Chapter 2
Nanobiology in Medicine

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2.1 Introduction to Nanobiology

The term 'nano' is a Greek word for 'dwarf', meaning one billionth. It was first used by N. Taniguchi in 1974. A quest for nano began from the noble lecture, 'There is plenty of room at the bottom' presented by the Noble Laureate, Professor Richard Feynman in 1959. In the 1980s, K. Eric Drexler popularized the word 'nanotechnology'. His idea was to build machines on the molecular scale [1]. The principle behind this technology is engineering and manufacturing structures, devices, and systems that have novel properties at the atomic and molecular level. Later, scientists and researchers successfully employed nanotechnology to explore the boundaries of biomedical sciences. They made it possible to use biological processes to construct biocompatible nanostructures. There are several approaches to construct nanostructures and they are top-down (miniaturization) approach, bottom-up (building from atoms and molecules) approach and functional (building materials with desired functionality) approach [2].

Biological studies focused at extremely minuscule to molecular levels are termed as Nanobiology. Most of the fundamental biological functions take place at the level of molecular machineries that have a size range of less than 100 nm. Figure 2.1 demonstrates a good size comparison of biological structures in the nanometric scale [3]. The emergence of nanobiology made opportunities to better understand the functions of these molecular machineries with the help of scanning probe microscopy, modern optical techniques, and micro-manipulating techniques.

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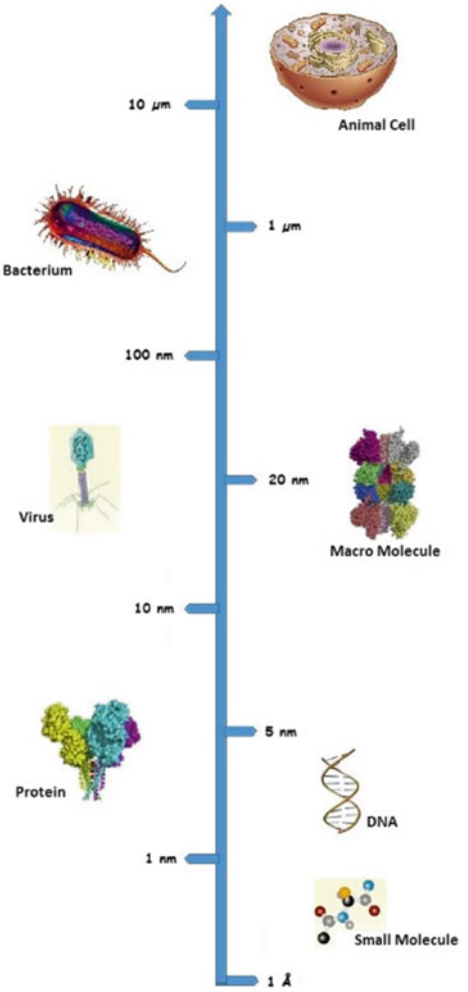

Fig. 2.1 Relative sizes of different biological structures in nanometric scale [3]

Nanobiology research interests can be roughly grouped into two basic categories: nanotechnologies applied to biological systems, and development of biologically-inspired nanotechnologies. The main reason for this categorization is to differentiate between the sources of inspiration. However, nanobiology research are mainly focussed at nanobiological structures and systems, biomimetics, nanomedicine, nanoscale biology, and nanointerfacial biology [4]. The tools, techniques, and technologies derived from nanobiology are applied to medical field directly and indirectly, giving rise to a new ground of medicine termed Nanomedicine. Nanobiology by itself is a blend of various different disciplines not limited to physics, chemistry, biology, computation, and engineering [4]. The different themes of nanobiology can be well understood from Fig. 2.2.

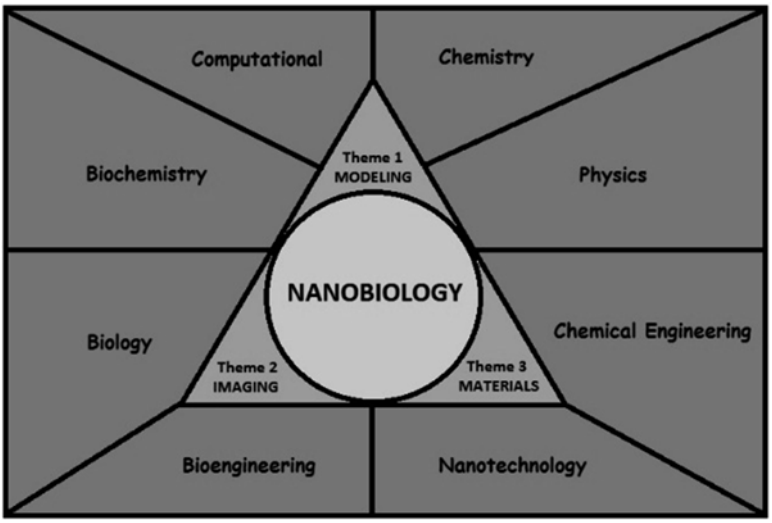

Fig. 2.2 Nanobiology map showing three different themes [4]

