity testing of nanomaterials in the 21st century: a paradigm for moving forward
David Y. Lai, WIREs NanomedNanobiotechnol2012, 4:1–15. doi: 10.1002/wnan.162

[78] J. Hutchison. Nanomaterial Design Guided by the Principles of Green Chemistry. In 2017 AAAS Annual Meeting (February 16-20, 2017); aaas, 2017.

[79] GyorgyScrinis (2007). "Nanotechnology and the Environment: The Nano-Atomic reconstruction of Nature". Chain Reaction97: 23–26. http://nano.foe.org.au/node/130.

[80] Ethical Aspects of Nanomedicine.htm

[81] Nanomedicine: current status and future prospects , S. MoeinMoghimi,*,1 A. Christy Hunter,* and J. Clifford MurrayFASEB J. 19, 311–330, (2005)
http://www.marketresearch.com/RNCOS-v3175/Nanotechnology-Forecast-6059361