

Original articles

A Comprehensive Review on Utilization of Nanotechnology in Biomedical Applications and Bibliometric Study Across Asia

Dinda Tria Kusuma^{1*}, Durriyatus Salsabila¹, Fanya Az-Zahra Fakhressy¹ and Huynh-Quang-Dieu Nguyen²

¹Department of Natural Science Faculty of Mathematics and Natural Science, Universitas Negeri Surabaya, Surabaya 60231, Indonesia.

²University of Colorado Denver, Anschutz Medical Campus, 2115 N Scranton Street, Aurora, CO 80045, USA.

*Correspondence: dindatria.22043@mhs.unesa.ac.id

ABSTRACT

Recent advancements in nanotechnology have significantly influenced biomedical science, facilitating substantial progress in the fields of diagnostics, therapeutics, and regenerative medicine. This review comprehensively explores the application of nanotechnology in biomedical applications, emphasizing the research initiatives in Asia, a region that has been recognized for its rapid advancements and innovations in nanoscience. Nanomedicine, defined as the intersection of nanotechnology, pharmaceutical, and biomedical sciences, has emerged as a vital field. It offers novel solutions for disease diagnosis, targeted drug delivery, and theranostic approaches. This review article presents a comprehensive bibliometric analysis to evaluate the evolution, distribution, and impact of research related to nanotechnology-based biomedical applications in major Asian countries such as China, Japan, South Korea, India, Iran, Singapore, and Taiwan. The analysis identifies leading contributors, influential publications, and collaborative networks, while also uncovering research trends and gaps. Furthermore, this review highlights the current challenges and limitations that impede the complete realization on the potential of nanotechnology in medical field. The objective of this findings is to provide a strategic foundation for guiding future research, fostering regional collaboration, and accelerating innovation in nanomedicine across Asia.

Keywords: Nanotechnology, biomedical application, Asian countries, bibliometric study.

INTRODUCTION

Recent advancements in nanomedicine have facilitated regeneration and reconstruction of damaged human tissues and organs, thereby establishing new avenues for the treatment of incurable disease [1]. It is acknowledged that there are several ways to define nanotechnology. Furthermore, it has been identified as an invaluable tool across a diverse array of scientific and industrial disciplines, particularly in the field of biomedical applications [2, 3]. All definitions, however, emphasize the design and development of highly ordered, bottom-up nanostructured materials that exhibit specific responses when exposed to certain stimuli [4]. The field of nanotechnology is focused on the precise manipulation of individual atoms, molecules, molecular clusters, or surfaces to construct novel materials and devices with distinctive properties, then applied in biomedical applications, which are known as nanomedicine [5-7]. The convergence of nanotechnology, pharmaceutical, and biomedical science has led to the rapid development of nanomedicine with new nanoformulations designed for therapeutic purposes, imaging agents, and theragnostic applications. In the past decade, nanomedicine has been investigated for its potential to treat a variety of diseases [8] and the main goal is to design and develop materials, instruments and systems that demonstrate essential properties alongside novel functionalities. Nowadays, nanomedicine offers enormous potential for the development of disease diagnosis, drug development, and targeted drug delivery [9].

Asia is the leading continent in the development and establishment of nanodistricts. A nanodistrict is defined as a regional hub in which nanotechnology research institutions and companies are concentrated, thereby facilitating collaboration in research, development and commercialization. The main objective of this concentration is to utilize common scientific and technical knowledge [10]. Several

Asian countries, including Japan, China, South Korea, Singapore, India, Iran, and Taiwan showed remarkable progress in the field of nanotechnology. These nations have become pioneers in the global advancement of nanotechnology, demonstrated by substantial investments, high numbers of patent registrations, and productive scientific publications in top-tier academic journals. Among numerous fields of nanotechnology research, the biomedical sector holds the highest commercial value and demand. This is driven by the urgent need for precise and rapid diagnostic and therapeutic solutions in healthcare, where nanotechnology-based innovations offer promising advancements to address complex medical challenges.

This review highlights the advancements made in nanotechnology research for biomedical cases and provides an overview of the development of research related to nanotechnology as a biomedical application in Asian countries, with a bibliometric analysis of research in the Asian. This approach enables the systematic identification of research trends, patterns of scientific collaboration, and the evolving contributions of Asian countries to the development of nanomedicine. Moreover, we assessed in-depth bibliometric analysis in terms of “Nanotechnology as a biomedical application around Asian countries” to serve a range of functions. (1) To assess the frequency and spatial distribution of scholarly publications within the field to gain insights into the evolution of research trends. (2) To characterize the research landscape by determining key authors and nations involved in the scholarly discourse, thereby highlighting areas of expertise and potential opportunities for collaboration. (3) To evaluate the impact of research through citation analysis, determining which studies have significantly influenced the development of the field. (4) To identify existing research gaps that may present opportunities for future investigations. (5) To quantify the overall research output related to the application of nanotechnology in biomedical sciences. Furthermore, this study identifies the main obstacles which impede the advancement of nanotechnology in biomedical applications, offering current insights that can serve as a valuable foundation for future research endeavors in this domain.

1. Nanotechnology Development

Nanotechnology, which involves the manipulation of matter at the atomic or nanoscale level (approximately 10^{-9} meters), has achieved notable advancements in recent years, driven by its vast potential applications across various sectors such as medicine, electronics, and energy (**Figure 1**). The fundamental concept of nanotechnology was initially introduced by a pioneering physicist Richard Feynman in his seminal 1959 lecture, "There's Plenty of Room at the Bottom," where he envisioned the possibility of manipulating and controlling individual atoms and molecules to construct novel materials and devices [11]. Regarding on this foundation, Eric Drexler wrote “Engines of Creation: The Coming Era of Nanotechnology” in 1986, indicating that molecular manufacturing could be used to create novel materials, machinery, and complex structure at molecular level. Since its conceptual inception, nanotechnology has advanced considerably, marked by continuous discoveries and technological innovations. A significant milestone in this progression was achieved in 1996 when Richard Smalley received the Nobel Prize in Chemistry for his pioneering work on fullerenes—spherical carbon-based molecules that have become fundamental to nanoscience. These development collectively underscore the capacity of nanotechnology to drive transformative change in science and engineering [12]. Since then, extensive research in nanotechnology has shown that working at the nanoscale frequently requires natural process mimics. It includes the development of self-cleaning surfaces, artificial photosynthesis, and the enhancement of material properties, such as tensile strength and elasticity, as well as the replication of complex biological mechanisms within the human body. Nanotechnology, particularly through the application

of engineered nanoparticles, facilitates the encapsulation and targeted delivery of therapeutic agents in a controlled manner. These nanoparticles are capable in mimicking cellular functions, such as overcoming the biological barriers which react to specific physiological stimuli, thereby improving the precision and effectiveness of drug delivery systems. Accordingly, it enable more targeted and efficient therapies, reducing adverse side effects and enhancing overall treatment outcomes [12]. These insights demonstrate that nanotechnology has become a pivotal instrument in tackling global challenges and promoting sustainable development.

