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NANOTECHNOLOGY IN HEALTHCARE: APPLICATIONS AND CHALLENGES

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ABSTRACT

New generations of nanostructures have been created in this era of nanoscience as a result of advancements in nanotechnology. These nanostructures are distinguished by their exploratory use in a variety of biomedical and bio-engineering applications. It is anticipated that these applications will greatly enhance the therapeutic and diagnostic aspects of numerous illnesses. The materials have been investigated and documented as highly effective drug delivery platforms and as parts of biosensors. There have been reports of a small number of clinically useful nanomaterials; however they are not consistently effective. This might be as a result of nontoxicity, a possible drawback to its application in biological systems. A brief review of the development of nanostructure for biomedical applications over time, including new materials and our knowledge of their interactions with the body, may lead to better biocompatible nanostructures.

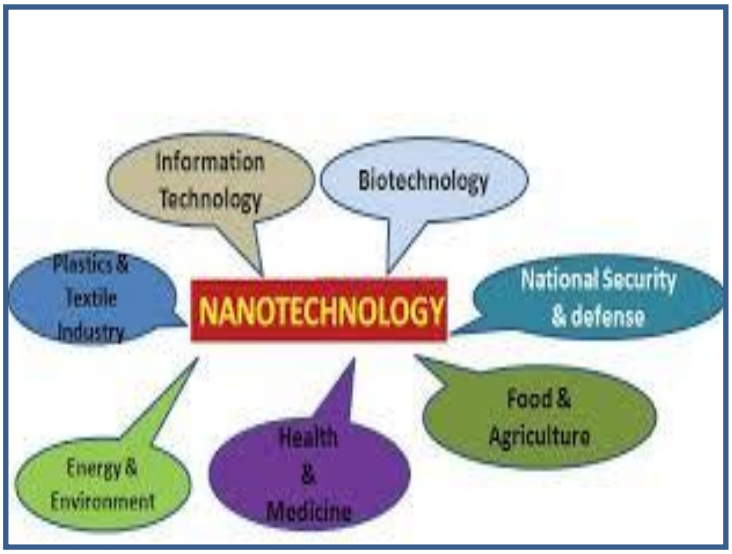
KEYWORD: difficulties, applications in healthcare, nanotechnology, and nanotoxicity.

INTRODUCTION

At the moment, nanotechnology and the science of nanomaterials are rapidly expanding and developing scientific fields that offer appropriate potential in material engineering. The study of regulating, modifying, and constructing systems according to their atomic or molecular specifications is its definition.[1] The core of nanotechnology, according to the US National Science and Technology Council[2], is the capacity to modify matter at the atomic, molecular, and supramolecular levels in order to produce newer structures and devices. This field of study often deals with structures that are at least one dimension in size and involves the manufacture and modification of nanomaterials and nanodevices. It has persisted as a subject

of considerable scientific investigation in a number of domains, including biological, optical, and electrical. Nanoparticles like viruses (75-100 nm), proteins (5-50 nm), nucleic acids (2 nm wide), and atoms (0.1 nm) can be easily absorbed or internalized by bacterial, plant, and mammalian cells that are larger than 100 nm. A 1000 nm nanofiber is 50,000 times smaller below a single human hair, resulting in a diameter of 50 µm.[3] In 1959, the brilliant late Nobel scientist Richard P. Feynman came up with the concept of molecular manufacturing.

This growth path is unavoidable, according to the renowned scientist who first proposed that materials and technology would one day have atomic requirements.[4] For years, researchers have been examining the incredibly unique physico-chemical properties of nanoparticles.



Review of Literature

Perspectives of Nanotechnology

Applications in Medicine and Health

The way an illness is diagnosed and treated could be significantly impacted by nanotechnology. Nanomaterials' unmatched sensitivity and performance, increased durability and flexibility, and special physicochemical characteristics have been used in target-assisted clinical therapy (Table 2), regenerative medicine (Table 2), and medical diagnosis (Table 1) for the early detection of diseases.

Medical diagnostics

The global revolution in biosensors toward point-of-care testing by glucometer for blood glucose monitoring has been a remarkable phenomenon. It evolved from an extremely basic enzyme-based technique to a principle based on amperometry and an extension of the reverse

iontophoresis technique. From in vitro diagnosis to in-vivo blood glucose monitoring, the method has changed from invasive to non-invasive monitoring.

Comparable to this, a variety of nanodevices and nanobiosensors have been created to monitor biomolecules at incredibly low concentrations, allowing for the early detection of disease. They have the potential to be an innovative and effective cancer detection system tool. Conventional diagnostic methods are less accurate in distinguishing between benign and malignant stages of cancers and cannot identify them in their early stages. Unlike conventional methods, novel nanoparticles (NPs) can generate targeted imaging of affected areas.

