Nanotechnology is a contemporary medicine: A future of clinical translation study

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Abstract

In recent thirty years there has been a substantial amount of research conducted in the area of nanotechnology. This attention is brought on by materials with special optical, electrical, magnetic, chemical, and biological capabilities that are 10,000 times smaller in size than the diameter of a hair strand. Large libraries of nanomaterials can now be characterized and synthesized thanks to techniques pioneered by researchers, who have also shown how useful they are in preclinical settings A new stage in the development of nanomedicine has begun, with the goal of utilizing these technologies are designed to assist anyone in need of medical care. This review paper provides an overview of the unique attributes of nanomedicine, the current status of the discipline, and evaluates the challenges associated with clinical translation. To establish a reciprocal relationship between laboratory research and clinical practice, we conclude by talking about the necessity to develop and enhance collaborations between engineers and physicians. This collaboration will direct basic research on the biological effects of nanoparticles, addresses clinical issues, alter the growth and assessment of new treatment technique , imaging tools , and drug delivery systems.

Keywords: Translation Nanomedicine Chemical

Introduction

Nanotechnology is the design and application of technologies with a size of 1–100 nm [1]. The practice of using nanotechnology in medicine to promote health is referred to as nanomedicine [1, 2]. Nanomedicine advancements depend heavily on nanoscale structures, materials, and particles. These entities have distinctive physical, chemical, or biological characteristics that can be utilized as innovative foundational elements in the development of medical devices and systems for the purpose of detecting and treating illnesses (see Figure 1). Quantum dots, for instance, are fluorescent semiconductor nanoparticles with controllable emissions due to changes in their size, shape, and chemical make-up. By applying biocompatible polymers and antibodies on their surface, they are employed as probes for in vitro and in vivo microscopy [3]. After laser excitation, gold-based nanomaterials in the form of rods can generate heat from their surface [4]. The clinical use of these materials for tumour thermal ablation has been investigated. Iron oxide nanoparticles has superparamagnetic properties, making them suitable for capturing biological components for detection in magnetic resonance imaging (MRI) and medical laboratory tests [5]. The engineering of a

nano system for simultaneous therapeutic and diagnostic applications results from the fusion of various nanoparticles into a single component. Nanomaterials possess a diverse range of physicochemical and biological properties, both on their surface and within their core, owing to their diminutive dimensions (Fig. 1). Platforms for nanotechnology are helpful in biology and medicine due of these characteristics. The inspiration originates from fundamental biological interactions, which take place at the nanoscale regime and ensure cell viability [6]. These include processes including receptor-ligand binding, neurotransmitter release, oncogenic pathway activation or deactivation, intracellular trafficking, synthesis, degradation, and oncogenic pathway activation. In these interactions, Biomolecules are interconnected by domains that possess dimensions smaller than 10 nanometres. Organelles and vesicles, which are biological structures that are 100 nm or smaller, perform sorting, processing, and degrading processes. Due to their small size, nanoparticles may be able to enter a variety of biological structures and disturb molecular interactions there. Researchers are currently endeavouring to fabricate nanomaterials with the aim of altering the course of diseases by intervening, rectifying, or modifying the interactions occurring at the nanoscale [2]. The use of nanoparticles for diagnostic and therapeutic purposes is currently discussed in this review article we highlight the accomplishments as well as the present obstacles to translation. The primary factor contributing to delays in translation is the disproportionate emphasis placed on the development of nanomaterials, while insufficient attention is given to investigating their interactions with biological systems. The goal of this research was to inform and involve the clinical community in identifying areas where nanomedicine could be used in healthcare to produce creative solutions.

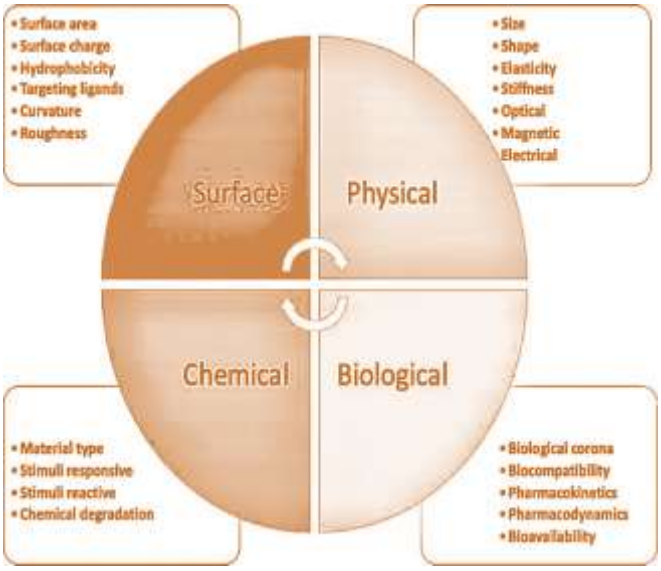

Fig.1 A wide range of adjustable properties are available in nanomaterials. Physical, chemical, surface, and biological qualities can be categorized among them.