Nanobiology can make significant contributions to medicine by achieving success in early detection and diagnostic strategies, and in treatment and prevention of fatal diseases. Based on enhanced efficacy, nanoparticles of polymers, metals or ceramics can conflict life challenging conditions like cancer, AIDS, heart and brain disorders. They can invade bacteria, virus, parasites, etc. Nanoparticles are generally characterized based on their size distribution, shape, surface area, surface reactivity, surface charge, chemical composition, and aggregation state. Factors such as specificity, solubility, stability, biocompatibility, biodegradability, and pharmacokinetics are to be considered predominantly while using nanoparticles in medicine. The purpose of employing nanobiology in medicine is to diagnose diseases early and accurately; and to treat them effectively without any side effects. It has proven potential to cure human cancer by specifically killing the targeted cancer cells leaving the surrounding healthy tissues harmless. Nano-drug delivery system can provide new insight for the treatment of tuberculosis (TB). DNA-based nanotechnology is a new arrival in molecular medicine [5]. Nano-drug therapy sounds promising compared to traditional therapies [6]. It is strongly believed that nanobiology has all the probability to benefit mankind by improving the quality of life, without any doubts.

2.2 Nanobiology and Human Biology

In terms of medical application, the main thing to consider about nanomaterials is their sustainability in the human body. These small materials exhibiting unique surface properties at nanoscale size could be toxic, causing adverse ill effects.

Table 2.1 FDA-approved gold based nanomaterials used in therapeutics [8]

Product/ brand name	Component/ active ingredient	Delivery route	Target	Company	Current status
Verigene	Gold	In vitro diagnostics	Genetics	Nanosphere	FDA-approved
Aurimmune	Colloidal gold nanoparticle coupled to TNF-α and PEG-Thiol (~27 nm)	Intravenous	Solid tumor	Cyt-Immune sciences	Phase-II
Auroshell	Gold coated silica nanoparticles (~150 nm)	Intravenous	Solid tumor	Nanospectra biosciences	Phase-I
Combidex (Ferumoxtran-10)	Iron oxide nanoparticles (17–20 nm)	Intravenous	Tumor imaging	Advance magnetics	NDA filed

The nanomaterials used on purpose should be able to dissolve inside the body without leaving any side effects when they are no longer needed. Nanomaterials have an unknown behavioural property when compared with bulk materials. For example, nanomaterials made of inert element like gold become extremely active at nanometric dimensions [7] and it is one of the most used nanomaterial in medicine. A few FDA-approved gold based nanomaterials which are currently used in therapeutics are listed in Table 2.1. In a research conducted by Han et al., functionalized gold nanoparticles proved to be highly attractive for drug delivery because of their distinctive dimensions, surface tenability, and controlled drug release [9].

The nanoparticles enter human body through four major routes: nasal, oral, dermal and intravenous. Upon entry, they can be distributed throughout the body including brain, heart, lungs, gut, liver, spleen, kidney, and skin. Inside the body, nanoparticles behaviour can be disturbed or altered by factors such as hydrophobic, hydrophilic, lipophobic, lipophilic, active catalysis or passive catalysis. Nanoparticles enter the cell by one of the following four mechanisms: passive diffusion, facilitated diffusion, active transport, and endocytosis. The passive diffusion is achieved by electrochemical or concentration gradient driven mechanism. Positively charged small particles of approximately 20 nm size undergo passive diffusion. Facilitated diffusion is for small particles of size 10–30 nm and these particles get internalized via selective membrane protein channels and concentration gradient driven mechanism. The active transport and endocytosis are meant for larger particles of size ranging from 50 to 500 nm. The former is facilitated by transport protein and are energy dependent, against concentration gradient whereas the later is collective term for energy dependent internalization of substances, forming vesicles.