Clinical therapy and drug delivery systems

In addition to serving as effective imaging tools for locating diseased tissues, the novel NPs are perfect delivery systems for anticancer medications and other therapeutic medications, ensuring that they reach the target spot with maximum effectiveness and no harm to nearby healthy tissues. Nowadays, intracellular molecular targets rather than the cell itself are the focus of the therapeutic approach. Biocompatible packing materials can be used to transfer gene-encoding DNAs, gene-silenncing short interfering RNAs, or recombinant proteins intracellularly. Liposomes, bacterial toxins, or viral NPs are the most often employed packaging scaffolds; however, they are typically broken down and removed from circulation early, or they might not reach the possible target site. Because bioreducible polymers can be molecularly programmed using sensors that can react to changes in ion concentrations in the microenvironment and distinguish between extracellular and intracellular regions, recent advancements in this field have drawn increased attention.[22]

Table 1: nanomaterials that are utilized in analyte biosensing to diagnose some diseases early.

Nanomaterial	Use and its Principle	References
Graphene oxide	Mansoori GA, Soelaiman TAF, and Soelaiman TAF (2005) very few cancer cells (three to five per milliliter of blood)	Yoon et al.[5]
Single-walled Carbon nanotubes (SWNT)	In inflammatory illnesses, keep an eye on the blood nitric oxide level. It makes use of the fluorescent signal idea.	Iverson et al.[6]
DNA hairpin probes tagged with Raman dye and silver-based nanoparticles	Focuses on particular illness indicators. makes use of the surface-enhanced Raman Scattering (SERS)	Wang et al.[7]
The first genetically based technique	Concept to detect intracellular mRNA in living	Halo et al.[8]

for detecting cancer cells in blood is known as nanoflares.	cells. Its foundation is the fluorescence principle.	
Protease-coated iron oxide nanoworm particles (matrixmetalloproteases, cathepsins) for early detection of cancer	It may harbor a tumor and interact with cancer proteins to create thousands of biomarkers that mass spectrometry can identify in a patient's urine.	Kwong et al.[9]
Target specific magnetic nanoparticles	It makes it possible to track glioblastoma multiforme microvesicles in blood in real time. They are picked up by a handheld, miniature gadget.	Shao et al.[10]
Silicon nanowires wrapped in polydimethylsiloxane and covered with an anti-EpCAM antibody compose the structure of the NanoVelcro chip.	To identify and separate the tumor cells that is in circulation. It makes use of the laser micro-dissection (LMD) principle.	Lu et al.[11]
Silver nanorod array substrate	Biological agents such as bacteria and viruses in food, urine, saliva, and blood can be separated and detected on-chip. It makes use of the surface enhanced Raman spectroscopy (SERS) principle.	Negri et al.[12]
Gold nanoparticles covered in antibodies specific to influenza A.	To identify the influenza virus present in the specimen. The dynamic light scattering (DLS) principle serves as its foundation.	Driskell et al.[13]
Gold nanoparticles modified with monoclonal anti-hemagglutinin antibody (mAb)	To identify influenza A blood virus. It makes use of the colorimetric immunosensing principle.	Liu et al.[14]
Nanoparticles that form clumps	To identify the presence of viral indicators such as p24 in low HIV viral load and cancer biomarkers such as prostate specific antigen.	de la Rica et al.[15]
μQLIDA (microfabricated Quantum dot-linked immune-diagnostic assay)	Myelopeoxidase (MPO) nanomolar concentration is detected using an in vitro diagnostic test. It is a cost-effective and quick immunofluorescence sensor that can detect nanomolar concentrations of MPO or other analytes in 2 μl of analyte solution.	Yu et al.[16]
Silicon quantum dots and fluorescent nanodiamonds	These luminous nanoprobes are extremely stable, biocompatible, and nontoxic. In addition to being a non-toxic drug delivery vector, it may be the perfect diagnostic tool for long-term bioimaging.	Montalti et al.[17]
Peptide-coated iron-oxide magnetic nanoparticles (poly-dopamine)	To identify clusters of malignant cells during photothermal cancer treatment with near-infrared laser irradiation and magnetic resonance imaging (MRI).	Wu et al.[18]
[18F]-FAC family of imaging agents for positron emission tomography	On PET scans, tumors that respond to chemotherapy medications show up as bright pictures.	Braas et al.[19]
Nano-MRI agent	Attach to the surface of freshly formed blood vessels' avβ3-integrin.	Liu et al.[20]
Gold nanoparticle based molecular diagnostic platform	FDA-approved nanosensor for warfarin sensitivity genetic testing. It allows testing for other genetic targets	Lefferts et al.[21]

Table 2: Nanomaterials have been used in clinical treatment for a number of illnesses.

