Nano-regenerative medicine towards clinical outcome of stem cell and tissue engineering in humans

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Introduction

Nanotechnology and nanoengineering are the science and engineering involved in the design, synthesis, characterization, and application of materials and devices. Its smallest functional organization (in at least one dimension) on the nanometre scale ranges from a few to several hundred nanometres. The bulk of nanoengineered substrates are designed with very specific and controlled chemical and physical properties. It further results in strong control over the molecular synthesis and assembly designs. These materials and devices with a high degree of functional specificity interact with cells and tissues at a molecular (i.e. subcellular) level, thereby allowing a degree of integration of technology with medicine and physiology that was at all not previously attainable. The significance of nanoscience and latest nanotechnologies for human health and the associated opportunities, and developments is well addressed [1].

In all tissue types, a specific three-dimensional microenvironment surrounds every cell. This microenvironment comprises several other cells, extracellular matrix (ECM), proteins and a range of soluble as well as ECM-bound factors. The ECM is composed of a variety of molecules (ranging several hundred nanometres) that include collagens, glycoproteins, glycosaminoglycans and proteoglycans [2] and its primary function is to provide structural support to the composing cells. It also includes several distinctive constitutive structures in the basement membrane like pores, fibres and ridges of nanometre dimensions. The topographies present in the surrounding environ-

Abstract

Nanotechnology is a fast growing area of research that aims to create nanomaterials or nanostructures development in stem cell and tissue-based therapies. Concepts and discoveries from the fields of bio nano research provide exciting opportunities of using stem cells for regeneration of tissues and organs. The application of nanotechnology to stem-cell biology would be able to address the challenges of disease therapeutics. This review covers the potential of nanotechnology approaches towards regenerative medicine. Furthermore, it focuses on current aspects of stem- and tissue-cell engineering. The magnetic nanoparticles-based applications in stem-cell research open new frontiers in cell and tissue engineering.

Keywords: nanotechnology ● magnetic nanoparticles ● nanomaterials ● regenerative medicine ● stem cells ● tissue engineering

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ment of cell directly affect the cellular behaviour such as cell adhesion, migration, proliferation and differentiation. The fundamental understandings of biological and physical interactions of cells with their surrounding environment are the key to excel in the field of regenerative medicines [3]. Nanotechnological principles support the creation of these smart materials, but this approach is still much far from being achieved. A technique to replace/repair diseased tissue or organs by in vitro and in vivo pathways is regenerative medicine. These medicines have potential to restore the function of lost, damaged cells or ageing cells by replacing them with new ones in human body. Cells usually need some scaffold material for their proliferation. The surrounding environment is composed of nanometre-scaled particles that provide distinctive biological signals, which finally decide the reaction and behaviour of the cell [3]. Regeneration can be achieved with living cells, which are capable of division on some material that acts as scaffolds and must produce correct signals to get the desired cell behaviour. The commercialized relevance of nanotechnology is as effective as biological ones; in addition, it produces the supporting material for technological advancements.