The physicochemical properties of nanomaterial

Nanomaterials' physicochemical characteristics will be covered in this part, and the applications in medicine will follow. Divided into organic and inorganic components, nanomaterials are frequently thought of in this way. Then, each of them may be created with certain surface, chemical, and physical characteristics to provide the required biological characteristics and function (Fig. 1). Organic nanoparticles are made from polymers, nucleic acids, proteins, lipids and carbohydrates can be produced synthetically or biologically [7]. Organic nanoparticles often have a wide range of functions and are biocompatible. Due to their mostly carbon, nitrogen, and oxygen-based chemical makeup, they are normally harmless and exhibit little immunological reactions. The applicability of the statement is limited to non-biological polymers, as the precursor reagents and chemical bonds present in synthetic polymers can vary from those observed in biological molecules. Consequently, scientists have conducted comprehensive investigations to assess the potential acute toxicity and immunogenicity of synthetic polymers. These organic nanostructures are frequently preprogrammed to bind particular cells and transport therapeutic substances through chemical or physical characteristics. An great illustration of a practical organic nanoparticle is the FDA-approved anticancer liposome nanoparticle doxil is made up of doxorubicin, polymers, and phospholipids [8, 9]. Doxorubicin is contained within the center of the nanoparticle and is protected from the solvent by a lipid bilayer comprised of phospholipids and cholesterol. A charge headgroup on the liposome surface allows the liposomes to interact with aqueous solvents. Polyethylene glycol (PEG) polymer has been coated on the surface of this nanoparticle with the intention of lowering the process of serum adsorption and the preservation of serum stability by means of hydrophilic contacts [10, 11].

To accomplish cellular targeting, scientists have further altered organic nanoparticles by surface conjugating molecules (such as antibodies, aptamers, and peptides). This enables the targeted distribution of these nanoparticles by allowing them to attach to a wide variety of biological molecules, including receptors, nucleic acids, polymerases, peptidoglycans, and glycoproteins. One example of a protein-coated dendrimer is a substance that inhibits the attachment of the human immunodeficiency virus (HIV) to its receptor sites [12]. Additionally, nucleic acids and small-molecule medicines that can alter gene expression or interfere with RNA expression can be carried by nanomaterials [13–15]. Utilizing organic nanomaterials, researchers are creating vaccinations, immunotherapy, diagnostics, and combinatorial medicines. Additionally, being developed for use in medicine are inorganic nanomaterials [16, 17]. These nanostructures' adjustable qualities set them apart from other materials. By modifying the physicochemical structure of the nanoparticle, the researcher may change its electrical, optical, and magnetic capabilities. These substances range from molecules like iron oxide and calcium phosphate through metals like gold, copper, zinc, and aluminum. They also contain semiconductors like cadmium selenide and zinc oxide. The uses of inorganic material are determined by their physical qualities. Gadolinium, iron oxide, and radioactive copper nanoparticle compositions, among others, have been employed in the field of medical imaging for diagnostic purposes, specifically in computer tomography, magnetic resonance imaging, and positron emission tomography. Ferumoxytol, classified as a

nanoparticle, has obtained approval from the Food and Drug Administration (FDA) for its application in the treatment of iron deficiency anaemia. It is also utilised off-label as a contrast agent in magnetic resonance imaging (MRI) procedures [18, 19]. Gold nanoparticles play a crucial role as agents in the fabrication of colorimetric diagnostic assays. The solution containing monodispersed gold nanoparticles has a red hue, however, the colour of the solution transitions to blue upon aggregation of the nanoparticles induced by the presence of target molecules or alterations in salt concentrations. In addition to that, scientists have the capability to artificially produce gold nanoparticles of different shapes and sizes, allowing for the customization of their optical and thermal characteristics (Figure 2). Dots of quantum serve as probes in the context of multicolour fluorescence imaging and single-molecule tracking [3]. Nevertheless, the use of inorganic nanomaterials may be restricted due to concerns regarding their stability, biocompatibility, and immunogenicity [3, 20]. These challenges can be effectively addressed through the use of protective measures such as the application of coatings or the encapsulation of the components within polymers, polysaccharides, or other organic substances. Scientists have successfully devised techniques for producing a diverse range of organic and inorganic nanoparticles, altering their surface properties through chemical modifications, and showcasing their effectiveness in a range of preclinical applications. The subsequent phase involves the progression of nanomaterials in the context of patient care. In the subsequent section, we will examine the fundamental concepts of nanomedicine and provide an overview of its current status in terms of clinical translation.