Several pathways of nanoparticle endocytosis include, phagocytosis, Clathrin-mediated endocytosis, Caveolae-mediated endocytosis, macropinocytosis, other Clathrin- and Caveolae-independent endocytosis, transcytosis (occurs in epithelial cells in blood brain barrier). The possible fates of internalized nanoparticles in the

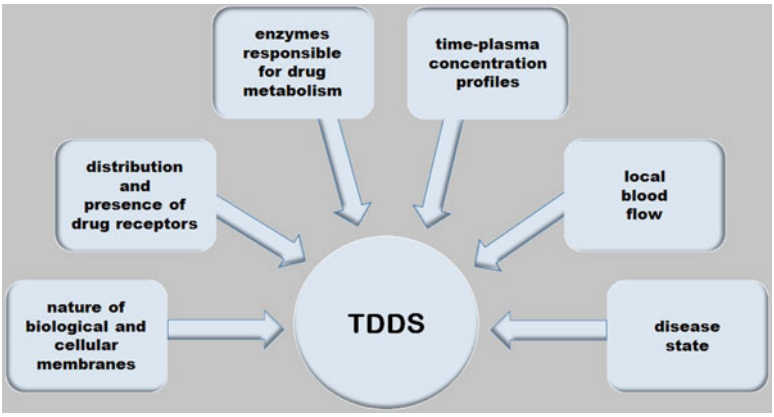

Fig. 2.3 Parameters to be considered for designing effective targeted drug delivery system (TDDS) [8]

cells are: enzymatic degradation or destruction by pH effect (acidic), exocytosis or transcytosis, transportation to intracellular locations escaping from endolysosomal compartment. The internalization of nanoparticles in the cells can cause molecular irregularities and incompatibilities resulting in fatal disorders ranging from interstitial fibrosis in respiratory system to acute coronary syndrome in vascular system. Because of some unresolved complications, not all the nanoparticles are readily used for medical applications. Only very few nanoparticles such as liposomes, dendrimers, organic polymers, quantum dots are tested to be safe in medicine and are found to be promising for in vivo imaging, in vitro diagnostics, and drug delivery. A few important parameters that are to be considered while designing an effective targeted drug delivery system are shown in Fig. 2.3.

2.3 Nanomaterials for Medicine

Materials with structural elements having dimensions in the range of 1–100 nm are termed as nanomaterials. Nanomaterials is a common term applicable for nanoscale materials, nanophase materials, and nanostructured materials. These three materials are different from one another; nanoscale materials, where the material itself fall under nanoscale regime; nanophase materials, these are hybrid materials having nanoscale phase or component; nanostructured materials, here the material structure will have nanoscale size or features [10]. Nanomaterials exhibit unique characteristic properties when compared to their bulk states. These improved properties along with large surface areas made them ideal for use in medical field. Nanomaterials play vital role in medical diagnosis and therapeutics ranging from fluorescent imaging to site-specific targeted drug delivery. More recently, Zhang et al. discussed how the nanomaterials could be designed based on their interactions with biological systems to

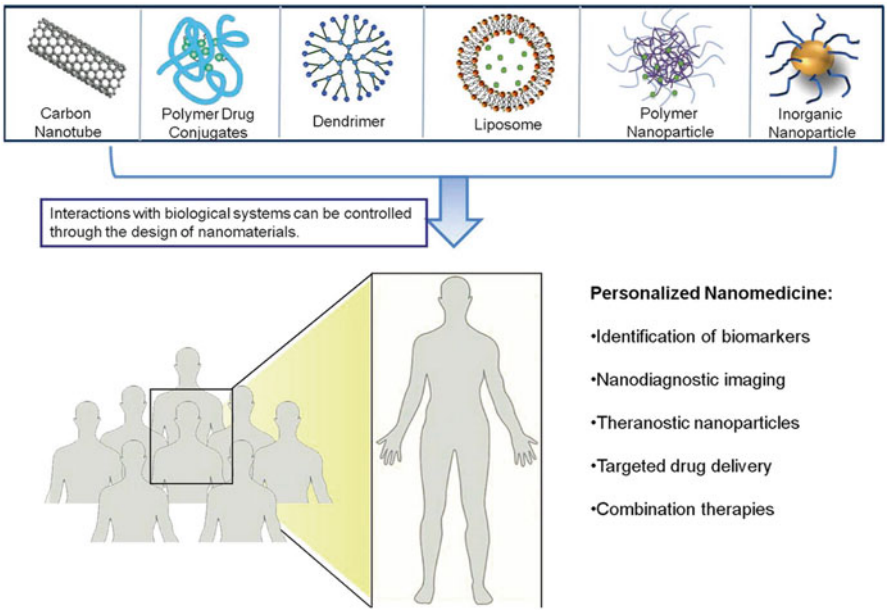

Fig. 2.4 Designing nanomaterials for personalized medicine [11]

meet their role in medical diagnostic, imaging and therapeutics [11]. The graphical view of the above context is depicted in Fig. 2.4. Nanomaterials of biological interest are mainly from two distinct groups: organic nanoparticles such as dendrimer, polymer; and inorganic nanoparticles such as gold, silver, iron, titanium dioxide. The other miscellaneous groups include carbon-based nanoparticles, organic and inorganic hybrids, liposomes, and protein and peptide-based nanoparticles.