Along with tissue engineering, nanotechnology provides the basic grounds for the development of regenerative medicines. Nanotechnological elements used for regenerative medicine include nanoparticles, nanofibres and nanodevices. Nanoparticles were used for specific and controlled delivery of growth factors, drugs and DNA molecules to the target site, whereas, nanofibres are used for preparing tissue scaffolds and for modifying the surface of implantable materials, nanodevices such as biosensors [3]. Embryonic, foetal, amniotic, umbilical cord and adult stem cells are capable of generating multiple therapeutically useful cell types. The generated cells are used for the treatment of various genetic and degenerative disorders such as age-related functional defects, osteoporosis, spine injuries, haematopoietic and immune system disorders, heart failures, chronic liver injuries, diabetes, arthritis, muscular, skin, lung, eye and digestive disorders, Parkinson’s and Alzheimer’s diseases, and aggressive and recurrent cancers [4]. Stem cells are the ideal raw materials for regenerative medicines, as these are capable of generating all types of cells, tissues, and shows unlimited growth morphology. These cells have revolutionized the field of regenerative medicine as well as cancer therapies. Main target of regenerative medicine is the in vivo regeneration. In few cases, in vitro regeneration has also been performed for some complex functional tissues. Both in vivo and in vitro regeneration strategies involve the use of porous scaffold on which stem cells are loaded. These scaffolds can be natural or may be synthesized manually. Depending upon the cells that need to be targeted, functionalization of scaffold is done accordingly with a variety of biological molecules. In addition to functionalization, entrapment of growth factors, drugs or genes, peptide sequences, such as arginine–glycine–aspartic acid or proteins in nanoparticles for continued release in controlled manner will boost the success rate of regeneration [5]. The in vitro tissue and cell regeneration is carried out in bioreactors under controlled conditions. In addition, for commercial large-scale industrial applications, these devices proved very beneficial, as these are integrated with a variety of BioMEMS (Micro electromechanical devices) for optimizing and controlling the specific operational conditions needed for tissue regeneration [5]. For real time monitoring and detection of specific cellular processes, several biosensors and laboratory-on-a-chip are integrated inside the bioreactors. The in vitro cell and tissue regeneration stem cells from the patients are first harvested, and then finally being seeded on the 3D scaffolds within a bioreactor. The hybrid construct in the form of tissue matrix is thus formed and implanted back into the patient’s body. Both harvesting and stem-cell expansion need great efficacy and efficiency for the regeneration operation to be successful. Major problems concerned with the in vitro regeneration include isolation of stem cells from the patient, proliferation of stem cells outside the body through in vitro systems, process of culturing stem cells in bioreactor and the time lapse during implanting the engineered hybrid construct in patient’s body [3]. Another strategy for tissue regeneration makes use of some intelligent materials capable of sending signals to the stem cells present inside the body. Stem cells receive the signal surrounding the damaged or diseased tissue of the body and then perceive the signals from these smart materials and trigger the regeneration process substantially. For the first time, In 1997, Whitman et al. [6] had initiated integrated platelet rich plasma (PRP) in fibrin glue. Further studies [7] reported that PRP was able to induce bone regeneration of the jaw. The study on regeneration confirms the fact that stem cells of bone marrow origin are responsible for repair of mesenchymal organs. Therefore, the stem cells with multipotent differentiating potential and biological products (PRP or its gel formulation Platelet Gel, PG) with stimulating proliferation efficiency aid in tissue repair and regenerative therapeutics. Addition of biomaterials acts as potential support in proper functioning of stem cells and PRP in repair particularly in bone repair system. A complex biological phenomenon of tissue repair is affected by several factors such as age, site depth of the lesion and co-morbidity. In the regeneration process, cells produce growth factors (GF), which crucially help in exchange of biochemical information to stimulate the regeneration process [8]. The combination of clinical applications employing cell infusions, PG or both, sometimes in combination with biomaterials, is now called regenerative medicine. It is currently applied to situations where no other therapy is available. The clinical application with the best results recorded as yet includes vascular surgery, maxillo-facial surgery, orthopaedic surgery and aesthetic medicine.

A meeting of traditional sciences such as chemistry, physics, materials science and biology together generates an emerging scientific discipline of nanotechnology. Figure 1 demonstrates schematic illustration of bio & nano technology in medical sciences. The present review explores the significance of nanoscience and latest nanotechnologies for regenerative medicinal therapeutics. Addressing the collective expertise, the review also suggests how to manage far-reaching developments in these novel technologies. The successful implementation of nano-regenerative medicine will definitely be a boon to the field of clinical therapeutics in future.

Stem-cell nano-engineering

A key challenge towards regenerative medicine and cell-based therapy is to expand and derive stem cells into a specific alignment by
Tissue engineering involves diverse physiological microenvironments. The review of synergetic effects will further help in designing experiments, and their standardization in a toolkit has been designed specifically for stem-cell biologists. The kit addresses investigative challenges, a micro- and nanotechnology-driven modern approach.

Pancreatic effects [21] recently introduced to examine more about the role of stem cells in biological sciences. The great challenge is to depict the mechanism of interaction, function and metabolism between stem-cell biology and biomaterial technology recapitulates the molecular events involved in the production, clearance and interaction of molecules involved in regeneration/replacements of tissues/organs for novel clinical therapeutics [23].