Nanomedicine therapeutics

Drugs are often delivered to the specific sick site using nanomaterials as delivery systems. There are potential medications that exhibit excellent efficacy in vitro for a variety of disorders. Poor pharmacokinetics and pharmacodynamics, however, impair in vivo performance [22, 23]. Once injected into the body, small molecule medications, proteins, and nucleic acids encounter a number of difficulties. They take up serum proteins that identify them so that the immune system can handle them. Endonucleases are enzymes that degrade nucleic acid medications, which are excreted below the renal filtration threshold of 6.5 nm. Consequently, the body's innate immune system recognises these molecules as exogenous entities [24–27]. Moreover, the liver exhibits a comprehensive first-pass metabolism of many medicines. In this context, the hepatic enzymatic process of drug metabolism leads to a reduction in the concentration of pharmacologically active drug molecules at the intended site of action. Organs that are not affected by infection, such as the liver, spleen, skin, and other tissues, have the ability to bind the medicine, thereby reducing its accumulation in target organs. These locations are susceptible to recognition by off-target cells, which might result in substantial side effects and organ damage, which restricts their practical application [28]. Although there are several therapeutic possibilities, the body's recognition and processing of them results in limited accumulation at the targeted region and adverse effects, which creates a translational hurdle for these medications. In order to overcome these difficulties, nanomaterials serve as a delivery system that can safeguard the active medication in vivo. Drugs can be incorporated into nanoparticles in a variety of ways. The location of

nanoparticles in relation to their intended biological interaction might vary, with three possible arrangements: internal encapsulation, integration into the material matrix, or surface presentation [29, 30]. When pharmaceuticals are incorporated into nanomaterials, a new entity is created that differs from the original drug in terms of shape, size, and surface chemistry. The first justification for using nanomaterials in medications is to avoid the acute immunological response over intravenous infusion. Small molecules, nucleic acid, and proteins are identified and designated to breakdown as a result in which they interact with immune cells, enzymes and serum proteins. Nanoparticles serve the purpose of safeguarding drugs during circulation, thereby impeding immune recognition and the associated processes. Furthermore, the utilisation of nanoparticles has been shown to effectively prolong the elimination half-life of several drugs. Certain polymers, such as polyethylene glycol (PEG), have been seen to impede the adsorption of proteins associated with the complement cascade and the innate immune system on the surface of nanoparticles. Furthermore, the kinetics of elimination are notably impacted by the size of the nanoparticles. The renal system eliminates nanoparticles and compounds of a size below 6.5 nm. Larger nanoparticles than 6.5 nm will go to different organs.

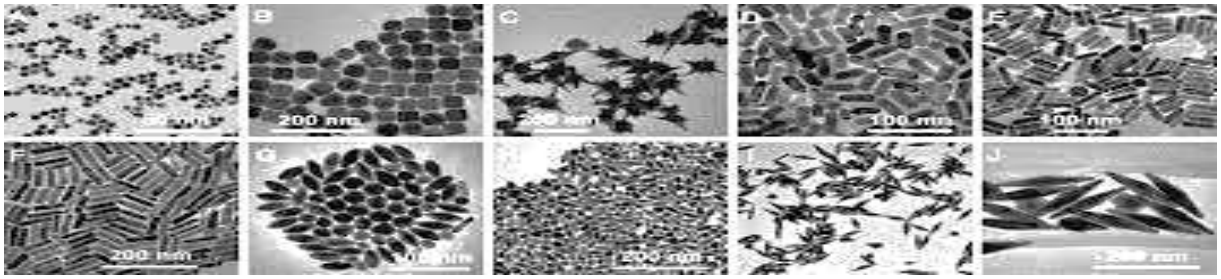

Fig.2 Typical TEM pictures of variously sized and shaped gold nanoparticles. Figure reprinted from article under reference [21].

The serum adsorption of nanoparticles can be decreased by covering them with neutral polymers. Proteins that undergo adsorption onto nanoparticles while in circulation are present in a relatively small yet potentially significant fraction. In-depth research is being done on this protein corona and how it affects nanoparticle destiny. In vitro investigations employing that lines of macrophages have revealed that the protein composition adhering to nanoparticle surfaces is contingent upon the size, shape, and surface chemical characteristics of the particles. [31, 32]. Based on the composition of the corona protein, computational models can forecast cellular absorption. Based on the observed adsorption patterns of protein during the process of circulation, complementary in vivo studies have been conducted to develop supervised learning systems capable of predicting organ absorption [33]. Currently, research is being done to determine the function of certain proteins such complement, immunoglobulins and lipoprotein. In order to mediate future cellular interactions, these investigations [34–36] concentrate on carefully manipulating the architecture of protein and its relative orientation of the epitopes. Designing delivery systems can be done more logically if there is a better knowledge of the interactions that occur between proteins and nanoparticles in living things. For instance, we may create a nanoparticle that preferentially

