Al-Salam Journal for Medical Science
Journal Homepage: http://journal.alsalam.edu.iq/index.php/ajbms
E-ISSN: 2959-5398, P-ISSN: 2958-0870

Nanotechnology in Molecular Genetics: A literature review

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DOI: https://doi.org/10.55145/ajbms.2025.04.02.004
Received March 2025; Accepted July 2025; Available online August 2025

ABSTRACT: Nanotechnology extends the limits of molecular diagnostics to the nanoscale. This study describes some of the details of how the body interacts with nanoparticles. Biological tests measuring the presence or activity of selected substances become quicker, more sensitive, and more flexible when certain nanoscale particles are put to work as tags. Particular emphasis is placed on the effects of surface changes on body-borne particles, their transport within the body, and the dose-response effect. Other considerations include the definition of "persistent" in the context of therapy, FDA scientific committees, and the need for nanoparticle tracking. In short, there have been dramatic changes in molecular and genetic research findings, as well as in diagnostics and therapy using nanotechnology. Numerous ethical challenges and concerns, including biocompatibility, biodistribution, and long-term toxicity, among others, accompany this. A careful and critical consideration of these challenges and concerns will lead to the improvement and design of "best-fit" nanomaterials for molecular genetics and the treatment of genetic disorders.

Keywords: NP, NM, Nanoparticles, Nanomaterials

1. INTRODUCTION

Nanotechnology can be considered a bridge between two important fields: molecular genetics and biotechnology. To understand nanotechnology in the context of molecular genetics, one must have an overview of both fields [1]. Molecular genetics is a branch of biology that studies genes as carriers of genetic material. It was the molecular geneticist George Beadle who showed in 1941 that a gene is related to a particular protein. Watson and Crick were the first to propose that the structure of DNA is a double helix [2]. The molecular genetics revolution began in 1953, when the double helix of DNA was described. Then, the great revolution in molecular genetics began with the development of combined procedures between molecular cloning and recombinant DNA technology [3]. The term nanotechnology was first mentioned in a book that discussed the coming era of nanotechnology. It can be described as a technology that can be developed between materials and devices with a length of about 1-100 nanometers. It possesses unprecedented manipulation power over nanomaterials and has an amazing potential, enabling the design of new materials that can be processed and engineered for research and gene therapy [4].

This article aims to provide basic knowledge of nanotechnology of importance in molecular genetics and the treatment of genetic diseases.

2. PREVIOUS MOLECULAR NANOSCIENCE WORK

Research and development in nanotechnology, despite being a correction to existing technologies, is one of the most exciting areas of biotechnology and materials science in recent years [5]. One of the major medical applications is the use of nanoparticles as highly sensitive imaging agents, which enable clinicians to detect low-density genetic diseases in human subjects through minimally invasive techniques. However, a fundamental understanding of the control of dynamic biological processes at the subcellular level is essential for developing personalized therapeutic and diagnostic interventions [6]. This ushered in a new of study into the structure of nucleic acid molecules, the creation of new analytical instruments, and DNA-based investigations that have resulted in the description of synthetic cells or organelles and the building of nanoscale technologies, These nanomachines and nanoobjects may soon be used in real-world applications, the diagnostics and research areas of medicine [7]. Single-cell analysis has also revealed vital