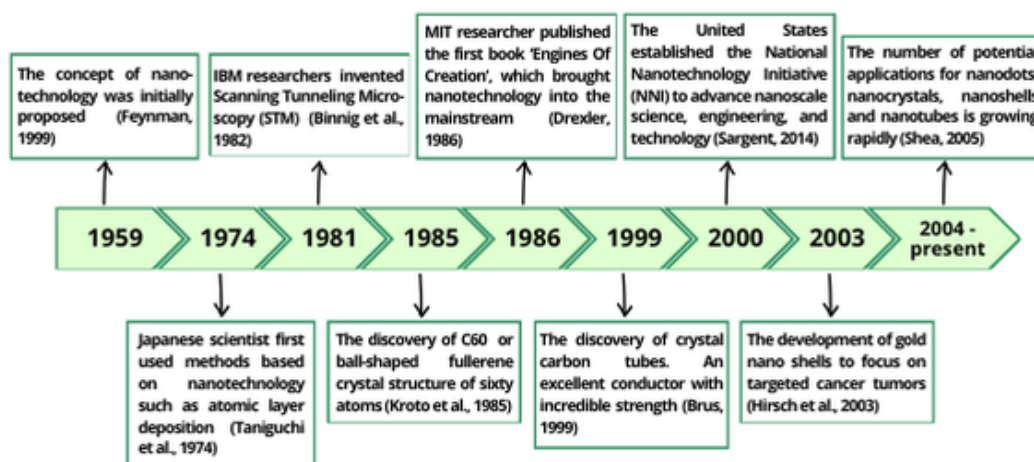


Figure 1. Nanotechnology development timeline

2. Implication of Nanotechnology Development in Multiple Biomedical Application

2.1 Nanotechnology as drug delivery platforms, therapeutics and vaccines

The development of vaccines is one of the most remarkable accomplishments in medical research and a vital component of worldwide public health. The pharmaceutical formulations are engineered to stimulate an adaptive immune response through the introduction of specific antigens, thereby conferring protection against targeted pathogens. Approximately 2 to 3 million live are saved worldwide annually thanks to vaccines which perform a significant role in preventing disease and effectively reduce the incidence of many infectious diseases [13, 14]. Despite the significant benefits of vaccines, developing an effective vaccines for certain diseases remains challenging due to limited understanding of disease pathogenesis, a lack of suitable animal models, and the complexity of inducing both antibody-mediated (humoral) and cell-mediated immune responses [15].

Biotechnological developments, including recombinant DNA technology, have led to the significant advance vaccine's technology. Notably, nucleic acid-based vaccines—such as DNA and mRNA vaccines—have emerged, with mRNA technology serve as a critical platform for several authorized COVID-19 vaccines. This platform is now being expanded to target diseases beyond COVID-19 [5, 16-18]. This technology offers several advantages, including high efficacy in preventing severe disease, the ability to provoke both cellular and humoral immune mechanisms, and a strong safety profile with a low risk of mutagenesis. Additionally, mRNA vaccines enable simpler, faster, and scalable production processes, reducing the risk of cross-contamination compared to traditional vaccine manufacturing methods [18, 19]. In contrast, DNA vaccines, which function by delivering a gene of interest via plasmid vectors to transfect

immune cells for subsequent antigen expression, encounter challenges such as relatively low immunogenicity and the theoretical risk of genomic integration. Therapeutic vaccines for cancer offer a novel paradigm that differs from conventional preventive vaccines, as they are designed to treat established tumors rather than prevent disease onset. Other promising strategy involves the encapsulation and delivery of tumor-associated antigens along with adjuvants using the special benefits of nanocarriers to improve the effectiveness of cancer immunotherapy [20, 21]. The effective mRNA delivery systems employed in lipid nanoparticles (LNPs) for some COVID-19 vaccines are now being repurposed for cancer vaccine development, wherein mRNA sequences encoding tumor-specific antigens are delivered to elicit targeted anti-tumor immune responses.

2.2 Nanosized vaccine delivery systems

Nanoparticles represent the most extensively used nanometric platforms in vaccine development. The use of nanotechnology has significantly propelled the field forward, resulting to the commercialization of multiple nanotechnology-based vaccines, alongside numerous candidates undergo clinical evaluation. These nanoplatforms are specifically designed to augment antigen immunogenicity, enhance vaccine stability, and facilitate controlled delivery and sustained release of both antigens and adjuvants [22]. Nanoparticles exhibit dimensions like those of biological entities, such as proteins and vesicles, that naturally interact with immune cell membranes. Due to their similar sizes, nanoparticles can penetrate cells more effectively and enhance the delivery of antigen via endocytic pathways [23]. Many nanoparticles are characterized by additional benefits, including reduced toxicity, biodegradability, and biocompatibility [13]. These attributes make nanoparticles apart from traditional adjuvants, which are often associated with inflammatory reactions at injection site, such as pain, erythema, and swelling commonly caused by aluminum salts and mineral oil emulsions [24, 25]. Traditional adjuvants present challenges in terms of stability, bioavailability, size and surface charge. Nanoparticle-based systems overcome these challenges by offering more stable and efficient platforms for the delivery of antigens and adjuvants, thus enhancing vaccine efficacy [26].

Conventionally, vaccines have been administered via parenteral routes, mainly through intramuscular (IM) and subcutaneous (SC) injections [19]. The SC immunization route shows more efficient vaccine drainage to the lymph nodes and elicit stronger immunogenicity compared to the IM route. Nevertheless, IM administration is associated with fewer and less severe local side effects than SC immunization, even when adjuvants are included in the vaccine formulation [27]. Intravenous (IV) administration of nanoparticles offers advantages such as efficient delivery through widespread systemic distribution and rapid therapeutic response. Additionally, IV delivery circumvents degradation by proteolytic enzymes and avoids first-pass metabolism [28]. Recent progress in nanotechnology has allowed for the design of next-generation vaccines that employ nanoparticles to enhance vaccine delivery and efficacy. These nanoparticles, defined as nanoscale particles that replicate the structural characteristics of viruses, are well-suited as platforms for developing innovative vaccines [29]. Vaccines can be delivered using nanocarriers through various approaches, including antigen encapsulation within the nanocarriers or conjugation of antigens onto their surfaces. Encapsulation protects antigens from enzymatic degradation, while surface conjugation enhances antigen uptake by targeting specific immune cells. Beyond their role in delivery, nanocarriers also exhibit intrinsic adjuvant

properties by activating immune cells, thereby contributing to the development of more effective vaccines [30].

In recent years, the FDA's approval of multiple adjuvanted vaccines has contributed to the growing incorporation of nanosized delivery systems (NS-DS) in immunization approaches (**Figure 2**). Nanostructures can act as delivery vehicles for antigens and/or immunostimulants or function as intrinsic adjuvants themselves. To achieve both effective and safe vaccination, it requires incorporation of antigen with adequate immunogenicity, immunostimulants to boost the immune response, and, when necessary, a delivery system tailored to the desired outcomes. Modern vaccine development aims to closely emulate the features of natural pathogens to enhance immunogenicity while minimizing the limitations of traditional vaccines. Prominent examples of this approach include liposomes, lipid polymer nanoparticles (LPNs), virus-like particles (VLPs), and viral vectors. These nanosystems not only mimic pathogen characteristics but also serve as efficient delivery platforms for antigens and immunostimulants.