**Molecular imaging**

The genetically encoded fluorescent and bioluminescent tags offer surplus information towards the living body images at the molecular level to enhance our understanding of human biology. In addition to the progress that has so far been made with the molecular agents, SPECT/CT hybrid systems capture functional information on molecular and cellular levels. They often provide anatomical detail of a targeted molecular structure more quickly, efficiently and clearly than standard imaging devices. The resultant images help in multi-functional applications such as the rapid identification of tumours, analysis of appropriate treatment, delivery of targeted therapy to precisely destroy target cells, and follow-up to assess treatment effectiveness. The novel light-producing transgenic animal model (GFAP-luc) Xenon (Society for Molecular Imaging’s 3rd Annual Meeting) aids in tracking damage and repair in chronic neurological conditions such as post-ischaemic stroke or Parkinson’s disease. To analyse the functioning of heart muscles, clinicians usually recommend ultrasound-contrast imaging to assess the heart’s condition. SonolysisTM, are gas-filled microbubbles for novel therapeutic applications. The transient effect of microbubbles imaging discriminating it as one of the crucial sensitive and flexible method. It easily disrupts the pattern by adopting finer incident and reflective lights. One such example, Definity®, commonly known as Sonolysis™, are gas-filled microbubbles for novel therapeutic applications. An intravenous injection of microbubbles or local administration in vascular graft dissolves vascular thrombosis [24].

The targeted action of ultrasound is applied externally or internally (catheter) over the area of the blood clot to provide localized...
prognosis of the infected patient. The microbubbles act on the principle of micromechanical device to defuse the clot. For blood clot dissolution, ultrasound pulses and blows the bubbles in the field leading to sound diffusion. Sonolysis nanosurgery is one amongst the best locally targeted noninvasive therapy for treatment of vascular thrombosis. It affords potential merits over the alternative therapeutic approach of mechanical thrombectomy and is faster than the conventional drug therapy with less risk of bleeding for treating thrombosis effectively. A new radio diagnostic agent, NeutoSpec™, has eliminated the need for removal and re-injection of blood into the patients. It directly labels white blood cells and myeloid precursors in less time. NeutoSpec™ is available for more than 5-year-old patients with equivocal signs of appendicitis. In addition, NeutoSpec facilitates visualization of the gamma camera-generated images, thereby, allowing the physicians to locate the sites of infection [25]. It reduces the time delays and risks normally associated with alternative white blood cell labelling processes. A first class volumetric CT system, eXplore Locus Ultra, is capable of quantifying physiological measurements, elaborate anatomy of tissues, tumours and organ perfusion. The Locus Ultra also performs dynamic imaging by image acquisition within sub-seconds. For the coupled and functionalized approach of nanoparticles with biomolecules, an enhanced conjunctive methodology of molecular biology, bioorganic chemistry, bioinorganic chemistry and surface chemistry are required. Nanomaterials can be synthesized to desired sizes, shapes with controlled physicochemical properties [24, 25].

Nanomaterials for regenerative medicines

Nanoparticles

Nanoparticle synthesis for regenerative medicines mainly focuses on development of entrapment and delivery systems for genetic material, biomolecules (growth and differentiation factors), bone morphogenetic proteins and for reinforcing the bioactivity of 3D scaffolds for tissue engineering. Microspheres, microcapsules, liposomes, micelles and dendrimers are the nanoparticles mainly used in delivery systems. As per the requirements, solid, hollow or porous nanoparticles are synthesized through molecular self-assembly, nanomanipulation, bioaggregation and photochemical patterning [26, 27]. For stem-cell regeneration, disease therapeutics and targeted drug delivery, the biodegradable nanoparticle carries immense potential for future endeavour.

Magnetic nanomaterials: iron oxide NPs

Simple synthesis methods and universal availability make iron oxide like inorganic Nps as the most promising candidate for stem-cell research. Iron oxide Nps have the tendency to bind on either external cell membrane or pierces into the cytoplasm. Particles bound on the surface may interfere with cell-surface interactions or at times get detached from the membrane without affecting the motility of the cell [28]. However, iron oxide Nps inside the cytoplasm modify their surface to increase the uptake efficiency with very less deleterious effect [28]. Polymer coating like dextran enhances the stability and solubility of superparamagnetic iron oxide nps (SPIONs) and prevents it from forming aggregates [29, 30]. The polymer-coated SPIONs help in tracing stem/progenitor cells with MRI. Magnetic iron oxide nps and their composites are sensitive and are emerging tools for MRI as compared with the conventional gadolinium-based approach [31]. SPIONs are now frequently used as in vivo cellular-imaging agent. The Nps label stem cells through endocytosis or pinocytosis route [32–34]. Dextran-coated SPIONs reduce the labelling efficiency of stem cells and therefore are unfavourable for endocytosis. Moreover, iron oxide nps, when dissolved in cells, may lead to elevation of free hydroxyl radicals and reactive oxygen species. These may cause toxic effects such as increased apoptosis or alteration in cellular metabolism [33]. Dissolved Fe²⁺ ions released from the iron oxide Nps exhibit toxic effect on cells. To protect stem cells substantially from the toxic effect, the SPIONs were initiated with gold coating. Gold coating provides the inert shell around NPs and protects them from rapid dissolution within the cytoplasmic endosomes [36]. In addition, the gold-coated inert shell clarifies MRI contrast drastically. The convenient coupling surface chemistry of gold with thiol or amine moieties allows SPIONs to interact with biomolecules more easily [37]. The stem cell labelled with SPIONs can be detected with MRI even after implantation within the body. The magnetic sorting techniques thus allow quick and easier retrieval of stem cells from the spleen and bone marrow proficiently [38].