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signaling pathways and intracellular biological components with key biological functions. Currently, efforts are being made to explore new technologies using various nano-carriers to enhance gene therapy, including polyethylene imine, chitosan, cation-based transduction reagents, liposomes, dendrimers, and inorganic-based nanoparticles [8]. The intersection of biotechnology and nanotechnology is a revolutionary area of scientific research, especially in the field of human health. Biotechnology and nanotechnology, which manipulate materials at the nanoscale, work together to transform treatments, diagnostics, and healthcare. Targeted drug delivery methods, like liposomal formulations, minimize overall side effects, and specially designed nanomaterials work with biological systems at the cellular and molecular levels [9]. The use of nanotechnology in plant biotechnology under controlled conditions has facilitated the understanding of important internal mechanisms of the plant biological system. The application of nanoparticles (NPs) in plant biotechnology has impact on in vitro plant growth and development. It has been concluded that more research is needed to understand the mechanism of nanoparticle delivery and translocation in plants to avoid any future hazardous effects of nanomaterials [10]. To improve the use of genetic engineering and nanotechnology, previous research has examined the CRISPR/Cas9 system to cut a specific region of the short arm of chromosome 21 (Chr21) and replace it with a specially designed new DNA construct containing the essential chromatin remodeling genes to inactivate an extra Chr21 chromosome. This requires mimicking the natural cytological pattern of inactivation of the extra X chromosome in females. Down syndrome (DS) is one of the most common genetic disorders in humans. Through a controlled dose of a suitable nanocarrier (poly-D,L-lactide-co-glycolide (PLGA) surface designed to integrate the relevant construct into Down syndrome brain cell culture media and then into a mouse model of Down syndrome, this has provided new insights into modifying Down syndrome [11].The development of DNA nanocarriers for intelligent drug delivery offers significant advantages over traditional treatments, such as immunotherapy, gene therapy, and chemotherapy. There is also discussion of the potential and difficulties in biomedicine based on DNA nanostructures, as shown in Figure 1 [12].

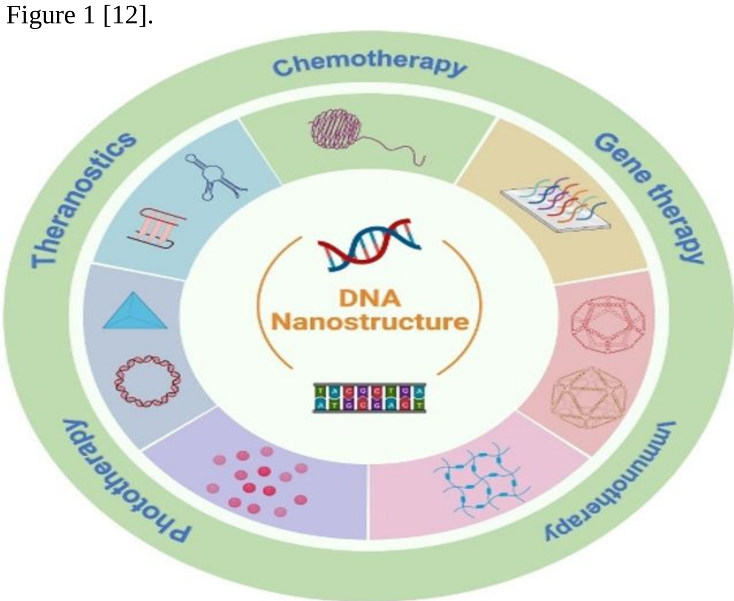

FIGURE 1. - Demonstrates the potential of DNA nanocarriers to deliver drugs intelligently compared to conventional therapeutics [12]

3. BASIC CONCEPTS IN NANOTECHNOLOGY

There is a significant difference between the physical and chemical properties of materials as the characteristic dimension crosses the bonding between molecules. A 3D set of atoms that has depth at the atomic or molecular level, has side dimensions between 1 and 100 nanometers, and has properties governed by size and other features that are inconsistent with their bulk components, is called a nanostructure [13]. Disease investigation, treatment, cell staining, and disease tracking are some of the areas where the application of biological and biocompatible nanomaterials is important from a technical and scientific point of view. They are used to study the fundamental behavior of biological systems and develop strategies for treatment [14]. In biomedicine, many nanomaterials are used due to their small size or large surface area and functionality, which improves their effectiveness and efficiency compared to drugs in solution. They are constructed from organic and inorganic components and are made using several procedures. The purpose of nanocomposites is to produce a material from more than one phase that has many properties. Although this type of design is impossible for more than a few microns, many of the dimensions of the external polysaccharide in the nanocomposite as shown in Figure 2 [15].