binds the targeted serum proteins while avoiding the immunogenic proteins. The bulk of the injected nanoparticles are sequestered in the reticuloendothelial system organs (spleen, liver and lymph nodes) [37–40]. These organs have largely developed to sieve out, stow away, and trigger an immune response to invading infections and materials. They contain characteristics in their structure and biology that encourage the sequestration of nanoparticles. An example of this can be observed in the liver's blood artery lining, where fenestrations serve to sieve nanoparticles and impede the smooth flow of laminar dynamics. Due to slower blood flow and the presence of immune cells, these organs have a lot of room to absorb nanoparticles. As a result, up to 99% of the nanomaterial that was injected is sequestered by these organs (Fig. 3), that has an impact on drug distribution, its metabolism, and clearance profiles. The function and efficacy of the medication at the target location can be changed by nanoparticles. Despite being physiologically active in vitro, tiny molecular medicines have negative pharmacokinetic and pharmacodynamic characteristics, necessitating this by adjusting their physicochemical characteristics, nanoparticles seek to influence these variables.

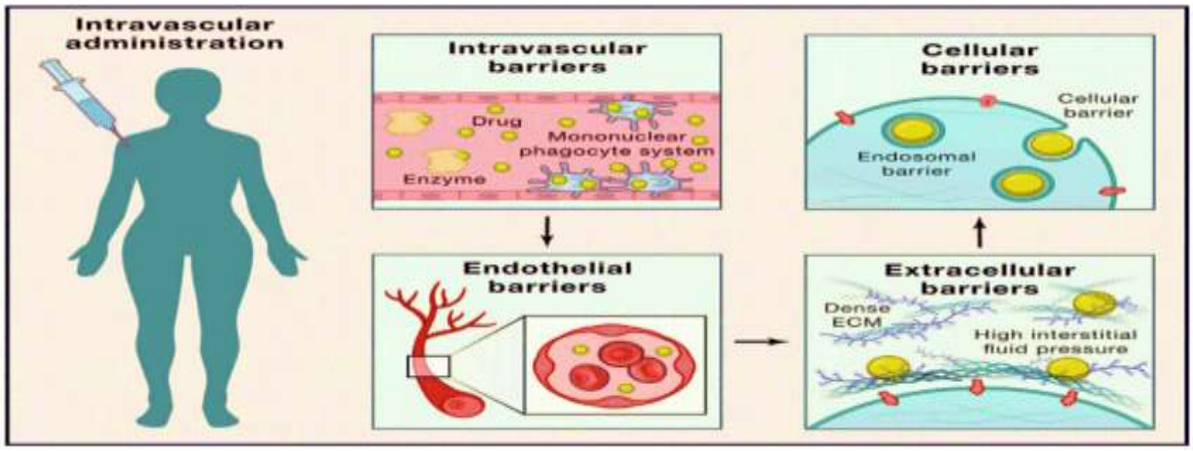

Fig.3 Biological impediments to the delivery of drugs to particular sites. Image is taken from article under reference [41]

The diseased target's exposure to the medicine is influenced by the nanoparticle design's effects on drug transport and release rates to the diseased location. Additionally, the drug's interaction with the target can be influenced by the avidity, valency, conformation, and presentation of the drug regarding nanoparticle surface. The target specificity and effectiveness of medications may be precisely controlled by fine-tuning the nanoparticle characteristics. We're still working to figure out how to limit a drug's ability to treat a disease at its intended target spot.

Cancer

The utilisation of nanoparticles in the field of cancer therapy is a highly investigated domain within the realm of nanomedicine. The area of study being discussed is referred to as cancer nanomedicine [42]. In the beginning, the primary objective of nanomaterials was to facilitate