Magnetic NPs for in vivo stem-cell tracking

Tissue regeneration through transplanting progenitor/stem cells is an emerging era of therapeutic research. For in vivo cellular imaging, various techniques such as MRI, bioluminescence, positron emission tomography and multiple photon microscopy are widely used. Amongst all, MRI offers high resolution, speed, easy accessibility and 3D capabilities with additional information regarding the surrounding tissues [31, 39, 40]. In this regard, magnetic iron oxide Nps with controlled size offer great potential towards MRI applications. The nuclear spins couple to create a large magnetic domain in the magnetic nanocrystals. At certain circumstances of fluctuating temperature and variable crystal sizes, these particles randomly become locked in one direction, making the material wise ferromagnetic [41]. The SPIONs surface coated with dextran are now commercially available as Endorem (Geurbet, France) [42]. Transfection agents are usually required to facilitate cellular uptake, which may potentially damage the stem cells. Higher concentration of transfection agents causes toxicity, whilst lower concentration is not sufficient for cellular uptake [28]. Therefore, such agents can be reduced by employing SPIONs, which are widely tagged for labelling human MSCs (hMSCs) and ESCs (hESCs). The other dextran-coated SPIONs such as Feridex and Sinerem are now being combined with commercially available transfection agents such as, Fungene, Superfect, Lipofectamine [28,
Nanofibres successfully replace the natural extracellular matrix porous scaffold that supports the tissue regeneration. These can be for host-cell colonization. Nanofibres can be assembled to form porous biodegradable structures that provide a suitable environment for the entrapped molecules. The properties of polymers act as a key for fabricating nanoparticles. Some polymers are capable of ‘stimuli-response’, with change in temperature, pH or magnetic field, which further results in conformational changes such as swelling or shrinkage. Polyelectrolyte can act as efficient drug carriers because these undergo ionization due to pH changes in surrounding environment [44]. Solid nanoparticles having surface modifications also find applications in regenerative medicines. Bone regeneration and osteoblast adhesion are found to be enhanced with hydroxyapatite nanoparticles functionalized with specific biomolecules [45]. The multifunctional ability of nanocarriers makes them ideal vehicles for treating multi-drug resistance (MDR) cancer. The nanocarriers improve the therapeutic index of drugs by diverting the effects of ABC transporter-mediated drug efflux, which is the primary mechanism of MDR, thereby breaching towards therapies by overcoming drug resistance [46].

Nanoparticle scaffold

Scaffolds are the 3D constructions that are capable of mimicking the structure of the tissue that requires repair [47]. These scaffolds are porous biodegradable structures that provide a suitable environment for host-cell colonization. Nanofibres can be assembled to form porous scaffold that supports the tissue regeneration. These can be synthesized artificially or at times may be naturally synthesized. Nanofibres successfully replace the natural extracellular matrix because of large surface area and aids in cell colonization as well as in efficient exchange of nutrients and metabolic waste between scaffold and its environment. In a recent breakthrough of bone marrow modelling, a spatial distribution of the different cells with 3D scaffold culture system resulted in better structural organization as compared with 2D culture systems [48]. Nanomaterial shows a new hope and avenue towards controlled drug release properties. Organ decellularization for bioscaffolds fabrication is a novel concept of future research. In addition, the electrophysiological properties of bioartificial myocardium, along with its associative multi-electrode network, could provide electrical stimulation for the improved coupling of grafted cells and scaffolds with host cardiomyocytes for the treatment of myocardial diseases [21].