Some examples of commonly used nanoparticles in medicine: multifunctional nanoparticles (best suited for intravenous delivery), lipid and polymer nanoparticles (trigger strong immune response), gold and magnetic nanoparticles (promising response in targeted drug delivery), virus based nanoparticles (acts as nanocarriers), dry powder aerosol (inhalable nanoparticles for lung specific treatment), smart nanomaterials (tunable by external stimuli).

Gold nanoparticles can be used for detection purposes. The gold nanoparticle with a DNA linker can result in a large size complex particle. A characteristic colour transition from pink to gray can be seen with naked eye. In medical diagnostics, gold nanoparticles can be used for laboratory analysis. Recently, a study on the development of a gold nanoparticle amplified agglutination system for weak blood group determination has been reported by Wiwanitkit et al. [12, 13]. In fact, gold nanoparticles found its entry in medical filed way back in 1800s. It was used as an important ingredient in many classical Chinese medicinal remedies. Jung et al. treated site-specific coupling of protein G to DNA oligonucleotide with a biolinker for efficient antibody immobilization [14]. The study reported that antibody targeting

on glass slides could be immobilized using this linker system without modifying or spotting antibodies, and the protein G-DNA conjugate brought a simple but effective method to label DNA-functionalized gold nanoparticles with target antibodies. Jung et al. concluded that the DNA-linked protein G construct introduced in this study offered a useful method to manage antibody immobilization in many immunoassay systems [14].

Silver nanoparticles is another commonly used nanomaterial for medical research which is proven to have promising antibacterial properties. Silver nanoparticles changes its colour with size. Silver particle having a size smaller than 10 nm appears to be golden yellow in colour. The colour further changes into red and black when the particle size increase. In 2006, Panacek et al. reported that the size of silver particles have a significant impact on their antibacterial activity. The study revealed that a very low concentration of silver gave antibacterial characteristic and thus the bactericidal property was found to be size-dependent of the silver particles [15]. In another quoted work, Gogoi et al. reported that above a certain concentration, silver nanoparticles were found to reduce the sizes of treated bacteria in addition to their characteristic bactericidal activity [16]. Pal et al. identified that silver nanoparticles underwent a shape-dependent interaction with *Escherichia coli* in their work on determining the antibacterial properties of differently shaped silver nanoparticles against the gram-negative bacteria both in liquid broth and on agar plates [17]. Also, an increase in the antibacterial activities of penicillin G, amoxicillin, erythromycin, clindamycin, and vancomycin in the presence of silver nanoparticles was reported by Shahverdi et al. [18]. As like gold nanoparticle, silver nanoparticles can also be used in the DNA linker system.

Superparamagnetic iron oxide nanoparticles are widely used in molecular and cellular imaging [19]. The major advantages of using iron oxide-based nanomaterials are their nontoxic property and biocompatibility. In a study reported by Thorek et al. superparamagnetic iron oxide nanoparticles demonstrated their utility as a novel tool for enhancing magnetic resonance contrast, allowing researchers to monitor physiological and molecular changes, in addition to previously monitored anatomical changes [20]. Hu et al. fabricated magnetic sponge-like hydrogels called ferrosponges by using an *in-situ* synthesis of magnetic iron nanoparticles in the presence of various concentrations of gelatin [21]. By using these unusual magnetic sensitive properties of the ferrosponges, a new drug delivery system can be designed to use in medicine. Titanium dioxide is another inorganic oxide nanoparticle which is recently found to be useful in medical application. Nano TiO_2 is studied to have good antibacterial properties as like silver nanoparticles. An effective organic degradation process was documented by Peralta-Hernandez et al. in their work on investigating the photo catalytic properties of nanostructured TiO_2 – carbon films obtained by means of electrophoretic deposition [22].