Nanomaterial	Use and its Principle	References
Biomimetic nanosponge	For the treatment of detoxification	Hu et al.[23]
Nano-composite film of carbon nanotubes (CNTs)	For ultrasonic treatment that is non-invasive. It disrupts cells by turning light into sound and producing high-pressure sound waves. "Invisible knife for non-invasive therapy" is another name for it.	Baac et al.[24]
Gold/Bismuth based nanoparticles	To target cancerous tumors with radiation therapy by concentrating radiation.	Cooper et al.[25]
Poly (ethylene oxylated) single-walled carbon nanotubes	Keeps the blood flowing through the brain.	Alqathami et al.[26]
SWNT functionalized with HER2 antibody	To destroy breast cancer cells specifically	Bobadilla et al.[27]
GRGDS-NPs are polyethylene glycol copolymers comprising poly (lactic-co-glycolic acid) and poly-ε-L-lysin targeting ligands that are ended with arginine, glycine, and aspartic acid.	In order to encourage coagulation and reduce trauma-related bleeding, these novel hemostatic NPs are administered intravenously.	Xiao et al.[28]
Fidgetin-like 2 (FL2) small interfering RNA (siRNA) nanoparticles	To encourage wound closure and regeneration, the siRNA contained in nanoparticles targets FL2, the regulator of cell migration.	Shoffstall et al.[29]
Fullerene nanoparticles	Minimize allergic responses	Charafeddine et al.[30]
Carbon nanotube based nanofiber scaffold	Engineering cardiac tissue	Ryan et al.[31]
Thymosin β4 coated poly (ε-caprolactone) nanoscaffolds	Following any cardiac event, the coated nanoscaffolds have the ability to replace the heart because they promote the proliferation and differentiation of cardiomyocytes into functional cardiac tissue.	Oh et al.[32]
BIND-014, a prostate specific membrane antigen (PSMA)-targeted NP containing docetaxel	Used to treat chemotherapy-naïve metastatic castrate-resistant solid cancers.	Kumar et al.[33]
siRNA encapsulated in a cyclodextrin based nanoparticle	To prevent cancer cells from producing essential enzymes	Mita et al.[34]
Gelatin nanoparticles as acarrier for osteopontin (OPN)	Administered intravenously to treat ischemic stroke	Davis et al.[35]
Nanoparticles poly (D,L-Lactitide-co-glycolide)-(PLGA-) based polymer	Insulin delivery carrier for individuals with diabetes	Kanasty et al.[36]
Monodisperse microgels consist of a chitosan matrix, enzyme nanocapsules, and recombinant human insulin	In individuals with type 1 diabetes, the enzyme nanocapsule-containing microgels track insulin secretion and baseline blood sugar levels.	Joachim et al.[37]
Nanocrystalline silver	Antimicrobial compound with endosomal	Verma et al.[38]
Bioreducible polycations-polymer of Polyethylenimine (PEI)	Escape activity for wound therapy pDNA carrier	Gu et al.[39]

Tissue growth and regenerative medicine

The goal of tissue regenerative medicine research is to create scaffolds or implants that can administer hormones, growth factors, and medications to promote tissue healing. In order to support cell survival, invasion, and proliferation for tissue engineering, they offer sustained administration of bioactive chemicals. Complete tissue replacement and functional recovery are the anticipated results of this type of treatment. The use of CNT, nanowires, and nanoparticles improves the development of extracellular matrix. To speed up bone repair, growth factors are delivered via regulated biomolecules using biomimetic hydrogels.[40–42]

Comparing to standard composite microparticles, the nanofilled composites demonstrate higher compressibility, tensile strength, and flexure strength. A new scaffold for osteochondral repairing might be a crosslink agent consisting of nanocrystalline hydroxyapatite (nHAp) along with partially hydrolyzed polyacrylamide (HPAM).[43]

Chodritin sulfate nanoparticles (CSnps) have been utilized to treat wounds by forming a scaffold of chitin mixed with poly (butylene succinate).[44] Because it is biodegradable, biocompatible, and forms a porous layer for improved nutrient exchange, it offers a greater aesthetic sense. Hydrogel scaffolds based on polyethylene glycol help transplanted cardiac cells develop and stay in place after myocardial infarction.[45] Garphene oxide-coated glass slides promote human adipose-derived stem cell adhesion and osteogenic differentiation.[46] It is currently demonstrated that the components of the laminin matrix, chitosan, collagen, and chondroitin-6-sulfate support islet function in vitro and help with islet survival and vascularization following transplantation.[47] A comprehensive understanding of the nanoscale interactions between cells and the in vivo environment can help in the design and manufacturing of biomimetic scaffolds.

Toxic Outcomes of Nanostructures

Nowadays, nanotechnology is seen as a two-edged sword. Potential health benefits are represented by one edge, while potential health concerns are shown by the other. Among the many benefits of nanotechnology are its high performance, decreased mass, size, and power consumption, POC testing, and enhanced robustness and dependability. In order to examine the unique physicochemical properties of these nanostructures, the toxicity component is ignored. Because of their adjustable characteristics, they produce distinct and erratic biological reactions, as will be covered below.