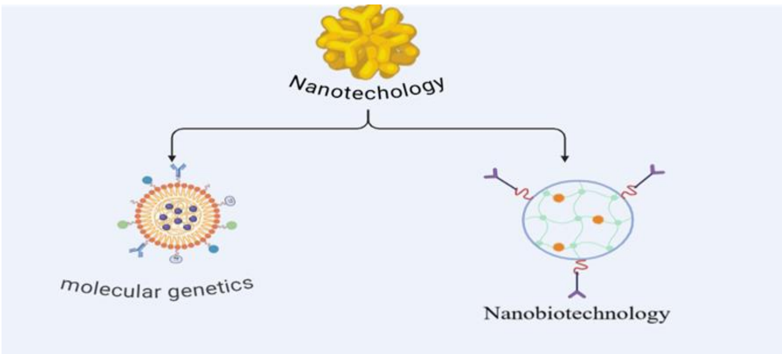

FIGURE 2. -The interface of bio-nanotechnology and molecular biology [15]

3.1 NANOPARTICLES AND NANOMATERIALS

Nanoparticles (NPs) by definition are discrete nanoscale entities composed of components in the crystalline or amorphous state and have typical dimensions ranging from 2 to 100 nm. Nanomaterials (NMs) are their extensions, reaching the sub-micron range [16]. Nanomaterials can be classified based on size and composition. Based on size, they are further classified as quantum dots, nanotubes, nanocrystals, and nanowires. The particle sizes typically range from ~2 to ~10 nm in the first two groups, while the diameters of nanotubes or nanowires range from ~100 to 1000 nm. The last category of particles having one of the three dimensions is included in the nano world since the true functionality is acquired when the given dimension is in the range of 1-1000 nm [17]. Considering one dimension in the micron range and the rest outside this range we may find a subdivision into nanorods, nanobelts and nanotetrapods and the functionalities in the two nanoscales only which are strongly perceived tend not to be classified in the nanoscale limit and can be interpreted for simplicity and classified as primary nanoparticles in the first place [18]. Nanomaterials consisting of a series of nanocomponents that are inside the outer micromatter can be produced as nanocomposites in hierarchical synthesis at the molecular level: (a) multimetallic nanoparticles, (b) tri-metallic core/shell nanoparticles, (c) tri-metallic core/shell nanoparticles, (d) alloy core/shell nanoparticles, and (e) at least, as bimetallic metal clusters, alloys and compounds on supports in the form of nanocatalysts [19]. These aspects of the dominant nanoscale size in nature make it necessary to introduce another scientific and industrial field beyond nanoparticle science: research, development, production, and applications of nanotechnology-based products. Nanoparticles. It has been proven after decades of investigations that there are two completely different types of physical behavior encountered at the nanoscale compared to both bulk matter at the microscopic scale and molecular compounds [20]. Nanomaterials are among the most advanced materials in current technology. The nature, composition, and classification of nanomaterials or nanoparticles are critical to their practical applications. Figure3 describes the classification and types of nanomaterials based on their composition [21].

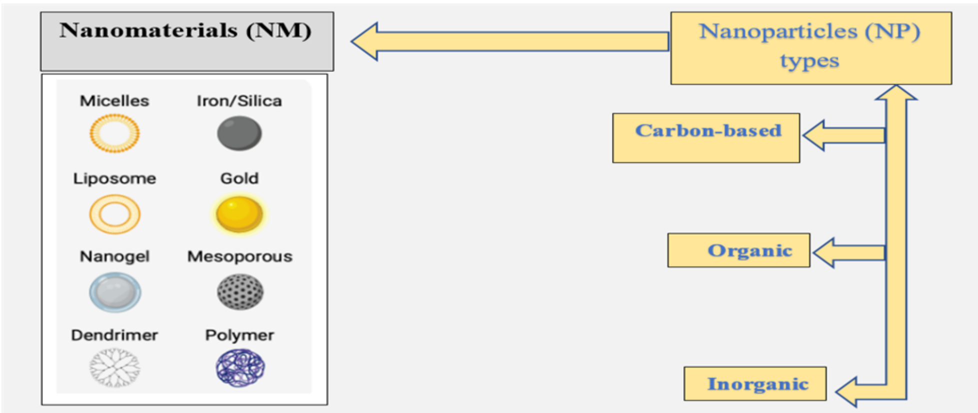

FIGURE 3. -Nanomaterial Classification and Nanoparticle Types [21]