Viral nanoparticles (VNPs) and Virus-like particles (VLPs) are naturally occurring bionanomaterials [23]. Both of them are very promising candidates for developing ‘smart’ devices which can be used in several medical applications ranging from tissue-specific imaging to targeted-drug delivery. The major advantages of using viral particles are their exceptional stability and biocompatibility. To add a

few more, they are monodisperse, programmable, multifunctional, and easy to produce on large scale [24]. Cohen et al. investigated the use of aptamer-labeled MS2 bacteriophage capsids for targeted in vitro photodynamic therapy [25]. In their study, they demonstrated a unique virus-based loading strategy for efficient targeted delivery of photoactive compounds for site-specific photodynamic cancer therapy using biologically derived nanomaterials [25]. More recently in a similar study, Zeng et al. affixed folic acid (FA) as targeting moiety on the rigid Cucumber Mosaic Virus capsid and stuffed the interior cavity of CMV with substantial load of doxorubicin (Dox) to design a controlled drug delivery system for cancer therapy [26].

2.4 Nanobiology: Applications in Medicine

Nanobiology can help medicine in many aspects by providing a new range of tools and techniques that can be applied in early detection, disease diagnosis, non invasive treatment, and also in disease prevention. Some of the applications of nanomaterials to medicine include: fluorescent biological labels for imaging, drug and gene delivery platform, detection of pathogens and proteins, probing of DNA structure, tissue engineering and regeneration, tumour destruction via heating, separation and purification of biological molecules, magnetic resonance imaging (MRI) contrast enhancement, and phagokinetic studies [27].

2.4.1 Diagnostic Applications of Nanoparticles

In medicine, nanoimaging and nanovisualization contributes a lot more in recent diagnostics. The use of nanoparticles in imaging can provide new insights to medical diagnostics. Nanomaterials and nanotechnology combined with novel devices have the potential to address emerging challenges in medical field. The application of nanomaterials for imaging and visualization will offer fast, sensitive, and cost effective solutions for the modern clinical laboratory. Rotomskis et al. reported that the properties of nanomaterials such as quantum effect and surface area effect could improve the sensitivity of biological detection and imaging at least by 10–100 folds [28]. Basically, the nanodiagnosis can be classified into naked eye diagnostic system, immunological diagnostic system, and molecular diagnostic system. The protein precipitation systems to qualitatively test the protein in body fluids are the best example for naked eye detection system. The colour changing property of nanomaterials due to aggregation of particles can be applied to diagnostic tests in medicine [29]. Wiwanitkit et al. proposed gold nanoparticle as an alternative tool for the detection of microalbuminuria [12, 13]. Normal urine triggers the precipitation of gold nanoparticle solution resulting in a gray coloured mixture, while urine samples with protein do not. In addition to protein detection, the naked eye detection system using nanoparticles can also be applied to detect small substances such as hormones in body fluid. Gold nanoparticle solution can be used for the detection of human

choriogonadotropin (hCG) in urine, which is a basic diagnostic test to confirm pregnancy in females. The cost of gold nanoparticle is cheaper than the urine strip test. In another study, Bauer et al. aimed at the direct detection of sub-molecular layers of DNA with naked eye, based on the understanding of absorption property of metal nanoparticles [30]. The study focused on the nanolayer coated metallized-PET-chip setup and on the synthesis of DNA nanoparticle conjugates suitable for resonance amplified absorption -point of care tests and the applied usage of those particles in the direct visualization of DNA-DNA binding events [30].

Immunodiagnosis by nanoparticle is the new stage of immunological test in medicine. Over the last decade, the immunological diagnostic systems using nanoparticles achieved considerable momentum in the field of medicine. Immunological diagnostic systems employ nanoparticle labeling. The best example for nano-enabled immunological diagnosis is luminescent quantum dot in immunoassay. Quantum dots are emerging as a new class of biological labels with properties and applied usages that are not available with traditional organic dyes and fluorescent proteins [31]. Zhu et al. reported quantum dots as a new immunoflorescent detection system for *Cryptosporidium parvum* and *Giardia lamblia* [32]. The study concluded that this new fluorescence system exhibited superior photostability, gave 1.5–9 fold higher signal-to-noise ratios than traditional organic dyes in detecting *C. parvum*, and allowed couple-colour detection for *C. parvum* and *G. lamblia* [33]. In addition to quantum dots, superparamagnetic nanoparticles are also used in immunoassays. Kuma et al. reported their development of a liquid phase immunoassay system using magnetic nanoparticles [34]. They developed a highly sensitive immunoassay system using Fe_3O_4 magnetic nanoparticles [34]. Other than these, nanoparticles like silicon di oxide, europium-doped lanthanum fluoride, europium-doped gadolinium oxide, cadmium telluride are also used in nanodiagnosis [35–38]. In another work, Hwang et al. proposed the use of gold nanoparticle-based immunochromatographic test for identification of *Staphylococcus aureus* from clinical specimens [39]. Hwang et al. reported that this detection method was fast, easy to perform, and had a long shelf life at room temperature [39]. More recently, Jiang et al. reported a single step synthesis method to produce water soluble Ag_2S quantum dots for in vivo fluorescence imaging [40]. This work proposed potential cadmium-free (and lead-free) quantum dots for nanodiagnostics and in vivo imaging [40].