Size, shape and surface area of the nanomaterial

These particles can readily enter important cells and organs due to their tiny size. They engage with the host cell and either stay attached to the surface or internalize by receptor-mediated endocytosis or translocation. By interacting with the subcellular organelles, they can also change the metabolism of the cell intracellularly. As the particles size decreases, its surface area "o" rises and the ratio to its surface to total atoms or molecules increases exponentially. The "size-dependent biological effects of silver NPs" were described by Ivask et al. Due to their higher intracellular bioavailability, silver nanoparticles smaller than 10 nm were found to be more hazardous than those larger than 10 nm in his study.[48]

Numerous researches based on carbon nanotubes, nanorods, nanospheres, silicas, copper, gold, and many other materials have also shown shape-dependent toxicity. Results from a study by Kennedy et al. comparing CuO nanorods to CuO nanospheres showed that the nanorods' larger surface area released more ions, making them more hazardous.[49] However, by improving the synthetic process, special qualities could be improved with few negative effects. In their research, Almodarresiyeh et al. developed a novel technique for creating rod-shaped zinc oxide (ZnO) nanoparticles when polymers (polyethylenimine and hexamethylenetetramine) were present. These ZnO nanoparticles are well suited for usage in optoelectronic devices due to their substantial excitation energy and wide band gap semiconductor.[50–52]

Solubility of NPs in the biological media

The solubility of nanomaterials in a medium is influenced by their size and surface ratio, which also affects their particle dispersion and aggregation state. Therefore, another element that determines the toxicity of NPs is the reciprocal action between the particle and its solvent. Longer TiO_2 nanofibers (15 mm) have a larger harmful effect than shorter ones, as demonstrated by Hamilton et al. This is because the longer fibers are insoluble in lung fluids and stay in the lungs longer, which causes the alveolar macrophages to mount an inflammatory response.[53] In their investigation, Yang et al. found that silver nanoparticles dissolved in a lower ionic strength were more hazardous than those dissolved in a higher ionic strength.[54] Because TiO_2 and ZnO have varying diameters in various biological environments, their toxicity varies as well.

Surface chemistry (charge/surface coatings)

The surface charge of an NP is another important variable determining how it interactions with the biological environment. According to the Dejaguin-Landau-Verwey-Overbeek (DLVO) theory, the Van der Waals forces and the particles' net electrostatic surface contacts determine how stable a particle is. A study by Stebounova et al. showed that in simulated lung fluid, polymer-coated silver nanoparticles with a greater surface charge were more stable than silver NPs with unidentified coatings.[55] Park et al. discovered that silica (SiO_2) nanoparticles with a negative charge were more harmful than those with a weak negative charge. Because of their improved opsonization by plasma proteins, articles have shown that positively charged SiO_2 is significantly absorbed by cells. Additionally, SiO_2 causes the production of intracellular reactive oxygen species (ROS) and uses oxidative stress to cause its harmful effects.[56]

Composition and degree of purity

Iron-containing nanomaterials are hazardous to brain cells[59], carbon-based nanomaterials cause lung cancers[58], and cadmium selenide (CdSe) nanomaterials are toxic to rat liver and renal cells.[57] In their investigation, Liu et al. demonstrated that cadmium sulfide (CdS) had cytotoxic and genotoxic effects on spermatozoa, liver cells, renal cells, and other investigated organs.[57]

Harper et al. evaluated how peptide-capped gold-glutathione (Au-GSH) nanoparticles' biocompatibility was impacted by the production process and purity. Dialysis-purified Au-GSH-(Trp)2 showed significant morbidity and death. Although Au-GSH-(Met)2 exhibited the least amount of toxicity, Au-GSH-(His)2 generated by ultracentrifugation or dialysis also shown significant toxic effects. NPs with improved biocompatibility and a high degree of purity can be produced by a meticulous synthesis method.[60]

Aspect ratio dependent toxicity

It is observed that the aspect ratio the ratio of the highest to the lowest dimension when the particles are of identical size is directly correlated with toxicity. Nanotubes, nanowires, and nanorods are examples of NPs with a high aspect ratio, while spherical, oval, and cubic shapes are examples of NPs with a low aspect ratio.[61] Less than 10 micron asbestos fibers induce lung cancer, 5 micron asbestos fibers produce lung mesothelioma, and 2 micron asbestos fibers cause asbestosis. The macrophages shorten and eliminate the longer asbestos fibers by breaking them down perpendicularly. Longitudinal cutting of smaller strands

produces additional fibers with smaller diameters that are more challenging to remove. Slow removal of broken-down particles, however, would cause longer fibers to accumulate in the alveoli, causing inflammatory alterations. When compared to spherical amorphous carbon black particles, the long aspect ratio of SWCNT has been significantly linked to lung toxicity.[62]

Aggregation state of NPs

All NPs exhibit aggregation, which facilitates the uptake of biomolecules by cells. Albanese et al. researched how different types of cells received collections of transferrin-coated gold nanoparticles. In HeLa and A549 cells, the aggregates decreased uptake by receptor-mediated endocytosis. On the other hand, through an unidentified mechanism, the aggregates internalized without the aid of the transferring receptor in MDA-MB-435 cells. According to the study, NP aggregates cause a variety of biological reactions.[63] Tripathy et al. offered proof of the influence of ZnO nanoparticle size and aggregation. Smaller aggregates typically dissolve more quickly and are absorbed by cells more readily, which produces ROS and triggers cellular death.[64]

Antigenicity of NPs

The physicochemical characteristics of nanoparticles determine their immunogenicity, and they may be antigenic in and of themselves. Plasma proteins have the ability to opsonize them, which activates the complement cascade. When compared to albumin control, nab-paclitaxel in pigs elicited an immune response, according to Trynda-Limiesz et al.[65] According to Abrams et al., the liposomal siRNA delivery vehicle LNP201 caused a cytokine storm, which is a manifestation of an uncontrolled innate immune response.[66]

Challenges for Nanotechnology

Even though the field of nanotechnology is expanding quite quickly, there are still several obstacles at different phases of development that prevent the product from becoming widely available. If the growth obstacles listed below are removed, the medical and health care industries could undergo radical transformation.