3.2 NANOFABRICATION TECHNIQUES

The ability to fabricate nanostructures at the molecular level with precise control is crucial for creating tools and devices that help manipulate materials such as genetic materials [22]. Several techniques have been developed for this purpose, which can be classified into two categories. Lithography is able to pattern nanostructures directly onto a substrate and is classified as a top-down technique. Alternatively, self-assembly methods enable materials to spontaneously arrange themselves into nanostructures and are classified as bottom-up [23]. Lithography and top-down methods provide exceptional control over spatial position and are capable of creating multiple copies of nanostructures with high reproducibility [24]. In contrast, self-assembly is generally more suitable for creating monodisperse structures and is typically faster and less expensive to generate prototypes. Chemical vapor deposition has recently attracted a great deal of interest due to its ability to produce high-quality nanowires and its increasing number of potential applications. It is important to study the engineering of these processes to translate these developments into practical devices and applications. One of the major challenges of many of the self-assembly techniques described here is the ability to scale up the techniques to produce microscopic assemblies or devices with the same structural nanocontrol that has been demonstrated at a smaller scale [25].

4. APPLICATIONS OF NANOTECHNOLOGY IN MOLECULAR GENETICS

Its basic approach and resulting products are of a type that will soon become the natural offspring of contemporary biotechnology and, in some ways, its radical application. Nanotechnology is often used as a scientific term for the molecular engineering of matter, and its basic principles are of great importance in molecular genetics [26]. Molecular biology is the study and understanding of the blueprint of life that is passed down through generations; nanotechnology is the application, modification, and development of new applications of this blueprint in our daily lives and human medical treatments [27]. This level of manipulation has begun in the development of various molecular tools, such as probes to monitor and modify cellular processes in living systems. Advances in nanotechnology enable new diagnostic tests that are better able to detect mutations in their structure and the mRNA associated with gene expression [20]. Another development that could soon be in the practical use of DNA chips is the ability to exploit stem cell banks where there may be hundreds of different types of suspected pathogens, creating populations or selective individuals based on personal genetic differences [28]. The best solution for diseases caused by pathologically overexpressed gene mutations is to identify all cells of a major organ. Several cell surface glycoproteins have been identified for which appropriate drugs can be administered. With the increasing availability of nucleotide sequence data, in vivo gene therapy and thus regulatory elements are key to the use of nanotechnology in regenerative medicine [29]. In addition, with an increasing number of estrogen receptors bound to DNA in some cancer cells, this ligand-binding hormone and the toxin-transporting oncogenes that digest ribosomal RNA complexes will locate the cancer cell. In addition, the scenario in which human touch will be used to evaluate as a sensor for the presence of specific genes in vaginally deposited sperm is anticipated based on nanotechnologies [30]. Exploiting the engineering aspect of nanotechnology has led to developments in medical intervention strategies that leverage molecular biology knowledge and combine it with nanotechnology tools to achieve outcomes, as illustrated in Figure 4 [31].

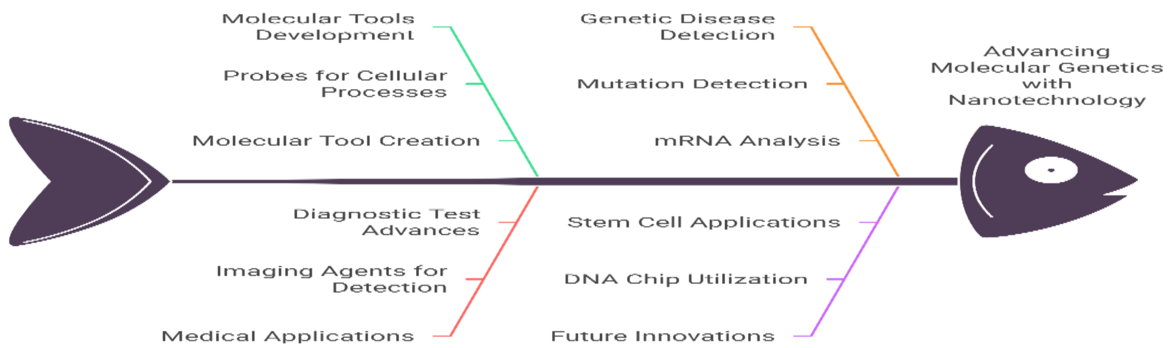

FIGURE 4. - Exploring Nanotechnology's Impact on Molecular Genetic [31].

