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Review Article

CURRENT STATUS AND FUTURE PROSPECTS OF APPLICATION OF NANOTECHNOLOGY IN STEM CELL RESEARCH: A REVIEW

GADE, N. E.?, DAR, R. M. AND MISHRA, O. P.

Department of Veterinary Physiology and Biochemistry, College of Veterinary Science and Animal Husbandry, Anjora, Durg 491 001 (Chhattisgarh). E. mail: nitingadeivri@gmail.com,

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Abstract: Current era of biological research is fascinated with novel tools like nanotechniques that have immense scope in various fields and huge potential applications. Stem cells are employed in regenerative therapies and further their appliance can be potentiated by use of modern techniques. In synergistic approach nanoparticles along with stem cells can improve their quality and utility in regenerative medicine. This review focuses on present use of nanoparticles in stem cell research and its prospects in near future.

Key words: Stem cell, Nanotechnology

INTRODUCTION

Concept of nano size was first revealed by Nobel laureate physicist, Richard Feynman though the term nanotechnology was coined later in 1974 by Norio Taniguchi. It deals with materials having size range from 1-100 nm and this nanoscale imparts numerous distinctive characters to these nanoparticles. They have high surface to volume ratio, surface adoptability, better solubility, high electrical and heat conductivity, and improved surface catalytic activity as compared to its parent molecule [1]. Moreover, it also have four unique features that is surface effects, quantum size effects, small size effects, and tunnel effects [2,3]. Nanotechnology has wide-ranging applications which give noteworthy impact on nearly all fields. It offers better constructed, enduring, cleaner, safer, and improved products for household, communications, medicine, transportation, agriculture and different industries. Wide notable arena includes chemistry, material science, biology, medical science, fuel industry, fabrics, electronics, food, space etc.

Emergence of nanotechnology has prominent prospects in biology as well as medicine; many researchers believe that nanomaterials may give solutions to major problems of biological sciences. Nanotechnology will provide wide range of new diagnostic and therapeutic opportunities such as imaging, diagnosis, drug delivery, disease detection and management [4]. In recent years, great progress has been made using nanomaterials for numerous applications in stem cell research [5]. In present review we will focus on existing status of applications of nanotechnology in stem cell research and their future prospective.

Stem cells have the capacity to renew themselves and differentiate into multiple cell types [6]. In mammals, stem cells are broadly classified as embryonic stem cells and adult stem cells. Embryonic stem cells are isolated from the inner cell mass of blastocysts [7] and adult stem cells are found in various body tissues such as bone marrow [8] , adipose tissue [9], umbilical cord blood [10], amniotic fuid [11], placenta, Wharton's jelly [12], dental pulp, tendons, synovial membrane and skeletal muscle [13]. Adult stem cells are further classified as hemopoeitic stem cells, mesenchymal stem cells, neural stem cells, skin stem cells, retinal stem cells etc.

In biological sciences, nanotechnology and stem cell research are now-a-days considered as promising research areas. Recently, stem cell nanotechnology research has emerged as a new exciting field, where focus is on application of nanotechnology in stem cell biology. The major challenges in stem cell research are the rapid, easy and efficient method for stem cell isolation, their long term maintenance and differentiation into specific cell lineages, suitable mimicking of microenvironment of stem cells *in vitro* condition, the development of novel regenerative therapies for chronic, debilitating and various unresponsive clinical diseases and disorders of animals as well as humans and understanding the stem cell functions [14]. These challenges can be tackled with the assistance of nanotechnology in better way. The applications of nanotechnology in stem cell research include Stem cell isolation and sorting with the help of magnetic and fluorescent nanoparticles [15]. Modification of *in vitro* microenvironment or three dimensional (3D) niches, which has a prominent role in the long term maintenance and differentiation of the stem cells into specific cell lineages [16]. Stem cell/tissue engineering to design scaffolds for organ / tissue regeneration [17]. Stem cell tracking and imaging will help to study the *in vivo* functions and application of stem cells in cell based regenerative therapy [18]. Stem cell transfection [19] with high efficiency and low cytotoxicity as well as use of molecular detection and biosensors to detect particular molecules in the stem cell pathway [20].

Stem cell isolation and sorting: Present scenario depicts that stem cells are omnipresent and their isolation is reported from different body tissues. Easy, rapid and low cost isolation is predominantly important in stem cell research moreover traditional methods have their own lacunae. Nanoparticles can be employed in the isolation and sorting of cells from mixture of multiple cell types [15]. Magnetic nanoparticle labeled stem cells were isolated by flow cytometry or magnetic force in cost effective, fast, and easier manner [21]. Functionalized magnetic nanoparticles and flurophores can be employed for stem cell isolation and expansion, stem cell sorting and separation.