Lack of knowledge NP components and their characteristics

Nanostructures come in a wide variety, each with its own unique composition and properties. These NPs' physicochemical phenomena in vitro and in vivo are poorly known. Therefore, finding an appropriate nanomaterial for the specific indication is essential. PEI is becoming

known as a great cargo for targeting intracellular nucleic acids. However, it is also thought to be a powerful cytotoxic agent. By attaching low molecular weight PEI to dithiodipropionic acid di (N-succinimidyl ester), techniques have been developed to lessen its toxicity due to its greater efficacy in drug delivery.[22]

Lack of uniformity of toxicity

Depending on their size, shape, or composition, nanomaterials may be hazardous to different cell types under various exposure scenarios. Nanoparticles' composition, size, shape, charge, aggregation, coating, and solubility all have an impact on the toxicity of the target cell and target moieties. While cell cultures exposed to 3.8 µg/ml show no cytotoxicity, CNTs at 400 µg/ml are harmful to human T-cells and 3.06 µg/cm2 on alveolar macrophages.[22]

Lack of standardization in model systems and test assay

To precisely explain the physical, chemical, and biological activity, there isn't a good in vivo model. Validating the results of NPs' interaction with cells is challenging since, even when test assay conditions are the similar, the results differ depending on the type of cells used.

Lack of standard synthesis protocol

Many harmful synthetic reagents are used in the production of nanomaterials. It is necessary to design an efficient synthesis process while avoiding the use of hazardous contaminants. A high-purity and superior biocompatible nanoparticle yield can be guaranteed by using synthetic materials wisely and according to safety regulations.

Lack of efficient analytical tools

Because nanotechnology works with nanoscale structures, new analytical techniques must be created in order to accurately describe nanomaterials in terms of their size, surface charge, chemistry, crystalline state, aggregation state, and dispersion. To forecast how nanoparticles will behave in biological media, new developments in metrological technology are necessary.

Lack of understanding of impact on biological system

Regarding cellular or organ toxicity, genotoxicity, or carcinogenicity, the impact on health and safety concerns is still unknown. These substances are sufficiently tiny to be breathed, and when they build up in the lung alveoli, they can cause inflammation or cancer. Because the workers will be at risk of occupational hazards, this would be of utmost importance.

Lack of in-vivo monitoring systems

The main obstacles to optimizing biological activities include the significant infrastructure required for in-vivo analysis of nanomedicines, the impossibility to monitor many probes, and the requirement that patients be hospitalized for analysis.

Lack of standardized safety guidelines

It is challenging to specify a specific safety recommendation for a given nanoparticle because of the complexity of nanomedicines and their multiform toxicity. Extensive pre-clinical testing and empirical evidence are required to develop a safety protocol.

Lack of well trained workforce

Expensive energy consumption results in extremely expensive manufacturing costs and limited accessibility for individuals. This is a significant obstacle to achieving the objective of doing proof-of-concept testing in remote places.

The effective manufacturing of "Safe by Design" nanostructures through green chemistry and the optimization of conventional synthesis, production, and clinical testing processes are urgently needed. In order to modify the set of regulations so that the occupational and health promotion benefits outweigh the cost and risk factors, scientific personnel, government officials, and representatives from the industry and workforce must contribute and evolve in the development of "Green Nanotechnology".[67]

CONCLUSION

Nanotechnology has enabled the creation of many very powerful products. The development of nanomedicines and nanodevices is still in its early phases. The breadth of the development processes is fairly broad because they are closely linked to information technology and biology. Products based on nanotechnology can get around the drawbacks of conventional techniques. However, its toxicity, environmental risks, production cost, and accessibility to remote and inaccessible regions remain the main obstacles.

REFERENCES

1. "Biomedical Nanostructures," Morrison D, Dokmeci M, Demirci U, Khademhosseini A (2008), John Wiley & Sons, Inc., ed. Kenneth G, Craig H, Cato TL, and Lakshmi N.
2. Rocco M, Alivisato P, and Williams S (2000) Research Directions in Nanotechnology: IWGN, "National Nanotechnology Initiative: Leading to the next Industrial Revolution,"

Loyola College, Maryland The National Science and Technology Council, Washington, DC, Interagency Working Group on Nanoscience, Engineering and Technology Committee on Technology, report.