4.1 GENE DELIVERY SYSTEMS

An important requirement in gene therapy is an efficient gene delivery system [32]. The studies of molecular genetics aim to exploit gene therapy as a potential treatment for many genetic abnormalities or malignant conditions. Nanotechnology-based gene delivery tools can improve the delivery and stability of genetic materials to target sites. Gene delivery systems can be used to deliver the target gene of genetic materials, such as mRNA, pDNA, siRNA, miRNA, and other nucleic acids [33]. Nano carriers, such as liposomes, dendrimers, Nano capsules, micelles, emulsions, inorganic nnoparticles, and cationic/thiolate Nano complexes of chitosan, DNA polyp lexes, polypsidorotoxanes and organic-inorganic hybrid nanoparticles increase the bioavailability of genetic materials by inhibiting nucleolytic degradation or accelerating their uptake into healthy or malignant cells Liposomes or protein carriers used in non-viral gene therapy are capable of carrying DNA to specific cells and sites, and the improvement in DNA delivery using DNA-peptide dendritic array demonstrates gene silencing activity [34]. A framework for nanotechnology to enhance gene delivery purposes can be obtained by modifying reliable physicochemical procedures by obtaining Nano carriers designed to protect their payload from inappropriate release by physiological enzymes during systemic circulation or while being trapped within packaging materials [35]. Current clinical trials used for siRNA-based gene therapies are in phase 1, while mRNA-based gene therapies are in phase 3. In vivo gene delivery through Nano carriers involves several parameters such as cellular uptake, mRNA expression level, protein yield, type of affected tissue, and biodistribution of gene material. These complex processes require improvements at several stages. There is a demand for developing a gene delivery system that can address complex questions and deliver gene materials to the affected tissues with high yield [36]. Patients with angioimmunoblastic T-cell lymphoma (AIT) and peripheral T-cell lymphoma (PTCL) are being diagnosed for a trial in which polymeric PD-1 blockade will be administered with therapeutic small interfering RNA (SIRNA) nanoparticles. Government agencies are also working in coordination with pharmaceutical companies and various universities across the world to develop the platform [37]. A novel triamcinolone liposome-like particle is being developed to test targeted delivery of small interfering RNA (SIRNA) to liver malignancies in uveal melanoma patients. In addition, gene delivery has recently received significant attention for treatment, monitoring, and diagnosis. These Nano carriers should not lead to any unwanted side effects, such as immunogenicity and tissue toxicity, when used in vivo. Bio-use is one of the solutions. Once the adverse effects of Nano carriers are resolved, ease of sterilization and longer storage are expected to escalate the demand for use in clinics [38].

4.2 GENE EDITING TOOLS

Genome editing is an innovative tool in molecular genetics in which genetic information is modified in a controlled manner [39]. Currently, there are many different gene editing techniques, the most important of which is the CRISPR/Cas9 system, followed by zinc finger nucleases and transcriptional activator-like effector nucleases . The CRISPR/Cas9 system is based on the modification of the DNA sequence, where a part of the existing code is replaced by another template through the CRISPR-Cas9-mediated homology-directed repair (HDR). Cas9 is activated in the presence of the appropriate gRNA(s) after directed mutation, and a new donor template containing the desired mutation is incorporated [40]. The negative selection method is based on the expression of a negative selected resistance gene when the wild-type Cas9 gene is modified into an inactive copy by a specific mutation, Due to the biohazards and ethical issues related to the use of whole microorganism carriers for functional delivery, a potential solution that has recently emerged is to combine viral or non-viral vectors in the form of nanoparticles with revolutionary genome editing tools such as CRISPR/Cas9 to directly knock out genes from the molecule [41]. Gene editing is usually mediated by classical methods that break double-stranded DNA molecules, leading to non-homologous end-joining repair. Such a powerful and HDR-unfriendly mechanism can generate non-specific off-site negative effects that may lead to detrimental outcomes, such as unwanted functional changes that directly cause off-target effects and unexpected genome damage [42]. However, the CRISPR/Cas9 system has recently developed new frontiers in such therapeutic field, showing more precise credentials to achieve site-specific genome editing through complete and precise therapy and complete gene knockout according to HDR. The only point we discuss is properly attributed to the ex vivo manipulation of cells taken from patients [43].