Stem Cell Tracking and Imaging: Outcome of stem cells therapeutics validates only after tracking the status of cells after transplantation and their real time imaging during healing and repair process. Stem cells can be tracked *in vivo* with various dyes however efficient labeling without side effects to stem cells is pre-requisite for selection of tracking dye. Nanoparticles offer great potential in area of tracking and imaging stem cells there are many reports on variety of nanoparticles [22].

Lei and co-workers [23] reported efficient entry of peptide conjugated quantum dots in mesenchymal stem cells and labeled stem cells were tracked to study their tissue distribution in nude mice. Quantum dots conjugated with anti-mortalin antibody can be internalized by MSCs and labeled MSCs maintain their mutilineage differentiation potential thus can be applied for *in vivo* tracking and imaging in mice [24]. Similarly another group reported that MSCs were efficiently labeled with non-toxic superparamagnetic iron oxide nanoparticles conjugated with protein transduction domain [25].

Molecular Detection and Biosensors: Stem cell development and differentiation involves numerous intracellular and extracellular molecules. Self-renewal pathways of stem cells and their differentiation potential can be elucidated by identifying and studying such molecules and their functions. Nanoparticles in form of carbon nanotubes, nanorods, nanospheres, nanowires can serve as novel tool for molecular detection in stem cell research. Gold nanopartciles-based surface-enhanced Raman scattering (SERS) was used for probing the differentiation of mouse embryonic stem cells [26]. Hwang and coworkers [20] monitored the mechanism of neuronal differentiation *in vivo*. Neuronal micro-RNA was sensed by quencher-based fluorescent beacon system to evaluate differentiation. Some researchers also developed nanosesors and studied the impact of internalization on mesenchymal stem cell culture [27].

Stem cell microenvironment: Maintenance of stem cell linefor long time and their multi-lineage differentiation potential are governed by the unique local microenvironment known as stem cell niche [28]. Stem cell microenvironment collectively comprises of secreted factors, stem cell interactions, extracellular matrix and mechanical properties [29]. Crucial challenge in stem cell microenvironment research is to develop an *in vitro* system that accurately recapitulates functions of the *in vivo* microenvironment [16]. Nanotechnology can be utilized to create *in vivo* like stem cell microenvironment and to determine mechanisms underlying the conversion of an undifferentiated cells into different cell types. Nanoparticles can be applied for controlled release of growth factors and biochemicals for more precise understanding of growth, self-renewal and differentiation. Micro/ nanopatterned surface can be used to study stem cell response to topography. Recent studies reported the effect of microgrooved topographies on alignment [30], morphology [31] and differentiation of stem cells [30,32]. Cell adhesion [33] and proliferation [34] is affected by microstructures.

Tissue Engineering: Enormous diseases and disorders can be treated with inventions in tissue engineering and uses of nanoparticles enhance the applications of tissue engineering in therapeutics. The novel nanomaterials are constructed in such a fashion that stem cells can be directed to grow and differentiate. Three-dimensional nanofiber moulds simulates extracellular matrix to grow stem cells in vitro. The nanopatterning of tissue constructs will also help in directed differentiation of stem cells into specific cell lineages. Recent reports indicate use of nanofibers for nerve, bone and vascular tissue regeneration [35].

In biological sciences, tissue engineering provides conduit for *in vitro* growth and development of cells with various growth factors [36]. Nanostructures and multi-dimesional constructs may be engineered to grow and differentiate stem cells. Such creation of microenvironment confers better in vitro culture conditions that mimics in vivo environment. 3-Dimenional scaffolds supports growth and allows proliferation and differentiation of stem cells. Development of nanomaterials scaffold will play crucial role in stem cell biology.

Stem cell transfection: Implication of transfection technique for genetic manipulation of stem cells, to study various gene functions, to control of stem cell differentiation, for cellular labeling and purification. Efficient stem cell transfection is the key for achieving the complete potential of stem cells [19]. Intracellular delivery is prerequisite for all these applications in stem cells and key challenge in transfection is to deliver genes to stem cells with high efficiency and low cytotoxicity. Traditional techniques of electroporation and nucleofection have high delivery efficiency but results in severe damage to stem cells [37]. Viral vectors can successfully transfect and manipulate cell differentiation but chances of mutagenesis, immunogenicity and the risk of toxicity is critical shortcomings [38]. So nanoparticles can be seen as most promising way for proficient transfection of stem cells.

CONCLUSIONS

Nanotechnology and its applications in various fields have enormous potential however still much research needs for unrevealing applicability of nanoscience. Currently, nanomaterials are used in engineering, electronics, material science, biomedical science, fuel industry, fabrics, electronics, food, space etc. Biomedical science have wide arena of problems that can be tackled using these multifunctional nanoparticles. Stem cell research more precisely can conquer novel avenues in concurrence with nanoscience. Stem cell isolation, labeling and tracking can become easier with application of nanotechnology. Stem cell differentiation, delivery, and engraftment for regenerative cell-based therapies is better with nanostructures that can mimic the natural environment of cells. Nanoparticles also provides good substitute for available molecular detectors and biosensors.

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