Finally, molecular diagnosis is rapidly advancing with the help of nanotechnology. There is a steady progress in the use of electrochemical biosensors for DNA analysis, over the past few years. In 2005, Shen et al. studied polymerase chain reaction (PCR) of nanoparticle-bound primers [41]. They concluded that with either one or two primers respectively bound to the nanoparticle surface, PCR could proceed completely under optimized conditions, having been subjected to certain rules [41]. Kalogianni et al. reported a simple and inexpensive assay that allowed visual detection and demonstration of the PCR-amplified sequences by hybridization within minutes [42]. According to their study, the nanoparticles bound to the target DNA through hybridization, and the hybrids were captured by immobilized streptavidin at the test zone of the strip, producing a characteristic red line [42]. In another quoted study, the use of plasmonics-based nanoprobes that acted as molecular

sentinels for DNA diagnostics were demonstrated. The plasmonics nanoprobe was composed of a metal nanoparticle and a stem-loop DNA molecule tagged with a Raman label, and the nanoprobe utilized the specificity and selectivity of the DNA hairpin probe sequence to detect a specific target DNA sequence of interest [43]. The study completely demonstrated the specificity and selectivity of the plasmonics nanoprobes to detect PCR amplicons of the HIV gene [43].

2.4.2 Therapeutic Applications of Nanoparticles

In recent days, the drug formulation and development becomes easier with the advancement of nanopharmacology. The application of nanotechnology in pharmacology is aimed at finding out novel pharmacological molecular entities; targeted site-specific drug delivery within the body; and providing personalized treatment to reduce side effects and increase drug effectiveness [44]. A graphical view on the beneficial effects of targeted drug delivery system (TDDS) are illustrated in Fig. 2.5 [8].

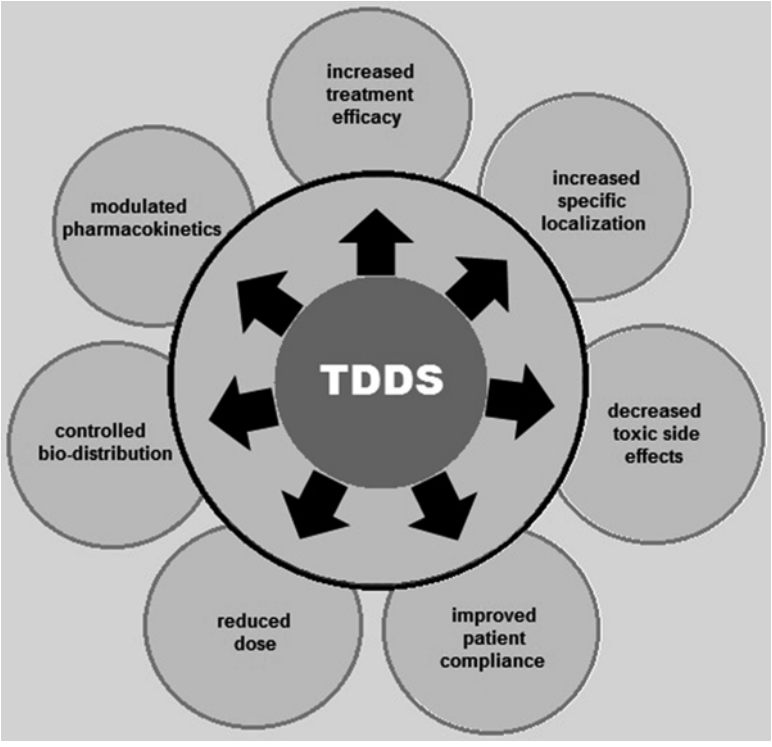

Fig. 2.5 Advantages of TDDS to improve drug efficiency for personalized treatment [8]

Table 2.2 Nanoparticles currently used in therapeutics

Type of nanoparticles	Material used	Application
Polymeric nanoparticles	Biodegradable polymers	Controlled and targeted drug delivery
Quantum dots	CdSe-CdS core-shell	Targeting and imaging agent
Nanopores	Aerogel, which is produced by sol–gel chemistry	Controlled release drug carriers
Nanowires or carbon nanotubes	Metals, semiconductors or carbon	Gene and DNA delivery
Nanoshells coated with gold	Dielectric (typically gold sulphide or silica) core and a metal (gold) shell	Tumor targeting
Liposomes	Phospholipid vesicles	Controlled and targeted drug delivery
Ceramic nanoparticles	Silica, alumina, titania	Drug targeting and biomolecules delivery
Polymeric micelles	Amphiphilic block co-polymers	Systemic and controlled delivery of water-insoluble drugs