5. CHALLENGES AND FUTURE DIRECTIONS

Despite the work on developing nanomaterials and delivery systems applicable to molecular genetic targets, many technical hurdles remain. Nanomaterials are often studied based on a single or few experiments that suffer from issues related to reproducibility. In addition, the safety of the material and the new demand for regulatory oversight by regulatory bodies have not yet been focused on [44]. Demonstrating the benefits of individual nanomaterials in a single laboratory cannot constitute a sufficient basis for investment in the case of gene therapy. It is now clear that appropriate controls and regulatory hurdles need to be addressed along the delivery system. Simply becoming part of gene delivery, as demonstrated in clinical investment in disease applications, also becomes a critical factor used in new development projects [45]. The challenges of working with nanotechnology in molecular genetics include developing reproducible, scalable, biocompatible, and stable nanomaterials. To achieve this goal, collaboration between molecular biologists, chemists, and engineers is required, often in the form of long-term relationships built over time [46]. Furthermore, except for actual gene delivery, the limitations of eukaryotic model systems that are accepted as the standard for commercial therapeutics often cannot be addressed, and model systems often have to be reoriented to human cytoplasmic applications. In the development of actual delivery systems, the necessary expertise is often under the control of chemists, biologists, and medical scientists, for example, physicians and clinical researchers [47].

6. ETHICAL AND SOCIETAL IMPLICATIONS

Generating health or developmental impacts of nanotechnology at the intersection of nanotechnology and human biology will predictably require attention to ethical, legal, and societal implications [48]. As we may use normalizing blood vessel growth in cancer patients and increasing the number of blood vessels in heart attack patients to eventually combat aging, in line with issues that have emerged in the field of genetics research, some have urged additional caution in how to handle the timeline of information revealed during genetic testing, while others have described their community as collaboratively collecting community genomics [49]. Describing nanotechnology as the creation of functional materials, devices, or systems by novel assembly methods, in the recently anticipated scenario of the future, the potential for this manipulation of biological organisms is limitless, to address these ethical challenges, researchers must continue to develop regulatory mechanisms that reflect interpretations of judicial rulings on how to allocate regulatory responsibility for novel activities such as the manufacture of molecular devices. The ability to control reproduction beyond natural human capabilities will have implications for species biodiversity and environmental health [50]. Advances in tissue regeneration and micro surgical implants using molecules could potentially help us rebuild our bodies and live longer. This ability is most problematic for disadvantaged populations, and decisions to move forward are confounded by societal concerns about equitable resource allocation, inappropriate incitement to research, assurance of choice, concerns about genetic underpinnings, and misinterpretation of opportunity and privacy for groups particularly vulnerable to genetic discrimination [51]. Although speculative imagination may be less clear when applied to new technologies, images of what MNT might one day bring vary widely and could thus influence educational and policy decisions. Moral forecasting and policy analysis provide a venue for discussing ethical issues as a function of a specific scenario or a different ethical assumption [52]. Reasonable foresight methods can be useful in formulating arguments about how to proceed with responsible development. While MNT is far from being realized, speculation about it serves as an emotional appeal to the public apology [53]. The focus is on the contribution of artificial intelligence to the advancement of science and technology, particularly in the field of bionanoparticles and their applications in agriculture, medicine, and environmental cleanup. This could lead to new data-driven insights and predictive modeling. Researchers can address societal needs and enhance environmental sustainability and human health by utilizing technologies based on artificial intelligence and bionanoparticles [54].

7. CONCLUSIONS

In conclusion, the benefits of integrating nanotechnology into gene therapy and research cannot be underestimated. Nanotechnology offers the potential to enhance currently used gene delivery systems as well as develop more effective tools for more efficient gene editing. In the past few decades, there has been a clear and rapid progress in research into nanomaterials, their synthetic protection, functionality, toxicity and biocompatibility. There is an urgent need to address multidisciplinary issues including research in biology, chemistry and materials science towards modern gene therapy applications. Translational medicine has gained acceptance in genomics and proteomics and has produced drugs and is moving towards personalized treatment for each individual.

Funding

None

ACKNOWLEDGEMENT

The authors would like to thank the anonymous reviewers for their efforts.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

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