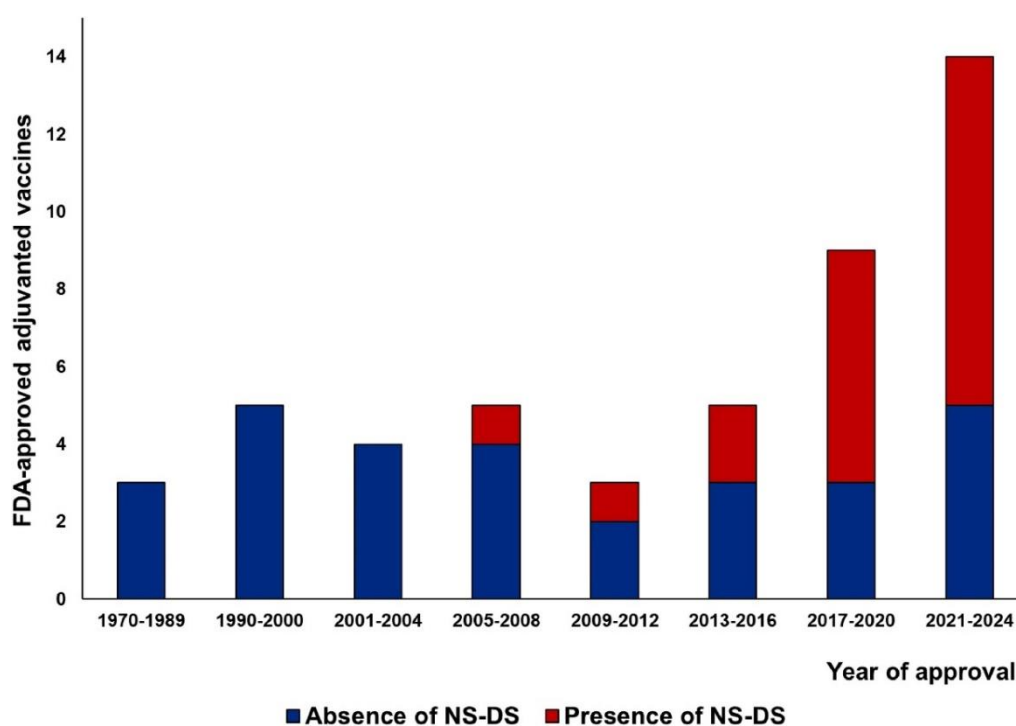


Figure 2. Comparative Analysis of the Presence and Absence of Nanoscale Delivery Systems (NS-DS) in FDA-approved adjuvanted vaccines over the years. Note: Vaccines based on Virus-Like Particles (VLPs), introduced in the 1980s, were excluded from this timeline. Reproduced with permission from ref [13]. Copyright 2024, Elsevier.

In order to achieve the efficacy and safety in vaccination necessitates, the addition of antigen with adequate immunogenic potential, immunostimulatory agents to potentiate the immune response, and a delivery system tailored to fulfill a specific immunological objective might be required. To improve the immunogenicity and diminish the drawbacks of conventional vaccination platforms, modern vaccine was design to mimic the structural and functional of natural pathogens, such as liposomes, LPNs, VLPs, and viral vectors. These nanostructured systems not only mimic pathogen-associated features but also act as efficient carriers for antigens and/or immunostimulants, thus it enables to optimize the vaccine performance.

As depicted in **(Figure 3)**, nanovaccines activate both innate and adaptive immune responses primarily by facilitating antigen uptake and presentation to antigen-presenting cells (APCs) such as dendritic cells (DCs), macrophages, and B lymphocytes, the latter via B-cell receptors (BCRs). This process is essential to elicit robust humoral and cellular immunity. Antigens distributed through nanoparticles are internalized by APCs either at the injection site or within lymph nodes, contingent upon the nanoparticles exhibiting suitable size parameters. This uptake predominantly occurs through endocytic pathways. The endocytic material creates vesicles in an exogenous antigen pathway, which then merge with lysosomes to degrade antigens and nanoparticles. The immunogenic effectiveness of particulate nanosystems is largely determined by their physicochemical attributes, including size, shape, surface charge, hydrophobicity, and biodegradability, which collectively modulate antigen [13]

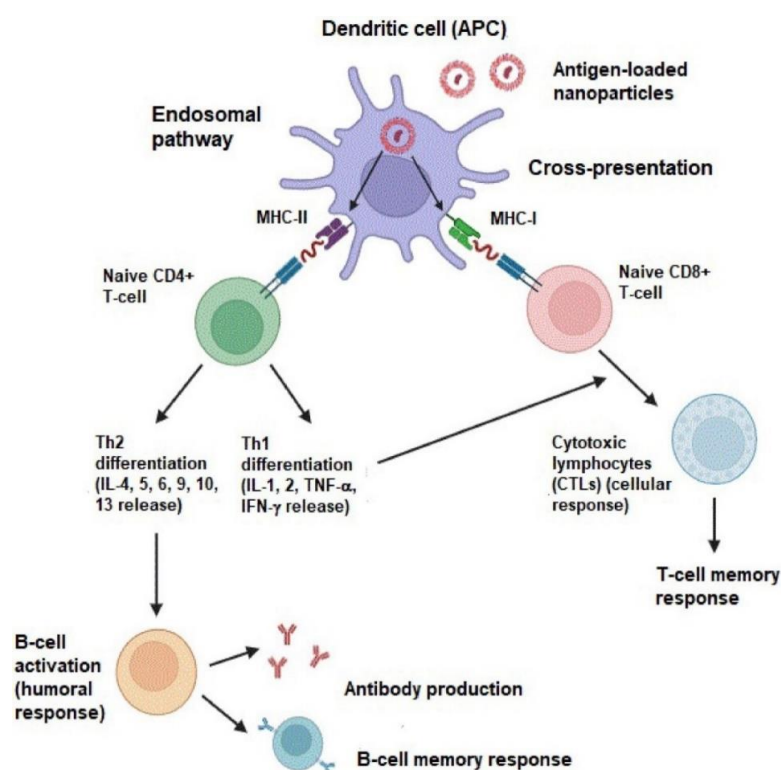


Figure 3. Uptake and antigenic presentation by nanoparticles to elicit humoral or cellular immune responses. Reproduced with permission from ref [13]. Copyright 2024, Elsevier.

Particle hydrodynamic size serves as a key determinant of vaccine development effectiveness [13, 31, 32]. The particle size range employed in vaccines is highly variable, with peptides, proteins, and viral subunits generally measuring up to 10 nm. In contrast, viruses, viral vectors, VLPs, and ISCOMs ranged from tens to hundreds of nanometers (until ~200 nm). Liposomes, virosomes, and emulsions can span from 100 nm to thousands of nanometers, and materials like mineral salts achieve 10 μm . The dimensions and morphology of nanoparticles play a vital role in mediating APC uptake, whereas these characteristics are less critical for the uptake of larger bacteria and microparticles [33]. The immune response is chiefly orchestrated in secondary lymphoid organs, where particle size is integral to optimizing antigen presentation and movement through lymphatic vessels. For example, particles sized 10–200 nm are ideal for

APC recognition and processing and for traversing the lymphatic network in a manner similar to viral particles. In contrast, larger particles require DCs to enter the lymphatic system, slowing the immune response. Soluble antigens smaller than 10 nm can pass through endothelial clefts too easily, reducing their functional concentration in lymphoid organs [33, 34].

Nanoparticles within the 10–200 nm size range exploit both major transport mechanisms for delivery to secondary lymphoid organs. Studies show that 25 nm Pluronic-stabilized polypropylene sulfide (PPS) nanoparticles achieve superior infiltration and transport within the lymphatic system, leading to elevated uptake by DCs in lymph nodes compared to 100 nm nanoparticles [35]. This targeted delivery approach enhances antigen interaction with follicular B cells within lymphoid organs, thereby strengthening the antibody response. The activation of T helper cells by DCs is also crucial, facilitating antibody class switching and the generation of long-lived plasma cells for sustained immunity [34].