the transportation of anticancer medicinal or diagnostic agents into tumours with enhanced efficacy. The objective was to address the limited accumulation at the intended location and the unintended effects of imaging agents and small molecule chemotherapeutics. The impetus for the advancement of nanomaterials originated from research conducted throughout the 1980s. proteins and dyes were introduced through injection and exhibited targeted accumulation in xenograft tumours as opposed to the skin [42-44]. The extravasation of macromolecules into the cancer microenvironment has been observed to occur through the presence of leaky vasculature, which is hypothesised to be a result of holes in the endothelial lining of tumour vessels. The phenomenon known as the Enhanced Permeation and Retention Effect (EPR Effect) has emerged as a fundamental principle in the field of cancer nanomedicine. The main objective of the design was to create nanoparticles that are smaller than the gaps in tumour vasculature, in order to facilitate their accumulating within the tumour. In current study, it was illustrated that the primary route of nanoparticle transport in the tumour microenvironment is an active process, specifically by the transportation of nanoparticles through endothelial cells (45). The discovery made in this new study has sparked a discussion over the method by which nanoparticles are able to penetrate solid tumours. However, scholars have provided a definition for the optimal cancer-targeting nanoparticle, which refers to nanoparticles that exhibit stability within the living organism, prevent unintended buildup in organs such as the liver and spleen, successfully penetrate the tumour, and selectively release their therapeutic payload within the tumour [46, 47]. Currently, there exist a total of 15 cancer nanomedicines that have been officially approved on a global scale [48, 49]. The majority of these entities consist of liposomal nanoparticles that have been encapsulated with chemotherapeutic agents. The initial liposomal nanoparticle, known as Doxil, was granted approval in 1995. This particular nanoparticle is designed to transport doxorubicin and is PEGylated. At now, it is considered a secondary treatment option following chemotherapy for the management of ovarian cancer and Kaposi's sarcoma. In clinical trials, it was observed that Doxil did not provide a significant improvement in patient survival. However, it effectively addressed the cardiotoxicity concerns associated with the medicine. Nevertheless, individuals experienced palmar-plantar erythrodysesthesia as a result of the deposition of the liposomal formulation on the skin. The introduction of this novel toxicity imposes constraints on the dosage of Doxil for administration to patients. Additional liposomal formulations have been approved as a result of modifications that have led to improved toxicity profiles. Several examples of liposomal drug formulations may be found in the market. These include DaunoXome, which contains daunorubicin, Myocet, a non-PEGylated variant of Doxil that is approved only in Canada, MARQIBO, which carries vincristine, MEPACT, which carries mifamurtide, ONIVYDE, which carries irinotecan, and Vyxeous, which carries cytarabine in a 5:1 molar ratio with daunorubicin. The majority of these nanoformulations did not provide a significant advantage in enhancing overall survival. Nevertheless, the clinical trial conducted for Vyxeous in phase III was a notable milestone as it demonstrated a noteworthy enhancement in patient survival rates for acute myeloid leukaemia (AML). Specifically, the survival duration increased from 5.9 months to 9.6 months. Vyxeous represents a pioneering achievement as the initial officially sanctioned nanomedicine that incorporates a meticulously calibrated combination therapy. Nanomedicines possess a notable advantage in comparison to small molecule

treatments due to their ability to transport and distribute several moieties simultaneously to the targeted region.

Nanomedicine analysis

Nanoparticles are increasingly recognised as crucial technology under in vitro diagnostic devices [56–58]. The primary objective of in vitro diagnostic techniques is to determine the presence of specific diseases in patients by detecting proteins, DNA, or other biomolecular biomarkers. Diagnostic devices commonly consist of two essential components: (a) the capture of molecule responsible for identifying the specific illness biomarker, and (b) the nanoparticle that facilitates the conversion or transduction of the captured biomarker. The capture molecules commonly employed in various applications include antibodies, peptides and aptamers. The transduced signal can manifest in several forms, such as alterations in colour, fluorescence, magnetism, or electrical properties. The extensive variety of nanoparticles facilitates the choice of the transducer signal. There exist two distinct categories of in vitro diagnostic technology, namely heterogeneous and homogeneous. One key distinction lies in the fact that homogeneous and heterogeneous experiments are conducted over surfaces and in solution, respectively. In a conventional diagnostic test with heterogeneity, the capture molecule is immobilised on a solid surface, such as polystyrene plates. This molecule is responsible for detecting and binding to the biomarker present in the patient's biological fluid, which might be blood or urine. The subsequent procedure involves the introduction of a buffer solution in order to perform surface washing, thereby eliminating biological molecules that are not bound. Subsequently, researchers introduce a nanoparticle that has been coated with a chemical capable of recognising the specific biomarker onto the surface. The secondary probe exhibits binding affinity towards the surface. The nanoparticle induces a modification in the detected signal at the surface, facilitating the identification of the biomarker's interaction with the capture molecule. One widely recognised illustration of a heterogeneous assay is the gold nanoparticle lateral flow immunoassay. In the context of a lateral flow immunoassay, a membrane is immersed into a biological fluid [59, 60]. The movement of the secondary probe, consisting of gold nanoparticles, through the membrane is facilitated by capillary force. through the fluid, the biomarker molecule interacts with the biorecognition molecule that is attached to the gold nanoparticles. Once the liquid flow traverses the capture molecule, the biomarker forms a binding interaction with the capture molecule. The gold nanoparticle is immobilised by the binding process, resulting in the manifestation of either a red or blue line, indicating a positive detection. In the event that the biomarker is absent inside the fluid, the absence of a visible line indicates a negative detection outcome. The red line corresponds to the presence of individual gold nanoparticles, whereas the blue line is attributed to the plasmon coupling of a far higher concentration of gold nanoparticles [61, 62]. Commercially available lateral flow immunoassays utilising gold nanoparticles are utilised for the diagnosis of cardiovascular disorders, diabetes, and infectious infections. One significant drawback associated with lateral flow immunoassays is the suboptimal analytical sensitivity exhibited by this particular method. Researchers are now involved in the advancement of lateral flow immunoassays that integrate fluorescent quantum dots, upconverting magnetic nanoparticles or nanoparticles as possible resolutions to this