3. Nanotechnology was first presented to the standards community in 2005 by Mansoori GA, Soelaiman TAF, and Soelaiman TAF. J ASTM Int, 2: 1–22.
4. Feynman R., Infinitesimal Machinery (1993). The talk was reproduced in the Journal of Microelectromechanical Systems.
5. Yoon HJ, Nagrath S, Lee K, Zhang Z, and Pham TM (2011) Graphene oxide nanoassembly for isolating circulating tumor cells.
6. Trudel LJ, Sen S, Iverson NM, Barone PW, Shandell M, et al. (2013) tissue-localizable near-infrared fluorescent single-walled carbon nanotubes for in vivo biosensing. 873–880 in Nat Nanotechnol, 8.
7. Surface-enhanced Raman scattering molecular sentinel nanoprobes for the diagnosis of viral infections Wang HN, Fales AM, Zaas AK, Woods CW, Burke T, et al. (2013). Acta 786: 153–158; Anal Chim.
8. NanoFlares for the identification, separation, and culture of live tumor cells from human blood by Halo TL, McMahon KM, Angeloni NL, Xu Y, and Wang W, et al. (2014). 17104–17109 in Proc Natl Acad Sci USA 111.
9. Murugappan G, Abudayyeh O, Mo S, von Maltzahn G, Kwong GA, et al. (2012) Mass-encoded synthetic biomarkers for multiplexed urine surveillance of illness. 63–70 in Nat Biotechnol, 31.
10. Shao H, Chung J, Balaj L, Charest A, Bigner DD, et al. (2012) Real-time glioblastoma therapeutic monitoring is made possible by protein typing of circulating microvesicles, 18: 1835–1840; Nat Med.
11. Wu D, Garcia MA, Shen Q, Lu YT, Zhao L, et al. (2013) NanoVelcro Chip for CTC enumeration in patients with prostate cancer. Procedure, 64: 144–152.
12. Negri P, Dluhy RA (2013) Surface-enhanced Raman spectroscopy based on Ag nanorods used for bioanalytical sensing. Biophotonics Journal, 6: 20–35.
13. Tripp RA, Jones CA, Tompkins SM, and Driskell JD (2011) Gold nanoparticles and dynamic light scattering are used in this one-step technique to identify influenza viruses, 3083–3090 the Analyst 136.
14. Liu Y, Zhang L, Wei W, Zhao H, Zhou Z, et al. (2015) used antibody-functionalized gold nanoparticles for colorimetric influenza A virus detection, 140: Analyst 3989-3995.
15. Stevens MM, De la Rica R (2012) Plasmonic ELISA for the highly sensitive visual

identification of illness biomarkers. 821–824 in Nat Nanotechnol 7.

16. Yu C, Papazoglou ES, Clark PM, Zubkov L, Kim GB, et al. (2015) an electrohydrodynamic mixing element in a microfabricated quantum dot-linked immunodiagnostic assay (μQLIDA), 209: 722-728; Sens Actuators B Chem.
17. Montalti M, Cantelli A, Battistelli G (2015) Nanodiamonds with silicon quantum dots: biocompatible and ultrastable luminous nanoprobes for extended bioimaging duration, 4853–4921 in Chem Soc Rev 44.
18. Wu M, Zhang D, Zeng Y, Wu L, Liu X, et al. (2015) Nanocluster of poly (dopamine)-coated superparamagnetic iron oxide nanoparticles for tumor photothermal treatment, magnetic field targeting, and ultrasensitive MRI. Science and Technology, 26: 115102.
19. Braas D, Ahler E, Tam B, Nathanson D, Riedinger M, et al. (2012) a metabolomics approach identifies a subset of liposarcomas that respond well to gemcitabine therapy. Discov, 2: Cancer, 1109–1117.
20. Zhang C, Liu Y (2013) A brief overview of using magnetic probes to target integrin αvβ3 in order to do magnetic resonance molecular imaging of tumor angiogenesis. J Nanomedicine Int, 8: 1083–1093.
21. Lefferts JA, Lewis LD, Lee HK, Dandamudi UB, Schwab MC, et al. (2010) used three distinct platforms to genotype warfarin. Transl Res Am J., 2: 441–446.
22. Wagner E, Klein PM (2014) Bioreducible Polycations as Transporters for Protein and Nucleic Acid Transfection for Therapeutic Uses. Signal of Antioxidant Redox, 21: 804-817.
23. Zhang L, Copp J, Luk BT, Fang RH, and Hu CMJ (2013) a biomimetic nanosponge that takes up poisons that cause pores. 336-340 in Nat Nanotechnol, 8.
24. Carbon nanotube optoacoustic lens for focused ultrasonic generation and high-precision targeted therapy, Baac HW, Ok JG, Maxwell A, Lee KT, Chen YC, et al. (2012). Sci Rep, 2: 989.
25. Gold nanoparticles and their substitutes for enhancing radiation therapy Cooper DR, Bekah D, Nadeau JL (2014). Front Chem, 2: 86.
26. Alqathami M, Franich R, Doran S, Blencowe A, Yeo UJ, et al. (2013) Bismuth oxide nanoparticle-induced enhancement of radiation effects for kilovoltage x-ray beams: A dosimetric investigation employing a new multi-compartment 3D radiochromic dosimeter. 012025 in J Phys Conf Ser, 444.
27. Bobadilla AD, Samuel ELG, Tour JM, Seminario JM (2013) Determining the Hydrodynamic Volume of Hydrophilic Carbon Clusters and Poly(ethylene oxylated)

Single-Walled Carbon Nanotubes. 343–354 in J Phys Chem B 117.Xiao Y, Gao X, Taratula O, Treado S, Urbas A, et al. (2009) Single-walled carbon nanotubes functionalized with an anti-HER2 IgY antibody for the purpose of identifying and eliminating breast cancer cells. BMC Cancer, 9: 351.