2.3 Integration of Nanotechnology in Tissue Engineering and Biomedical Implant Fabrication

Nanomaterials and nanostructures including nanoparticles, nanosurfaces, nanofibres, nanocoatings, and nanocomposites have been explored for a wide range applications in orthopedics and traumatology fields [9]. Existing nanotechnology-based strategies for enhancing tissue formation can be broadly categorized into two main approaches: nanotechnology-enabled surface engineering of biomaterials and the utilization of nanomaterials for next-generation implants.

2.3.1 Nanotechnology-Based Modification of biomaterial surfaces

Biomaterials are generally defined as non-living substances that interact with biological systems and are used in biomedical and pharmaceutical applications, such as drug delivery and tissue repair [36]. The implantation of biomaterials into the human body holds significant importance in the medical field and various biological applications. However, several critical challenges remain, including extending the lifespan of biomaterial implants, minimizing immune rejection responses, and reducing the risk of post-implantation infections. Thus, addressing these issues is essential to improve the efficacy and safety of implantable medical devices [37]. Modifying the surface of biomaterials can effectively change their inherent physical, chemical, and biological attributes, resulting in improved functionality and performance.

Surface modification of biomaterials enables control and customize its surface properties. It gives specific physical or chemical characteristics that enhance the compatibility of implanted biomaterials in human body [38]. One of the key advantages is that surface modification of implanted biomaterials constitutes a highly effective approach for enhancing biocompatibility and minimizing implant-associated infections [39]. It is a common practice to modify the surface of biomaterials without changing the properties of the substrates on a micro or nanoscale [40].

2.3.2 Nanotechnology for novel implants

A growing need for artificial implantable devices has emerged due to marked changes in the global population's age distribution. The percentage of the population comprising the age group of 60 years and above is increasing significantly, leads to a rise in demand for artificial medical implants [41]. Biomaterial implants and devices have become integral to contemporary medicine, serving to replace a wide range of vital organ and tissue functions when natural healing processes are insufficient [42]. Nanotechnology

has introduced a wide array of innovative tools for use in orthopedic applications, one of them through osteochondral implant materials. Employing implant coating materials, surface modification techniques, bone substitutes, and tissue engineering approaches represents essential strategies for minimizing implant failure, avoiding complications, and prolonging implant longevity [43]. Nanostructured implant coatings offer thermal insulation, preventing wear, corrosion, and erosion. Yang and coworkers[44] explored gold nanoparticles (GNPs) on the differentiation of mesenchymal stem cells (MSCs) and the associated molecular mechanisms due to GNPs showed good biocompatibility and surface specificity, thus it can use as osteogenic agents for bone regeneration (Figure 4).

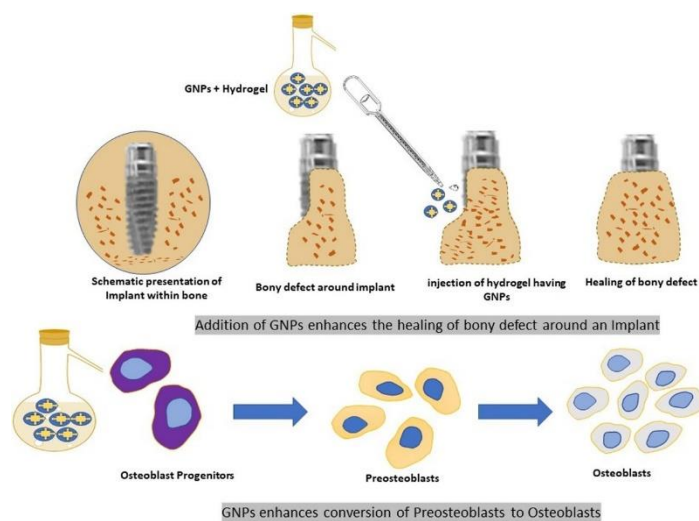


Figure 4. GNPs acts as an osteogenic agent for bone regeneration. Adapted with permission from ref [45], with permission 2020 Elsevier.

2.4 Nanotechnology for Control Infections such as Antibacterial Technology

Antibiotics have transformed modern medicine by effectively treating bacterial infections. Nonetheless, their indiscriminate use, misuse, and frequent abuse over time have contributed to the swift emergence of pathogenic strains exhibiting antimicrobial resistance (AMR) [46]. Surface modification of biomaterials is the most effective preventive measure before the maturation of bacteria adhered to a biofilm. Nanoscale materials exhibiting antimicrobial activity hold substantial promise in the treatment of highly pathogenic organisms. These materials possess unique properties that enable effective disruption of bacterial systems and enhance biofilms penetration. Most importantly, the core substance, surface chemistry, shape, and size of nanomaterials define their efficacy while avoiding the development of AMR. Nanomaterials facilitate access to antibacterial approaches that are novel for bacteria and not part of their intrinsic defense systems. The therapeutic benefits of nanomaterials are chiefly attributed to their nanoscale confinement, multivalent interactions, and increased surface-to-volume ratio. Nanosized metals, metal oxides, organic nanoparticles (NPs), and nanocomposites with potent antibacterial activities provide significant strategic benefits in safely managing superficial infections and infectious diseases. Inorganic NPs are made up of inorganic oxides of Si, Ag, Au, Zn, Mg, Mn, Cu, Se, Al, or Ti, hence they differ in shape, size, solubility, and

stability. Their characteristics are defined by pH, temperature, reduction time, concentration of the reducing agent, and aggregation behavior that impact their antimicrobial potency [47, 48].

Nanomaterials benefit from their controllable and nanosized structures in comparison to those of bacterial components [49]. A high surface area-to-volume ratio ensures strong surface chemistry in terms of multivalent interactions with bacterial cells or functionalization for a specific charge or targeted delivery. The primary forces that govern the nano-bio interface include van der Waals forces, electrostatic interactions, hydrophobic interactions, and receptor-ligand binding. Through electrostatic interactions, nanomaterials anchor to bacterial envelopes, induce changes in membrane potential, and cause depolarization accompanied by loss of membrane integrity. As the physical barricade is disrupted, transport discrepancy, respiration impairment, and intrusion in metabolic pathways are followed, resulting in cell death [50].

Additionally, ROS are intracellularly originated secondary metabolites of oxidative metabolic activity of a bacterial cell. The maintenance of cellular ROS levels is mediated by the endogenous antioxidant defense mechanisms. Nanomaterials produce four different types of ROS with diverse levels of dynamics and activity, including hydrogen peroxide (H_2O_2), singlet oxygen ($^1\text{O}_2$), superoxide radical (O_2^-), and hydroxyl radical (OH). Nanomaterials, such as carbon nanotubes (CNT), fullerenes, TiO_2 , ZnO , CeO_2 and AgNPs, induce oxidative stress as a major mechanism of their bactericidal property. Major causes for ROS development are (i) pro-oxidant functional groups on the ultra-reactive surface, (ii) multivalent surface of NPs due to involvement of transition metal ions in active redox cycling involving Fenton-type or Haber-Weiss reactions, and (iii) cellular internalization of NPs leading to activation of NADPH oxidase or mitochondrial respiration [51, 52].