problem. The diagnostic procedure in a homogeneous test takes place within a solution. A bead assay exemplifies the aforementioned sorts of assays. The buffer solution is comprised of 1-micrometre beads that have been coated with capture molecules and secondary probes. The identification of a biomarker, such as bacteria, viruses, antigens, or nucleic acids, in the fluid of a patient establishes a connection between the beads and the secondary probe. The secondary probe forms a tether with the surface of the bead and induces a modification in the optical signal of the beads, resulting in a positive detection (Figure 4a). The signal may be identified by several imaging methods, such as flow cytometry, camera of smartphone, and optical microscopy. The secondary probe is comprised of a biorecognition molecule that has been coated with a fluorescent substance, such as a dye or quantum dot. The use of nanoparticles has the potential to enhance the functional capacity of the beads. One possible approach is the utilisation of distinct emitting quantum dots to achieve optical coding of the beads. The utilisation of this coding facilitates the simultaneous detection of numerous biomarker targets [63–66] (see Figure 4). The integration of magnetic nanoparticles into beads offers a streamlined approach to the purifying process. The use of quantum dot barcoded beads has demonstrated the potential to accurately detect infectious illnesses and cystic fibrosis, exhibiting a clinical specificity and sensitivity over 80% [63]. An further illustration of a homogeneous test involves the phenomenon of gold nanoparticle aggregation. The solution undergoes a colour shift from red to blue as a result of the agglomeration of two or more gold nanoparticles in the presence of target molecules. The aggregation of gold nanoparticles is facilitated by the presence of a biological molecule on the surface of the nanoparticles, which exhibits specific affinity for the biomarker. The homogenous assay is often characterised by a faster reaction rate compared to the heterogeneous test due to the absence of kinetic limitations. Nevertheless, executing this test might be more intricate for anyone without specialised expertise.The reagents must be accurately measured and transported. The act of introducing reagents into tablets would effectively tackle the issue of transportation [67, 68]. Scientists are now engaged in the development of read-out devices specifically designed for tests that utilise nanoparticles. The utilisation of near-infrared cameras has been demonstrated to effectively detect thermal emissions resulting from gold nanoparticle signals in lateral flow immunoassay, as reported in reference [69].