Nanoparticles can easily cross any of the biological barriers in human body as their size falls in the nanometer range. A list of nanoparticles and their applications in medical therapeutics are given in Table 2.2. When compared with classical drug administrations, nanosystems provide more advantages with greater therapeutic effect. Nanotherapy has all the potential to deliver treatment for fatal diseases like human cancer, HIV-AIDS, etc., Nanoparticles act as vector in drug delivery systems. The drug can be directly attached (entrapped, coated, or functionalized) to the nanoparticles. After drug discovery, a large number of compounds failed to prove high solubility, stability and bioavailability and are dropped. Nanotechnology-based drug formulation could meet out all the requirements to sustain as a good drug agent [45]. Different nanoparticles such as micelles, liposomes, solid lipid nanoparticles, polymeric nanoparticles, pegylated nanostructures, nanocrystals, nanobodies, cyclodextrin, dendrimers, and metallic nanoparticles are used for drug delivery in medicine. By using these nanoparticles in drug delivery, a novel platform to deliver drug targeted to a specific tissue with a controlled release rate can be developed. Nanoparticles and liposomes (with or without pegylation), dendrimers and micelles are candidate carriers for tumor-specific drug delivery [46]. In medical therapeutics, nanoparticles are applied to surgical medicines, dentistry, gene therapy, stem cell therapy, tissue engineering and regeneration.

Nanosurgery is a new concept in surgical medicine. But, nanosurgery for human beings has rarely been achieved. There are some advents in eye surgery. Femtosecond laser pulses, emitted from lasers working in the near-infrared, based on multiphoton effects allowing both imaging and laser effects to be generated which are in the submicron range and which do not cause collateral damage are available [47]. Kohli et al. reported membrane surgery and nanosurgical cell isolation using high-intensity femtosecond laser pulses [48]. They demonstrated the applicability of using ultra short laser pulses for performing surgery on live mammalian cells [48]. In 2007, another study reported on corneal multiphoton microscopy and intratissue optical

nanosurgery by nanojoule femtosecond near-infrared pulsed lasers [49]. In this study, multiphoton microscopy including multiphoton autofluorescence imaging and second-harmonic generation was used as a new diagnostic tool to perform tissue nonlinear optical tomography with submicron resolution [49]. Nanoneurosurgery is another interesting emerging nanosurgery. In addition, nanocoated tools can also be useful for surgery and orthopaedics. Although bone is a very diverse tissue providing different functions within the body, recently identified nanobiomaterials shown promising solution to orthopaedic problems [50]. Chris Arts et al. reported the use of a bioresorbable nano-crystalline hydroxyapatite paste in acetabular bone impaction grafting [51]. In this work, destructive lever-out tests and in vivo animal tests were performed with various combinations of materials. Chris Arts et al. concluded that TCP-HA granules with a nano-crystalline hydroxyapatite paste could be a valuable addition when TCP-HA ceramic granules are being used for acetabular bone impaction grafting procedures [51].

Nanotechnology has a significant involvement in dentistry materials. He and Swain used a nano-based indentation system to determine the indentation stress-strain response of two kinds of dental ceramics, one kind of dental alloy and healthy enamel [52]. They reported that strong and tough materials with primarily elastic response, such as toughened ceramics, were required to enable dental crown/bridges to have long-term reliability [52]. In another study, Fu et al. studied effects of dental bleaching on micro- and nano- morphological alterations of the enamel surface [53]. The study concluded that the thickness of the enamel smear layer was significantly reduced due to the bleaching process [53]. Hairul Nizam et al. performed a nanoindentation study of human premolars subjected to bleaching agent [54]. According to their study, the exact mechanism by which hydrogen peroxide impacts the dentin and enamel had yet to be completely elucidated; however, it was observed to have an undermining effect on the nanomechanical properties of teeth [54]. Lee et al. reported the changes of optical properties of dental nano-filled resin composites after curing and thermocycling [33]. The objective of their study was to access the colour changes after curing, polishing, and thermocycling of a nano-filled resin composite. Lee et al. concluded that changes in colour and translucency after curing, polishing, and thermocycling varied by the shade group [33].