2.5 Nanotechnology in Wound Healing

The human body is enveloped by skin, the largest organ, covering approximately 2m^2 of an adult's surface area [53]. The skin serves as a protective barrier between the human body and the external environment. It performs multiple functions, including moisture retention, sensory perception, temperature regulation, maintenance of humoral balance, and defense against external pathogens [54]. With prolonged exposure, the skin tolerates the impact of numerous exterior stimuli, injuries triggered by the destruction of the skin's integrity led to ailments. The self-healing property of an organism results in wounds healing within three months, depending upon the injury's severity. The biological activity and behavior of nanoparticles have garnered significant interest among researchers, leading to the development of an increasing number of nanotechnology-based products designed to enhance and accelerate the healing process [43]. Nanotechnology is an emerging and promising field with numerous applications in skin regeneration. Wound healing management is becoming progressively more complex for clinicians, underscoring the urgent requirement for new materials and therapeutic approaches. Advances in nanotechnology, particularly in the areas of nanochemistry and nanomanufacturing, have led to transformative changes in the pharmaceutical and biotechnology sectors. Owing to their exceptional adsorption capacity, antimicrobial properties, and drug-loading capabilities, nanomaterials have recently been widely employed in wound healing [54-56]. Recent discoveries regarding nanomaterial-wound microenvironment interactions have illuminated the mechanisms that account for their therapeutic benefits. Yang and co-workers [57] developed a nanofibrous biomimetic scaffold containing nanoparticles functionalized for the controlled release of two different growth factors in a relayed manner

(fast and sustained release at various phases) (**Figure 5**). The nanofibrous mesh facilitated fibroblast growth and displayed antibacterial effects *in vitro*. With the designed quick releasing of VEGF and slow expelling of PDGF-BB, accelerated wound healing was achieved on a full-thickness rat skin wound model. VEGF helped angiogenesis in an early stage of the healing process, while PDGF-BB improved epithelium regeneration, collagen deposition, and functional tissue remodeling.

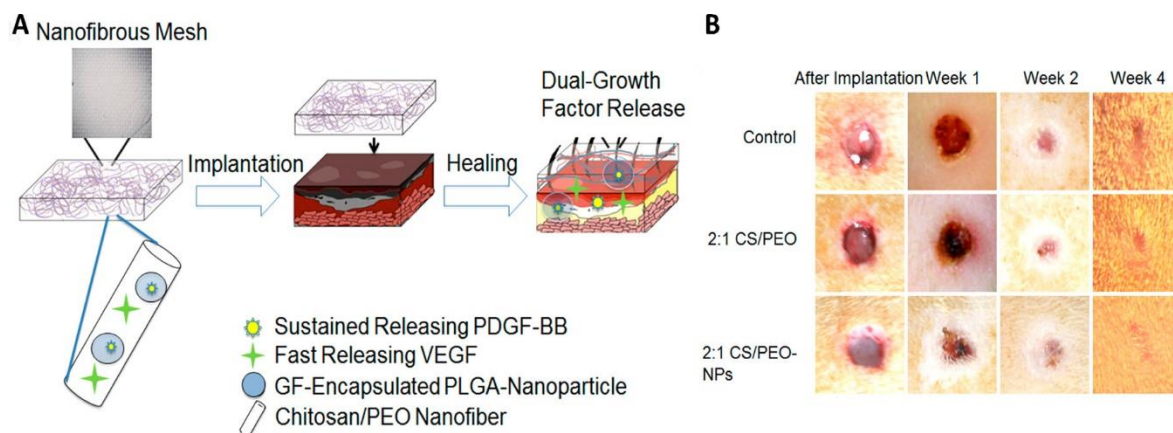


Figure 5. (a) Schematic representation of the nanoparticle-embedded electrospun nanofibers loaded with two growth factors VEGF and PDGF-BB for the wound healing and (b) representative macroscopic view of wound closure after treatment of rat wounds with control, 2:1 chitosan/PEO (CS/PEO) without growth factor, and 2:1 CS/PEO-NPs with nanoparticles and growth factors. Reproduced with permission from ref [58]. Copyright 2023, Elsevier.

The model dressing must penetrate the extracellular matrix (ECM) for a wet milieu, possess antimicrobial properties, and allow the proliferation of cells and angiogenesis, therefore, needing unique constituents with outstanding properties. Due to their structural similarity to the extracellular matrix, nanofibers have attracted significant attention in skin regeneration as scaffolds. Several types of polymeric nanofibers with unique properties have been developed and extensively studied for this purpose. Nanofibrous materials act as delivery systems for medicines, proteins, growth factors, and other compounds in addition to supporting tissue healing [59].

In recent years, a variety of biocompatible self-assembling nanoparticles (NPs) have been developed [60-62]. NPs involves the expansion of materials in the range of nanometers or in the molecular range [63]. Decreasing the size of a material to the nanoscale significantly increases its surface area and surface area to volume ratio, resulting in progressive physiochemical properties. Metal NPs, including silver, gold, and zinc, have shown advantageous properties, including the promotion of wound healing and antibacterial activity [54, 64]. It has been reported that the use of silver NPs shows a good release of anti-inflammatory cytokines in a rapid wound closure with small scare. They promote keratinocyte proliferation, which is essential for epidermal re-epithelization [65]. In the case of gold (Au) NPs, at low concentrations, Au NPs boost keratinocyte growth and healing, and inhibit microbial colonization, where this physiology plays a key role in the wound healing process.

2.6 Emerging nanotechnology applications in cancer therapy and diagnosis

Nano diagnostics refers to the utilization of nanoparticles in clinical diagnostic procedures, aiming to enhance the sensitivity, specificity, and speed of disease detection (**Figure 6**). Nanotechnology offers promising and advantageous approaches for cancer treatment and diagnostic evaluation. NPs have been used to assist traditional cancer which results in easier and faster process. It possess unique properties such as a large surface area, high volume proportion, and excellent targeting capabilities [4]. The integration of nanotechnology with conventional tumor therapies enhances the efficacy of chemoradiotherapy agents while simultaneously reducing the incidence of toxicity and other adverse effects [8, 66-69]. One of the primary benefits is its capacity to elevate the concentration of anti-tumor agents at the tumor site via the enhanced permeability and retention (EPR) effect. Additionally, NPs can target the tumor cell actively by functionalizing their surfaces with various ligands, including antibodies, aptamers, and sugars. It is noteworthy that nanotechnology improves the stability and solubility of antitumor drugs, enhancing their pharmacokinetics and resulting in better therapeutic outcomes. Their low toxicity toward healthy cells improves bioavailability and half-life by enabling effective penetration through epithelial fenestrations and tissue structures [4].

Recent advancements in nanomedicine indicate that nanotechnology-based drug delivery systems hold significant promise for cancer diagnosis, offering the benefit of reduced side effects [70, 71]. Although nanoparticles (NPs) are much smaller than cells, they are nonetheless large enough to encapsulate multiple small-molecule compounds. At the same time, the substantial surface area of nanoparticles enables effective functionalization with ligands (i.e., small molecules, DNA or RNA strands, and peptides). Such modifications can influence factors including blood half-life, biodistribution, interactions within the circulatory system, and reduced toxicity [72]. Several nanoparticle-based platforms are currently available for cancer treatment, including liposomes, polymeric micelles, and human albumin nanoparticles.