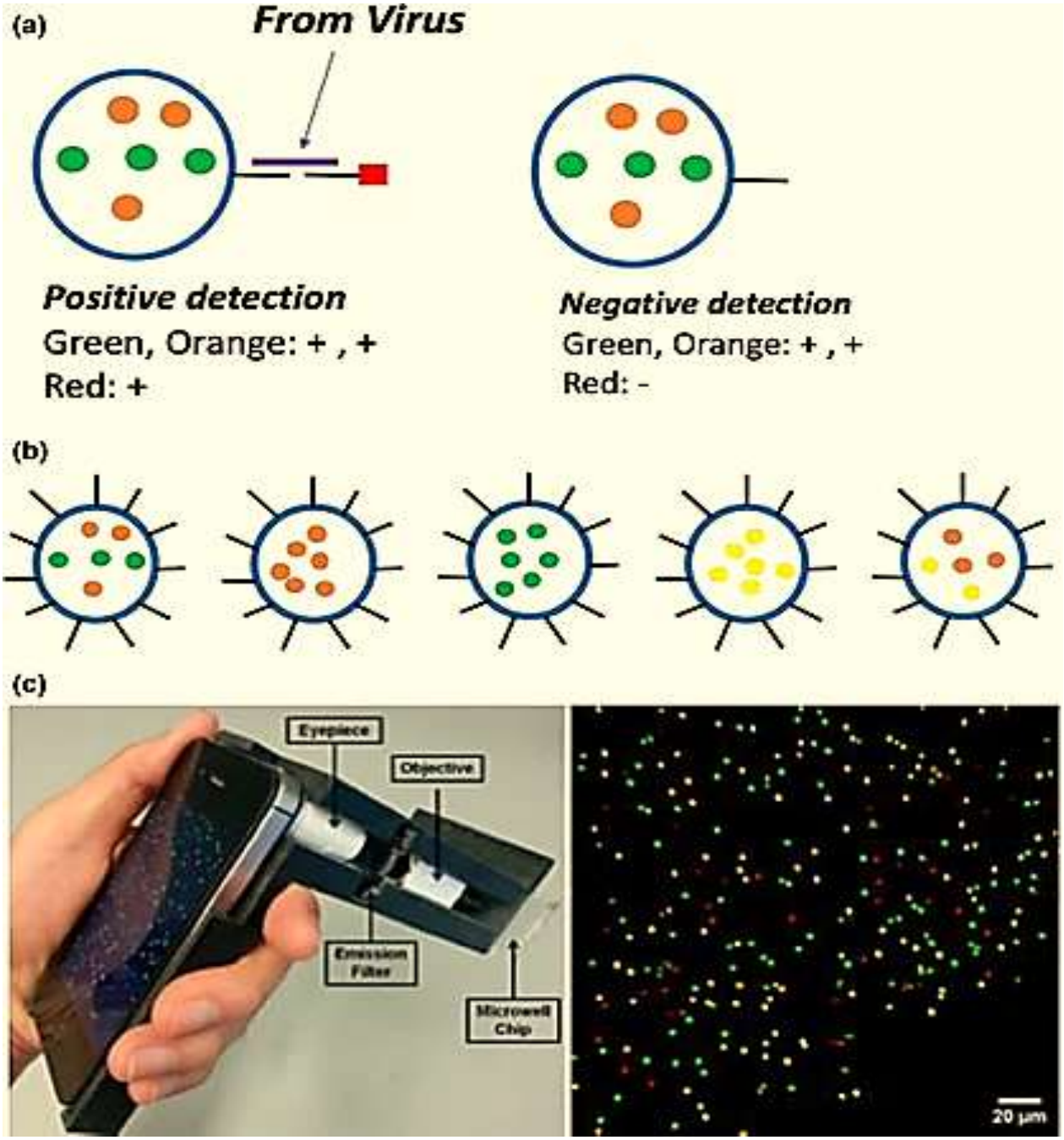

Fig.4 The design of quantum dot barcodes. The camera records the visual representation of quantum dot barcodes with varying emission properties that are arranged in an array on a surface. This figure is taken form article under reference [70].

The light emission produced by quantum dot barcodes may be detected using a smartphone camera (see figure 4) [70, 71]. Conversely, the magnetism in iron oxide nanoparticles can be measured using a miniaturised SQUID device [72]. There exists a significant endeavour to develop systems, devices, and software specifically for nanoparticles design with the purpose of diagnostic applications.

Challenges and outlook

In recent times, there has been a notable acceleration in the progress of clinical translation in the field of nanomedicine. One of the most notable achievements in the field is exemplified by Alnylam Pharmaceuticals, which has effectively utilised the lipid nanoparticle (LNP) platform in conjunction with nucleic acid alterations to successfully produce Onpattro, as previously elucidated. Additional recent achievements encompass the development of Vyxeos, as well as the creation of COVID-19 vaccines by Pfizer-BioNTech and Moderna. Nevertheless, numerous other firms have encountered setbacks in their clinical studies or are currently engaged in the ongoing pursuit of identifying the most effective design for their clinical applications [48,73]. The aforementioned failures have engendered a pressing necessity to comprehend the reasons behind the failures of formulations, trials, and companies. In current years, there has a notable increase in research endeavours aimed at comprehending the interactions between nanoparticles and biological systems, commonly referred to as nano-bio interactions. Although numerous optimisation studies were conducted in the 1990s to develop liposomes for drug delivery applications, many researchers regard the 2000s as the initiation of research on nano-bio interactions [74–79]. The primary emphasis of these studies was to investigate the systematic influence of nanoparticle design factors, such as shape, size, surface chemistry, and stiffness, on several biological functions including therapeutic effectiveness, immune response, delivery, and toxicity. The comprehensive research conducted have established a fundamental basis of overarching principles and have also prompted further investigations into the mechanisms underlying the interactions between nanoparticles and various biological contexts. The objective of nanobio interaction study is to investigate the interaction between nanoparticles and biological systems in order to establish a connection between nanoparticle design and their effectiveness in medical applications, such as therapeutic response and imaging signal. Nano-bio interactions have emerged as a crucial area of investigation within the realm of nanomedicine [80, 81]. The investigation of fundamental aspects pertaining to the process of delivery plays a crucial role in facilitating the translation of numerous concepts discussed during the 2009 JIM Nano conference. The process of delivery is influenced by both the physicochemical features of the nanoparticle carrier and the biological barriers it meets after injection.In 2016, Wilhelm et al. established a foundation for addressing the issue of delivery by quantifying the present condition [82]. The findings of their meta-analysis indicate that a median of less than 0.7% of given nanoparticles successfully reach solid tumours in animal models. The issue of delivery quantification has prompted researchers to prioritise enhancing delivery mechanisms through the study of nano-bio interactions, with 0.7% serving as a benchmark. The study conducted by Ouyang et al. demonstrated that the efficiency of delivery will experience an increase after the dose above a certain threshold value. This improvement was observed to range from 0.7% to a maximum of 12.0% [38]. Additionally, novel mathematical equations have been developed to provide a more precise description of the delivery mechanism of nanoparticles and the therapeutic substance [83]. The field of nanobio interaction studies is increasingly integrating machine learning and artificial intelligence methodologies to computationally establish correlations among nanoparticle design, transport mechanisms, potential side effects, and medicinal efficacy [33, 84, 85]. The elucidation of the link between nanoparticle design, biological