28. Intravenous hemostatic nanoparticles improve survival after blunt trauma injury, according to Shoffstall AJ, Atkins KT, Groynom RE, Varley ME, Everhart LM, et al., 2012; 33: 3850–3857 in Biomacromolecules 13.
29. Charafeddine RA, Diaz-Valencia JD, Makdisi J, Schairer D, O'Rourke BP, et al. (2015) Fidgetin-Like 2: A Wound Healing Regulator Based on Microtubules. Dermatol J Invest, 135: 2309–2318.
30. Fullerene nanoparticles suppress the allergic reaction, according to Ryan JJ, Bateman HR, Stover A, Gomez G, Norton SK, et al., 2007; 179, J Immunol, 665–672.
31. Oh B, Lee CH (2013) Cardiovascular tissue engineering using nanofiber. Drug Delivery Expert Opin, 10: 1565-1582.
32. Marks ED, Duvalsaint L, Desai M, Patel A, and Kumar A (2014) Nanofiber scaffolds coated with thymosin ß4 for the restoration of injured cardiac tissue. 12: 10 in J Nanobiotechnology.
33. Eisenberg P, Hart L, LoRusso P, Burris H, and Mita M, et al. (2014) Abstract CT210: BIND-014, a PSMA-targeted nanoparticle that contains docetaxel, is being given weekly to patients with resistant solid tumors as part of a phase 1 research. CT210-CT210 in Cancer Res 74 (19 Supplement).
34. Davis ME (2009) from concept to clinic: the first targeted delivery of siRNA in humans using a self-assembling, cyclodextrin polymer-based nanoparticle. Pharm Mol, 6: 659-668.
35. Anderson D, Vegas A, Dorkin JR, and Kanasty R (2013) materials for siRNA therapy delivery. Science, 12: 967-977.
36. Lee JK, Kim KK, Jin Y, Kim ID, Joachim E, et al. (2014) in a rat ischemic stroke model, gelatin nanoparticles improve the neuroprotective benefits of intranasally delivered osteopontin. Transl Res Drug Deliv, 4: 395-399.
37. In 2014, Verma A, Kumar N, Malviya R, Sharma PK, Verma A, et al. published Emerging Trends in Noninvasive Insulin Delivery. e378048 in J Pharm J Pharm 2014.
38. Glucose-responsive microgels combined with enzyme nanocapsules for closed-loop insulin administration Gu Z, Dang TT, Ma M, Tang BC, Cheng H, et al., 2013; 6758–6766 in ACS Nano 7.

39. A review of nanocrystalline silver dressings in wound care by Fong J, Wood F (2006). 441-449 in Int J Nanomedicine.
40. Oupicky D, Li J (2014) Bioreducible polycations in the delivery of nucleic acids: historical, contemporary, and prospective trends. Biosci Macromol, 14: 908-922.
41. Lienemann PS, Ehrbar M, and Lutolf MP (2012) Biomimetic hydrogels for regulated delivery of biomolecules to promote bone regeneration. Drug Delivery Advancement, 64: 1078-1089.
42. Koushki N, Majidi M, Jahanbakhsh A, Tavassoli H, Katbab AA, et al. (2015) A novel injectable biphasic hydrogel scaffold for osteochondral regeneration based on nanohydroxyapatite and partially hydrolyzed polyacrylamide. Advances in RSC., 5: 9089-9096.
43. Thitirat C, Furuike T, Tamura H, Viha CVS, Deepthi S, et al. (2014) Creation of Ternary Composite Hydrogel Scaffold for Skin Tissue Engineering using Chitin/Poly(butylene succinate)/Chondroitin Sulfate Nanoparticles. 6: Polymers 2974–2984.
44. Myocardial Matrix-Polyethylene Glycol Hybrid Hydrogels for Tissue Engineering (Grover GN, Rao N, Christman KL, 2014). 014011 in Nanotechnology 25.
45. Fu YX, Cao CH, Luo D, Lo CQ, Lu JY, et al. (2015) The Possible Mechanism Behind the Induction of Osteogenic Differentiation of Human Adipose-Derived Stem Cells by a Novel Self-Supporting Graphene Hydrogel Film. 20245–20254 in ACS Appl Mater Interfaces 7.
46. For the ectopic transplantation of islets, Ellis CE, Suuronen E, Yeung T, Seeberger K, and Korbutt GS (2013) bioengineered a highly vascularized matrix. Islets, 5: 216-225.
47. The size-dependent toxicity of silver nanoparticles to bacteria, yeast, algae, crustaceans, and mammalian cells in vitro was reported by Ivask A, Kurvet I, Kasemets K, Blinova I, Aruoja V, et al., 2014; One 9: e102108 (PLoS).
48. The fate and toxicity of CuO nanospheres and nanorods employed in Al/CuO nanothermites both before and after combustion were examined by Kennedy AJ, Melby NL, Moser RD, Bednar AJ, Son SF, et al., 2013; 11258–11267 in Environ Sci Technol 47.
49. In 2014, Almodarresiyeh HA, Abakshonok AV, Agabekov VE, and Eryomin AN synthesized ZnO nanoparticles from various zinc salts. Civil Engineering: An Encyclopaedia.
50. The impact of reaction conditions on the optical properties and structure of zinc oxide nanorods was examined by Shahab SN, Eryomin AN, Agabekov VE, Abakshonok AV,