The advancement of polymeric nanocarriers to enhance chemotherapeutic efficacy and facilitate intracellular delivery for cancer treatment has generated considerable interest within contemporary pharmaceutical technology [73]. Cheng and co-workers developed multiple hydrogen-bonded supramolecular nanocarriers to enhance the effectiveness of cancer therapy [74]. The results demonstrate that following the drug encapsulation process, a series of in vitro experiments confirmed that the hydrogen-bonded supramolecular nanocarrier material selectively induced apoptotic cell death in cancer cells without significant cytotoxicity toward healthy cells, while exhibiting nonselective cytotoxic effects on both cancerous and normal cells under certain conditions. This suggests that strengthening hydrogen bonding within nanogels is critical for improving the selective cellular uptake and cytotoxicity of drugs, thereby promoting apoptosis in cancer cells [74, 75].

Nanoparticles (NPs) exhibited considerable promises for cancer diagnosis and treatment owing to their capacity to selectively target the specific cells and tissues. NPs have been utilized as drug delivery systems targeting the central nervous system (CNS), where a major challenge owing to the presence of the blood-brain barrier (BBB) which effectively restricts therapeutic agents' penetration into brain tissue. Through precise engineering, NPs can be modified to cross the BBB and deliver drugs directly to the brain, thereby opening new avenues for developing therapeutic strategies against various CNS diseases and brain tumors [76, 77]. Progress in this field has led to one of the most promising applications of nanotechnology in cancer treatment, called nanotheranostics, a unified strategy that merges diagnostic and therapeutic functionalities

into a single platform to improve the effectiveness of cancer management. Nanotheranostics, which integrates imaging and therapeutic agents within a single nanostructure, offers significant advantages over conventional nanomedicine approaches. It enables non-invasive assessment of nanocarrier accumulation at target sites prior to drug release, facilitating patient stratification and enabling personalized nanotherapy based on real-time monitoring [78, 79]. Real-time monitoring and prediction of therapeutic outcomes at delivery site, high-density loading of agents to enhance imaging quality, and controllable activation triggered by biological stimuli or external energy sources collectively underscore the efficacy of nanotheranostics technology. Moreover, the system's intrinsic ability to directly report drug release events further enhances precision and control in cancer treatment strategies [70, 80]. Nanotheranostics has revolutionized cancer therapy by providing non-invasive assessment of nanocarrier accumulation in the absence of therapeutic payloads. This capability enables personalized interventions based on real-time monitoring and efficient delivery of both therapeutic agents and imaging components, thereby significantly improving the sensitivity and efficacy in cancer treatment [80].

Owing to their diverse biological applications, nanoparticles are categorized into various types—such as metallic, magnetic, polymeric, metal oxide, quantum dots, graphene, fullerenes, liposomes, carbon nanotubes, and dendrimers—which are extensively employed in cancer detection and imaging [81]. The distinctive chemical, optical, magnetic, and physical characteristics of these nanomaterials facilitate the development of imaging probes with enhanced contrast, increased sensitivity, controlled biodistribution, and superior spatial resolution across diverse imaging modalities, including MRI, PET, SPECT, and ultrasound (6). Imaging plays a fundamental role as an initial step in cancer diagnosis and therapy, consequently imaging technology continues to be developed to enable more effective detection of various cancer types.

Table 1. Application of nanoparticles in cancer diagnosis [4]

| Type of Nanoparticles | Application of Nanoparticles | Properties | Example of Cancer Diagnosis |
|------------------------------|---|--|---|
| Carbon-based nanoparticles | Used for cancer detection and diagnosis | Excellent physio-chemical properties, including high-level penetration into the cell membrane, high surface area, and high capacity for drug loading | Both in vivo and in vitro studies show that nanoparticles are an effective contrast material for both photoacoustic and ultrasound imaging. |
| Ceramic nanoparticles | For better drug delivery and cancer imaging | High biocompatibility | Clinical studies on gold NS-based photothermal therapy are under consideration for ablating repetitive head and neck |

| | | | |
|---------------------------|--|--|---|
| | | | tumors, as well as cancer imaging. |
| Metallic nanoparticle | Detection and imaging of cancer cells/ tissues | Magnetic nanoparticles are crucial for metastatic breast cancer detection and protection | Cancer imaging |
| Polymeric nanoparticles | Drug delivery and diagnostics | Surrounded by a polymer shell | Block copolymer-coated nanoparticles (TPIONPs) connected with RGD peptides and dye molecules to target tumors. |
| Lipid-based nanoparticles | Use as a drug delivery carrier and drug delivery system for cancer diagnosis | Better biocompatibility and low toxicity in comparison with inorganic nanoparticles | Conjugation of anti-HER2 antibodies on phospholipid-coated QDs revealed the ability to target HER2-positive tumors. |

The primary method to detect cancer cells relies on the binding of nanoparticle-conjugated probes to surface markers on cancer cells as well as to cells capable of internalizing the probes to detect genetic content wherein they are linked to specific targeting molecules such as proteins, short peptides, antibodies, or oligonucleotide aptamers [82].

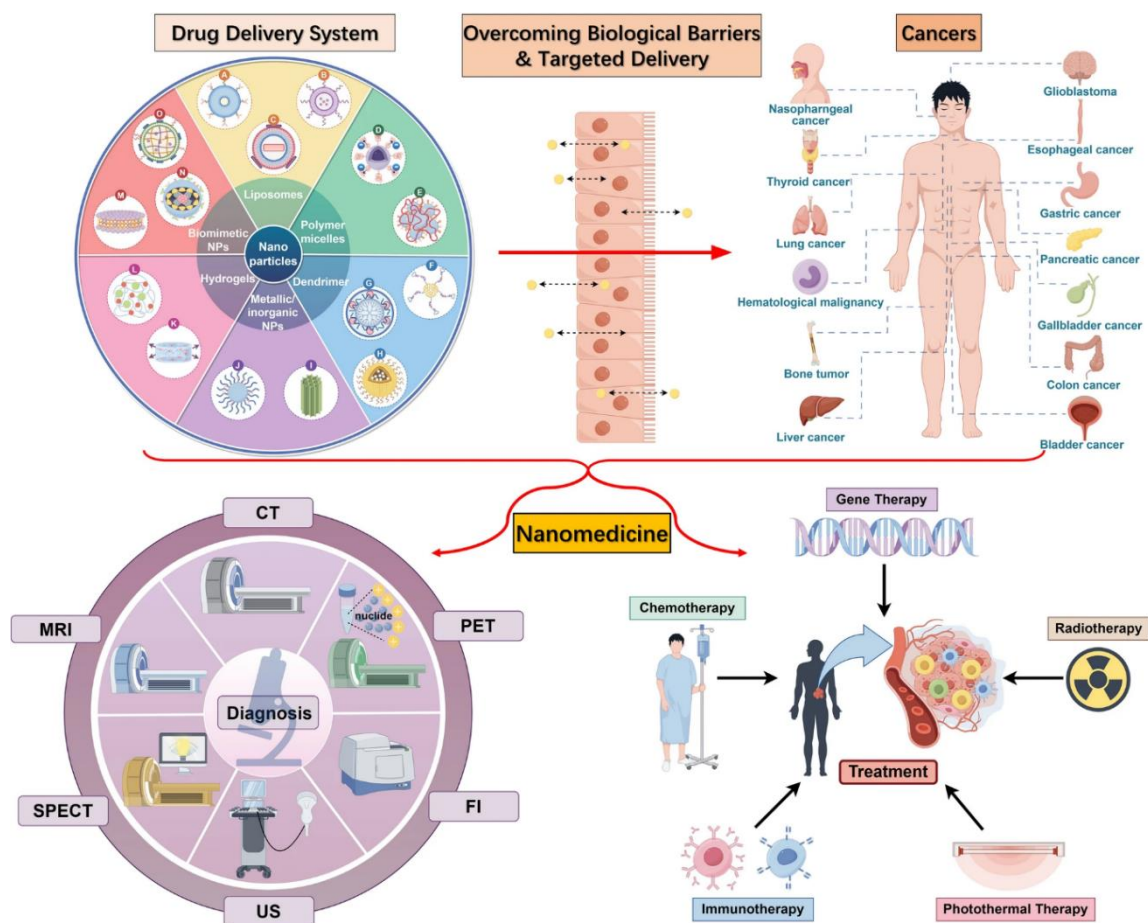


Figure 6. Applications of nanomedicine in cancer detection and therapy. CT computed tomography, MRI magnetic resonance imaging, PET positron emission tomography, SPECT single-photon emission tomography, US ultrasound, FI fluorescence imaging. Reproduced with permission from ref [8]. Copyright 2024, Nature.