interaction, and therapeutic outcome will require a significant amount of time. The result will contribute to a more logical and systematic approach in the field of designing nanomedicines. Gaining a comprehensive understanding of the obstacles, setbacks, and achievements associated with the utilisation of nanoparticles in clinical settings is crucial for the advancement and triumph of nanomedicine in the future [86]. The field of nano-bio interaction research has successfully identified significant hurdles in the distribution of nanoparticles to biological systems. These findings can be utilised to inform the identification of disease targets for therapeutic interventions. For instance, the process of transporting nanoparticles to solid tumours is intricate as it involves overcoming various barriers that impede their access to cancerous cells [22, 42, 82, 83]. This observation implies that nanoparticles may have more accessibility and efficacy when targeting other biological entities. Researchers have chosen to focus on hepatic illnesses due to the fact that nanoparticles tend to collect in the liver at larger concentrations. There is currently an increased emphasis on the utilisation of nanoparticles for the treatment of immunological illnesses due to the inherent tendency of immune cells to phagocytose nanoparticles (87-89). An additional field of investigation involves the precise localization of nanoparticles towards endothelial cells as a potential therapeutic approach for addressing cardiovascular disease [90]. The obstacles encountered during the transportation of nanoparticles to the desired destination play a crucial role in determining the efficacy of their delivery to certain cells and tissues.

As we embark onto a new era in the growth of nanomedicine, it is evident that a robust groundwork has been established. Initially, it is imperative to prioritise the implementation of measures aimed at expediting the process of translating scientific advancements into practical applications, so ensuring that patients can reap the benefits of the progress made over the last three decades. Furthermore, there has been significant progress in our comprehension of the destiny of nanomedicine inside the human body, and it is imperative that this knowledge informs the development of future designs. There is a discernible shift occurring in our current landscape, whereby the focus of projects is transitioning from being mostly directed by engineers and chemists to increasingly including doctors. Physicians are poised to assume a pivotal function in the narrative of nanomedicine, as we delineate many avenues via which they might effectively supplement and bolster the next stage of nanomedical advancements. Initially, it is important for doctors to ascertain the existing difficulties associated with present treatment methods. Furthermore, they should explore novel prospects for diagnostics and therapies, while also offering guidance in the development of experimental designs that will ultimately facilitate the clinical approval of nanomedicines. Furthermore, medical practitioners have the capability to provide clinical samples and actively contribute to the development of illness models. The availability of patient samples is of great value in the context of preclinical testing, since it enables the refinement of the technology for eventual usage in patients. For instance, doctors will play a crucial role in obtaining tumour samples for the purpose of developing patient-derived cancer models and analysing biopsy samples to get insights into the structural characteristics of diseased tissues. They have the ability to engage in collaborative efforts to ensure that the illness features seen in animal models align with the manifestations observed in their hospital wards and clinical settings. Furthermore,

they possess the capability to provide guidance to researchers throughout the whole of the engineering process, enabling them to explore parameters that are clinically important and conduct experiments that replicate real-world clinical circumstances. Finally, doctors possess the ability to enlist patients and other medical facilities, formulate research protocols, oversee the effectiveness of treatments, and devise strategies for managing unforeseen adverse reactions that may arise throughout the transition from preclinical to clinical stages of drug development. The collaboration between engineers and physicians is crucial for the progression of nanomedicines, ultimately enhancing patient outcomes. The rationalisation of nanomaterial design for biological applications is deemed necessary from an engineering standpoint. Engineers often focus on the technological aspects while developing nanotechnology, such as enhancing fluorescence or improving magnetic characteristics. Insufficient attention is given to the examination of nanotechnology's behaviour and interaction within the biological environment or system. The ultimate application is determined by doctors, and thereafter, the engineer must investigate the correlation between the physicochemical characteristics of nanomaterials and biological systems. Frequently, individuals lack awareness about optimal experimental models, designs, and suitable equipment for investigating nanoparticles. To illustrate, in the context of using nanomaterials for the treatment of cardiovascular ailments, it is important for an engineer to investigate the process of medication transportation inside vital organs like the kidney, lymph nodes, and liver. These organs possess the capability to eliminate therapeutic nanoparticles from the bloodstream prior to their specific targeting of cardiovascular ailments. These investigations will provide guidance for the development of an ideal nanoparticle design that enables effective transport to the intended region of action. The emergence of the field of nano-bio interaction is expected to assume significant importance as a crucial area of study in the 21st century. These studies play a defining role in shaping the engineering processes associated with the utilisation of nanotechnology in the medical domain. There is still a significant amount of knowledge and research that has to be explored and examined within the field of nanomedicine. Advancement in this particular domain of study necessitates a genuine collaboration among clinicians, biologists, and engineers. The use of nanomaterials in clinical trials for treatment of cancer and vaccine development is expected to generate significant interest and drive progress in these areas. Conducting comprehensive investigations at the laboratory level to elucidate the mechanisms by which these materials interact with the human body serves as a crucial foundation for the field of nanoparticle engineering. The integration of passion and insights will play an important role in the progression of nanomedicine for society’s betterment.

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