and Almodarresiyeh HA (2014). In: IOP Conference Series on Materials Science and Engineering [Online]. 012050 IOP Publishing.

51. Almodarresiyeh HA, Agabekov VE, Ariko N, Shahab SN, and Filippovich L (2014) zinc oxide nanoparticles with organic dyes to modify polyvinyl alcohol films. International Conference on Science and Applications of Thin Films, SATF, Izmir, Turkey.
52. In 2009, Hamilton RF, Wu N, Porter D, Buford M, Wolfarth M, and others The toxicity and bioactivity of titanium dioxide nanoparticles are dependent on their particle length. Fibre Toxicol Part, 6: 35.
53. Yang X, Liu J, Auffan M, Marinakos SM, Gondikas AP, et al. (2012) The toxicity mechanism of silver nanoparticles in Caenorhabditis elegans depends on surface coating and dissolved silver. 1119–1127 in Environ Sci Technol 46.
54. O'Shaughnessy PT, Kim JS, Park H, Adamcakova-Dodd A, Stebounova LV, et al. (2011) In a subacute inhalation paradigm in mice, nanosilver causes negligible lung damage or inflammation. Fibre Toxicol Part, 8: 5.
55. The impact of silica nanoparticle size and surface charge on cutaneous toxicity was examined by Park YH, Bae HC, Jang Y, Jeong SH, Lee HN, et al., 2013; 67–74 in Mol Cell Toxicol 9.
56. Liu L, Sun M, Li Q, Zhang H, Alvarez PJJ, et al. (2014) Analyzing the Differences Between Nanorods and Nanodots in the Genotoxicity and Cytotoxicity of Cadmium Sulfide Nanomaterials to Mice. 373–380 in Environ Eng Sci 31.
57. Guo NL, Porter DW, Pacurari M, Wan YW, Denvir J, et al. (2012) Gene profiles in the mouse lung caused by multiwalled carbon nanotubes may have prognostic significance for the prognosis and risk of lung cancer in humans. A., 75: 1129–1153, J Toxicol Environ Health.
58. Wu J, Ding T, Sun J (2013) Iron oxide nanoparticles' neurotoxic potential in the striatum and hippocampus of rat brains. 243-253 in Neurotoxicology 34.
59. In 2014, Harper B, Sinche F, Wu RH, Gowrishankar M, Marquart G, et al. examined how surface ligands and the synthesis process affected the toxicity of glutathione-coated gold nanoparticles. Nanomater 4, Basel, Switzerland, 355-371.
60. In 2007, Buzea C, Pacheco Blandino I, and Robbie K discussed the origins and toxicity of nanoparticles and nanomaterials.
61. Johnson VJ, Murray AR, Kisin ER, Mercer R, Shvedova AA, et al. (2005) Unusual pulmonary reactions in mice to single-walled carbon nanotubes, including inflammation and fibrogenicity. Lung Cell Mol Physiol Am J Physiol, 289: L698-708.

62. Albanese A, Chan WC (2011) Aggregation of gold nanoparticles and its impact on toxicity and cell absorption. 5. ACS Nano: 5478–5489.
63. The impact of ZnO nanoparticle aggregation on the toxicity of RAW 264.7 murine macrophages was examined by Tripathy N, Hong TK, Ha KT, Jeong HS, and Hahn YB (2014). 110–117 in J Hazard Mater 270C.
64. Desai N. (2012). Difficulties in developing medicines based on nanoparticles. AAPS J., 14: 282-295.
65. Abrams MT, Koser ML, Seitzer J, Williams SC, DiPietro MA, et al. (2010) Evaluating the Effect of Co-treatment with Dexamethasone on the Inflammation, Biodistribution, and Efficacy of a Strong siRNA Nanoparticle. Mol Ther., 18: 171–180.
66. Valsami-Jones E, Weiss C, and Lynch I (2014) a method for classifying nanomaterials according to important physico-chemical characteristics in order to create safer NMs by design. Today, 9: 266-270 in Nano.