3. Bibliometric Analysis of Nanotechnology as Biomedical Application in Asian Region

Nanotechnology presents opportunities for the development of revolutionary new products. The market potential for nanomaterial-based products is substantial, encompassing diverse industries such as environmental management, energy, healthcare, construction, textiles, automotive, household, and personal care. Various technological and business forecasts consistently affirm that nanotechnology will be a key driver and determinant of the future. Consequently, numerous countries, enterprises, and research institutions worldwide have taken these forecasts seriously and, after evaluating the prospects of nanotechnology, have invested significant financial resources. These projections have further intensified competition among research institutions, companies, governments, and other stakeholders. UNESCO has identified ten key nanotechnology applications aligned with the United Nations Millennium Development Goals (UN MDGs) - (a) Energy storage, production, and conversion; (b) Optimization of agricultural productivity; (c) Water treatment and reuse; (d) Diagnostic and screening procedures for diseases; (e) Drug delivery systems; (f) Food production and storage management; (g) Air pollution control and remediation; (h) Construction; (i) Health monitoring; and (j) Vector and pest detection and control. From these findings, it can be concluded that nanotechnology possesses limitless potential and can be applied across all fields of human needs. This has driven rapid advancements in nanotechnology, particularly in biomedical

applications such as disease diagnosis and screening as well as drug delivery systems, including in Asian countries. According to Scopus data from 2015 to 2025, there has been a significant increase in research output related to nanotechnology in biomedical engineering, as summarized in **Figure 7**. **Figure 7a** illustrates the annual growth trend of research documents on nanotechnology in biomedical engineering in Asia, **Figure 7b** shows the distribution of sources of these research documents over the same period, **Figure 7c** presents the types of research documents published, and **Figure 7d** depicts the main research topics within this field during the timeframe. These data demonstrate the substantial influence and pivotal role of nanotechnology in advancing various scientific disciplines in the future.

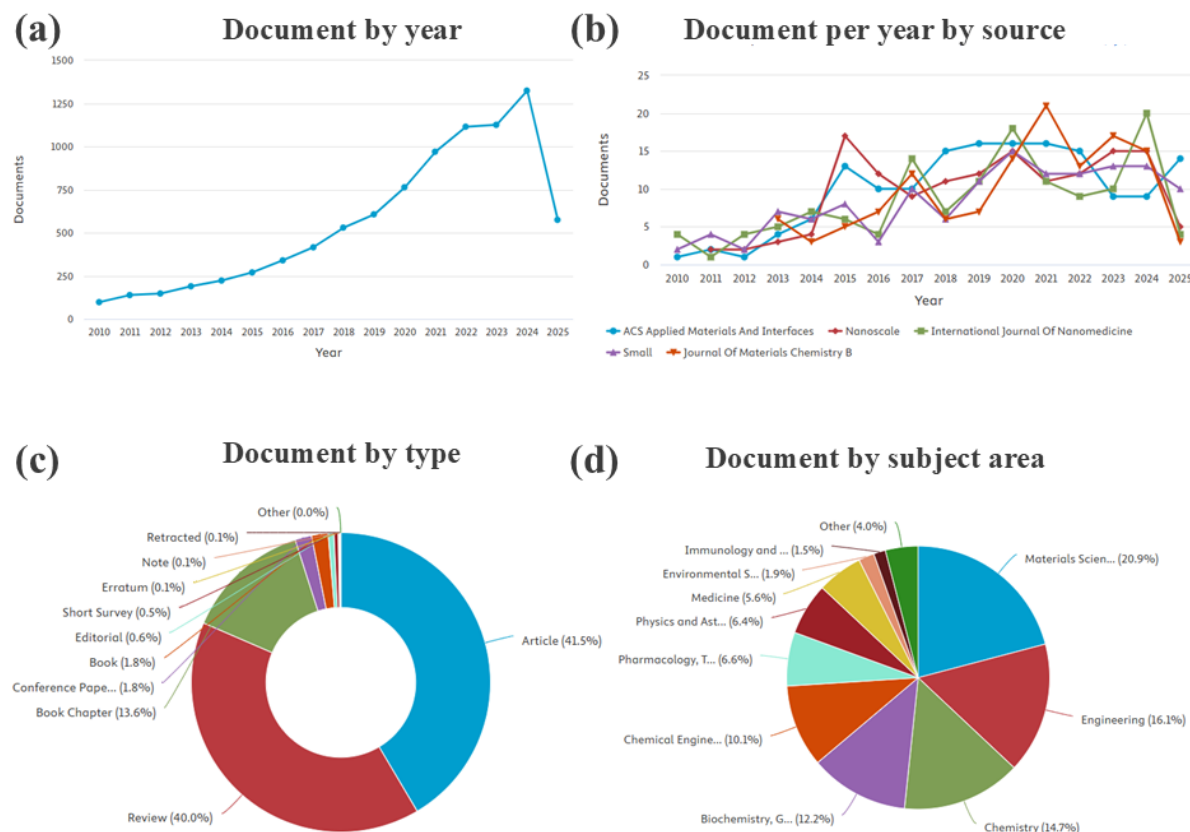


Figure 7. Summarized of nanotechnology in biomedical applications research around Asian region by Scopus 2015-2025

Furthermore, we conducted a bibliometric analysis on “nanotechnology as a biomedical application in the Asian region” using VOS viewer software (version 1.6.18, Liden University Center for Science and Technology), as illustrated in **Figure 8**. This software provides mapping tools to facilitate data analysis with a focus on the application of nanotechnology in biomedical fields. The data source was extracted from the Scopus database through a keyword search with the following Boolean operators TITLE-ABS-KEY: (“nanotechnology” OR “nanomaterial” OR “nanomedicine” AND “biomedical application” OR “biomedicine”). Scopus was chosen because of its extensive coverage of peer-reviewed journals in nanotechnology and the biomedical sciences. Our analysis included 8,813 Scopus documents from 2015–2025, concentrating on Asian countries and restricting subject areas to materials science (4,507 documents), chemistry (3,165 documents), engineering (3,473 documents), biochemistry, genetics, and molecular biology (2,628 documents), chemical

document, and no minimum citation threshold. The five countries with the highest levels of co-authorship collaboration were China, India, South Korea, Singapore, and Hong Kong. Furthermore, we conducted a co-citation analysis to identify documents that are frequently cited together by other articles. Through this approach, we examined co-citation patterns across countries to determine which countries are most frequently cited in the context of nanotechnology as a biomedical application within the Asian region. The 5 countries with the highest co-citation strength are China, India, Singapore, Malaysia, and Taiwan (**Figure 8c**). This is influenced by several factors: the strengthening of infrastructure for nanotechnology development, international cooperation between countries with research institutions, universities, and the biomedical industry, and a high level of investment in research and development (R&D). This indicates that global nanomedicine innovation is advancing in Asia as a major centre for research, particularly in the development of antibacterial agents, antibiotics, wound healing therapies and tissue engineering (**Figure 8d**). Additionally, we performed a keyword co-occurrence analysis to identify emerging research themes in the field of nanotechnology as a biomedical application across Asian countries. As shown in **Figure 8d**, the keyword co-occurrence overlay map visualizes 1,000 keywords organized into 4 major thematic clusters: medical applications, biomedical applications, nanotechnology, and drug delivery, those reflecting the dominant areas of research focus. Based on the yellow overlays in the map, it is evident that since 2021, research on nanotechnology as a biomedical application in the Asian region has expanded rapidly, encompassing the development of antibacterial agents, antibiotics, wound healing therapies, tissue engineering, and various other related fields.