Gene therapy is the advanced therapeutic concept at present. It involves gene manipulation and transfer. Gene therapy implies local or systemic administration of a nucleic acid construct that can prevent, treat and even cure diseases by changing the expression of genes that are responsible for the pathological condition. This therapy is the hope for treating presently incurable diseases. Viruses are used in most of the clinical experiments today; however, they do have significant drawbacks. Therefore, non-viral vectors based on lipids, hydro-soluble polycations, other non-condensing polymers and nano or microparticles/capsules have been proposed [55]. Both biodegradable and non-biodegradable inorganic particles can be completely fabricated on the nanoscale with the attributes of binding DNA, internalizing across the plasma membrane and finally releasing it in the cytoplasm for final expression of protein [56]. In addition to the classical intravenous injection system,

polymer-based nanoparticle technologies for oral gene therapy is in continuous development [57]. Pan et al. revealed that polyamidoamine dendrimers-modified magnetic nanoparticles might be a good gene delivery system and have potential applied usages in cancer therapy, molecular imaging and diagnosis [58]. In another study, Yamada et al. noted that hepatitis B surface antigen-L (HBsAg-L) particles were able to deliver payloads with high specificity to human hepatocytes. The study indicated that the L particle was a suitable cell- and tissue-specific gene/medicine transfer vector [59].

Stem cell therapy and tissue engineering are few other advanced therapeutic concepts. Stem cell therapy is mainly applied for the treatment of congenital defects and malignancies, whereas tissue engineering is targeted at regenerative medicine. Murugan and Ramakrishna reported that electrospinning was a straightforward, cost-effective technique that could be applied to the fabrication of nano-featured scaffolds suitable for tissue engineering, and it offered usefulness over conventional scaffold methodologies [60]. Chen et al. performed a meta-analysis of applied usage of electrostatic spinning technology in nano-structured polymer scaffold [61]. The study concluded that the nano-structured polymer scaffold could support the cell adhesion, proliferation, site, and differentiation, and this kind of scaffold had a considerable value in the tissue engineering field [61]. In another study, Huang et al. reported their development of nano-sized hydroxyapatite-reinforced composites for tissue engineering scaffolds [62]. In a more recent study, Corradetti et al. illustrated the use of affinity targeted biodegradable nanoparticles to mediate paracrine stimulation as an alternate to withstand the growth and pluripotency of mouse embryonic stem cells [63]. This approach will extremely contribute to the scalable manufacture of stem cells and the clinical delivery of new advanced cellular therapies for regenerative medicine [63].

2.5 Conclusions and Future Outlook

Nanobiology signifies the merger of biological research with nanotechnologies and it is a multidisciplinary field where a wide range of applications such as using bionanomaterials in engineering or engineered nanomaterials in biology and medicine are studied with diverse viewpoints. It confers innumerable welfare measures on humanity like advancement in medicine, nanoparticle coated zidovudine as in AIDS therapy, treating tumour of precise points, storage of hydrogen fuel and drug delivery material. The use of nanomaterials in surgical medicine could help in the development of many nanosurgical tools and nanoprosthetic devices. The concept of nanosurgery is to minimize blood loss, inter- and post-operative complications and to decrease the period of hospitalization for the patient. The advances in nanobiology could help the researchers to create future “SMART MATERIALS” that play an important role in diagnostics and in efficient drug delivery. Nanotechnology will also help in the formation of brand new molecular systems which might perfectly

resemble existing living systems. Though nanobiology has several achievements and promises to add to its credit, it also requires our much appreciated patience. One should always realise that nanobiology can be a promising avenue by which medicine can advance, instead of expecting it to revolutionise medicine.

Moreover, researchers are also working to discover the potential long-term toxicity of nanoparticles, and their metabolic and degradative mechanisms. It is necessary to understand the fate of the drug once delivered to the nucleus and other sensitive organelles. In order to avoid public distrust and address the risks and potential hazards of emerging nanotechnologies: methods and tools should be developed to identify and characterize nanomaterials in biological matrices; international guidance should be developed on the effective exposure control; well-characterized stable benchmark and reference materials should be developed and used for toxicology studies; required data should be collected on human exposure, biomonitoring, and health outcomes that might be related to exposure; education and training should be given to researchers, manufacturers, and users of nanomaterials regarding the safe development and use of nanomaterials; existing regulations should be evaluated and new regulations should be developed if necessary; international guidance should be developed and shared on the best available practices for working with nanomaterials.

The in depth journey through nanobiology will lead one to end up in picobiology. Also, in nature there are many things exist below 1 nm level. Many single molecules are in the picolevel. In volume sense, many substances such as vitamins exist in the picolevel. The science focusing on objects that fall in the range of 1–100 pm is believed to be the next for nanoscience. But, the main question is when we can reach picotechnology.

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