Nanocarriers

Controlled delivery of biomolecules is the critical point of concern in the support and enhancement of tissue growth during regeneration. Nanoscale carriers are capable of reaching the targets, which are otherwise inaccessible, like blood-brain barrier, tight junctions and capillaries. Nanocarriers are generated through a combination of various polymers (polyactic acid, polyglycolic acid, polyethylene glycol) with hydrogels. These nanocarriers possess different release properties for the entrapped molecules. The properties of polymers act as a key for fabricating nanoparticles. Some polymers are capable of ‘stimuli-response’, with change in temperature, pH or magnetic field, which further results in conformational changes such as swelling or shrinkage. Polyelectrolyte can act as efficient drug carriers because these undergo ionization due to pH changes in surrounding environment [44]. Solid nanoparticles having surface modifications also find applications in regenerative medicines. Bone regeneration and osteoblast adhesion are found to be enhanced with hydroxyapatite nanoparticles functionalized with specific biomolecules [45]. The multifunctional ability of nanocarriers makes them ideal vehicles for treating multi-drug resistance (MDR) cancer. The nanocarriers improve the therapeutic index of drugs by diverting the effects of ABC transporter-mediated drug efflux, which is the primary mechanism of MDR, thereby breaching towards therapies by overcoming drug resistance [46].
surfaces, leading to accelerated calcium deposition and improvement in integration with surrounding bones as compared with core conventional titanium surfaces [56–59]. In another application of regenerative medicine which includes cartilage, nano-structured polyalactic-co-glycolic acid (PLGA) surface induction has been shown to stimulate chondrocyte adhesion and proliferation, as well as extracellular matrix production tremendously [60–62]. In addition, vascular graft (PLGA) and stent titanium surfaces with nanometre surface roughness values drastically improve inner endothelial vessel cell functions as compared with naked nanosmooth polymer and titanium surfaces [63–67].

Furthermore, with conventional biomaterials, various intrinsic nano-sized materials such as hydrophobic carbon nanotubes [68–72] and hydrophilic helical rosette nanotubes [72, 73] are still under keen investigation in regenerative medicine. These novel carbon-based nanomaterials speculate vigorous cellular interactions over currently implanted materials.

Contemporary strategies for the development of novel biomaterials in medicine can be grouped into two chief categories. The first strategy is all the way through altered chemistry; for example, titanium use is much better as compared with stainless steel for orthopaedic applications or using controlled drug release to form implant surfaces [74–77]. The second strategy takes up amendment in the physical implant properties like surface roughness for generating nanometer surface features. For these reasons, selectively chosen biomaterials can be tailored to stimulate favourable cellular interactions by varying both chemical and physical factors. This review also discusses the importance of nanotechnology in active and passive implants of tissue engineering.

Passive implants and tissue engineering

The life span of passive implantation such as artificial joints, artificial hips, finishes normally after ~15 years leading to wear or implant loosening and therefore further surgeries are required to re-cope with the common human life [78]. Nanotechnologies could help reduce such kind of problems. To reduce these problems, a thin layer coating of a nanocrystalline structure over the implants made of titanium, cobalt or chromium alloys can be provided to make it harder, smoother, and consequently, more resistant to wear. This results in less wear of the polyethylene artificial socket. Moreover, the coated over-layer ensures better biocompatibility of the implant. The other suitable coating materials include diamond, metal ceramic and hydroxyapatite [79]. A natural component of the bone hydroxyapatite constitutes 70% of the mineral component, with the remaining 30% constituent of organic collagen fibres. New coating production methods in implants have now provided to make it harder, smoother, and consequently, more resistant to wear. This results in less wear of the polyethylene artificial socket. Moreover, the coated over-layer ensures better biocompatibility of the implant. The other suitable coating materials include diamond, metal ceramic and hydroxyapatite [79]. A natural component of the bone hydroxyapatite constitutes 70% of the mineral component, with the remaining 30% constituent of organic collagen fibres. New coating production methods in implants have now been shown to stimulate chondrocyte adhesion and proliferation, as well as extracellular matrix production tremendously [60–62]. In addition, vascular graft (PLGA) and stent titanium surfaces with nanometre surface roughness values drastically improve inner endothelial vessel cell functions as compared with naked nanosmooth polymer and titanium surfaces [63–67].

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extracellular matrix is pathologically and deeply altered. Therefore, an associative procedure for regenerating both myocardial cells and the extracellular matrix is a mandatory condition for the cure. The improved efficiency of cellular cardiomyoplasty via tissue engineering is a feasible and safe approach reported for intra infarct cell therapy associated with a cell-seeded collagen scaffold grafted onto infarcted ventricles [95]. A new method of tissue engineering was proposed to improve the contractile function of engineered cardiac tissue cardiomyocyte viability, differentiation and their surrounding three-dimensional collagen environment. A novel in vitro method that couples arginine–glycine–aspartic acid–serine (RGD+) peptides on cross-linking with a collagen matrix drastically improves the performance of collagen-cell scaffolds. This newly designed scaffold might also serve as a potential platform for improving/engineering cellular transplantation in a true myocardium [96]. Towards this investigative challenge, a biodegradable tri-dimensional matrix seeded with cells and grafted onto the infarcted ventricle is currently under research [21, 97].

**Active implants and tissue engineering**

An active implant has a rich and chief source of energy. Based on their functional role, active implants are categorized into two groups. The first group with long life span contains administering medicines, which include insulin, and morphine pumps. Recent research is underway for the long-term storage and controlled release of active substances on implantable microchips [98, 99]. The potential merit of administering medicine is their target and controlled drug delivery; it goes directly to the location where they are needed at varying rates. The controlled release could also be detected by a biosensor that responds to variable physiological parameters [100]. The second group neural prostheses aid in repair or take over nerve functional responses. They are potentially used to bridge damaged nerve paths, induce muscular impulses and at times employed to replace senses. This group includes cochlear implants (for restoring hearing), pacemakers and defibrillators (for regulating the heart beat), bladder stimulators (for controlled emptying of the urinary bladder by spinal cord lesion patients), deep-brain stimulators (to combat tremor in patients with Parkinson’s disease), as well as peroneus stimulators (to combat drop foot)-based responses.

For some years now, to enable thought-oriented devices, various research groups in the United States have also been working on neuroprostheses [101–106]. For instance, electrode-adhered microchips are fitted to the motor cerebral cortex, which record the electric signals associated with the thoughts commonly referred to as brain-machine interfaces. A major success has been achieved in enabling rats to operate handles by ‘brain power’ and in monkeys to operate the cursor of a computer or a robot arm by their thoughts [103, 104]. A few years ago, an electrode has been implanted in the cerebral cortex to enable the patient to operate a computer device in an amyotrophic lateral sclerosis patient [107]. According to the findings presented at the annual meeting of the American Academy of Physical Medicine and Rehabilitation, in Phoenix in October 2004 [108], a neuroprosthesis has been fitted to a paralyzed man. It enables him to operate the cursor of a computer device by thought, play video games, operate a light switch, and select a television channel. The ultimate goal, which is still far-off and under research, is to enable patients to operate arm, leg prostheses, and controlled restoration of their paralyzed limbs [102, 105].

**Conclusion**

Nanobiological research is a speculation area of interest in many countries and its relevance within physical sciences, molecular engineering, biology, biotechnology, and medicine is expected to increase in the future. In recent years, studies of interaction between nanomaterials, nanostructures and stem-cell nanotechnology has emerged as a new exciting field. The theoretical and experimental potential of nanotechnology to the fundamental developments in regenerative medicines for treatment of injuries and degenerative diseases has been widely speculated. In particular, a new interdisciplinary frontier in regeneration medicine is the effect of nanoparticles in molecular imaging. Nanomaterials such as fluorescent magnetic nanoparticles have been used for molecular imaging, scaffolds for tissue engineering, and designed nanostructures have been used in stem-cell treatments and tissue implants. The multidisciplinary applications of nanotechnologies for discovering new molecules and tailoring those could be incredible in its potential to improve human health. In the future, we could envision a world where nanodevices would be routinely getting implantation to participate in the repair of cells that deviate from the normal routine of mechanism. The successful development and implementation of nanotechnology with regenerative medicine foster a global perspective on research and bring together the spin-off benefits to human diseases in general. This broad sweep of knowledge traditional sciences like chemistry, physics, biology and materials science aids to bring together the required collective knowledge and expertise for the development of these novel nano-technologies. Current trends in nanotechnology have evolved hopeful revolution in medicine to increase the quality of human life, and to increase the initial formation of tissue necessary to prolong implant lifetime. Incorporating tissue cell–biomaterial interactions and cell-nanotopography interactions at the nanoscale and develop methods to create unique nanoscale surface features applicable to numerous medical fields is a major clinical goal of nanomedicine. Thus, it has become evident that nanotechnology will become a critical tool in the fight to resolve eventual medical issues. Other critical future challenge includes catalysing the development of biologically inspired nano biomaterials whose functions can stimulate the capabilities of natural organs and tissues.

**Conflict of interest**

The authors declare that they have no conflict of interest.
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