4. Current Challenges and Future Opportunities

The application of nanotechnology in medicine plays a pivotal role in balancing therapeutic efficacy and toxicity. The integration of chemical, biological, and physical properties within nanotechnology enables more comprehensive exploration of *in vivo* behavior. A critical aspect of translating nanomedicine into clinical applications involves evaluating the biodistribution of nanocompounds following administration in both preclinical and clinical studies. Each imaging and monitoring technology possesses distinct characteristics, limitations, and capabilities in assessing real-time nanoparticle accumulation at the cellular, tissue, and organ levels. While numerous benefits of nanotechnology for biomedical applications have been extensively discussed, several key challenges remain to be addressed in their development. One of them is the potential side effects of nanomedicine, which differ significantly from conventional drugs. The toxicity profile of particulate matter is distinct from that of chemical substances, which may or may not dissolve within biological matrices, thereby substantially influencing the possibility of organ exposure. Due to their nanoscale dimensions, nanoparticles can traverse multiple physiological barriers within the body. One of the most critical barriers is the blood-brain barrier (BBB), its penetration by nanoparticles can potentially affect brain function through various mechanisms. Furthermore, the nanoscale size of nanoparticles allows them to readily permeate cellular membranes, intracellular organelles, and even the nucleus. Nanomedicine-based drug delivery systems can leverage a wide range of biological substances and chemical structures, as previously discussed. However, it is important to note that the potential for nanoparticle-cell interactions that may induce toxicity is highly dependent on the specific structure and formulation of the nanoparticles. It is noteworthy that the evaluation of nano compound biodistribution post-administration remains a key factor in the translational assessment of nanomedicine. Various studies have demonstrated that each technology used in this analysis offers

unique strengths, limitations, and capabilities in monitoring real-time nanoparticle accumulation across cellular, tissue, and organ levels.

CONCLUSION

Nanotechnology has emerged as a transformative force in biomedical science, enabling breakthroughs in diagnostics, targeted drug delivery, vaccines, tissue engineering, wound healing, infection control, and cancer theranostics. The narrative review highlights how nanoscale materials such as liposomes, polymeric nanoparticles, metallic nanoparticles, nanofibers, and gold nanoparticles, enhance therapeutic precision, reduce toxicity and side effects, improve drug bioavailability, and support tissue regeneration through mechanisms like controlled release and immune modulation. Bibliometric analysis of 8,813 Scopus documents (2015–2025) confirms Asia's leadership, with China, India, South Korea, Singapore, and Taiwan dominating publications, citations, and collaborations in key themes like drug delivery systems, biomedical materials, tissue engineering, and antimicrobial technologies. These findings reveal an expanding interdisciplinary research ecosystem and identify gaps in toxicity research addressable through enhanced regional cooperation.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the financial support of internal funding in Riset Kolaborasi Internasional dengan Perguruan Tinggi Luar Negeri (RKI PT LN) Universitas Negeri Surabaya.

CONFLICT OF INTERESTS

The authors declare no competing financial interest.

REFERENCES

- Berthiaume, F., T.J. Maguire, and M.L. Yarmush, *Tissue Engineering and Regenerative Medicine: History, Progress, and Challenges*. 2011. **2**(Volume 2, 2011): p. 403-430.
- Ramos, A.P., et al., *Biomedical applications of nanotechnology*. *Biophys Rev*, 2017. **9**(2): p. 79-89.
- Goncalves, A.G., et al., *Recombinant protein polymer-antibody conjugates for applications in nanotechnology and biomedicine*. *Advanced Drug Delivery Reviews*, 2022. **191**: p. 114570.
- Alrushaid, N., et al., *Nanotechnology in Cancer Diagnosis and Treatment*. *Pharmaceutics*, 2023. **15**(3).
- Thi, T.T.H., et al., *Lipid-Based Nanoparticles in the Clinic and Clinical Trials: From Cancer Nanomedicine to COVID-19 Vaccines*. *Vaccines (Basel)*, 2021. **9**(4).
- Bayda, S., et al. *The History of Nanoscience and Nanotechnology: From Chemical-Physical Applications to Nanomedicine*. *Molecules*, 2020. **25**, DOI: 10.3390/molecules25010112.
- Bayda, S., et al., *The History of Nanoscience and Nanotechnology: From Chemical-Physical Applications to Nanomedicine*. *Molecules*, 2019. **25**(1).
- Wang, B., et al., *Current advance of nanotechnology in diagnosis and treatment for malignant tumors*. *Signal Transduction and Targeted Therapy*, 2024. **9**(1): p. 200.
- Saji, V.S., H.C. Choe, and K.W.K. Yeung, *Nanotechnology in biomedical applications: a review*. *International Journal of Nano and Biomaterials*, 2010. **3**(2): p. 119-139.
- Youtie, J. and P. Shapira, *Mapping the nanotechnology enterprise: a multi-indicator analysis of emerging nanodistricts in the US South*. *The Journal of Technology Transfer*, 2008. **33**(2): p. 209-223.
- Feynman, R., *There's plenty of room at the bottom*, in *Feynman and computation*. 2018, CRC Press. p. 63-76.

12. Elzein, B., *Nano Revolution: "Tiny tech, big impact: How nanotechnology is driving SDGs progress"*. Heliyon, 2024. **10**(10): p. e31393.
13. Márquez, P.G., F.J. Wolman, and R.J. Glisoni, *Nanotechnology platforms for antigen and immunostimulant delivery in vaccine formulations*. Nano Trends, 2024. **8**: p. 100058.
14. Rodrigues, C.M.C. and S.A. Plotkin, *Impact of Vaccines; Health, Economic and Social Perspectives*. Front Microbiol, 2020. **11**: p. 1526.
15. Delany, I., R. Rappuoli, and E. De Gregorio, *Vaccines for the 21st century*. EMBO Mol Med, 2014. **6**(6): p. 708-20.
16. Pardi, N., M.J. Hogan, and D. Weissman, *Recent advances in mRNA vaccine technology*. Curr Opin Immunol, 2020. **65**: p. 14-20.
17. Park, J.W., et al., *mRNA vaccines for COVID-19: what, why and how*. Int J Biol Sci, 2021. **17**(6): p. 1446-1460.
18. Zhou, W., et al., *Vaccines' New Era-RNA Vaccine*. Viruses, 2023. **15**(8).
19. Heng, W.T., J.S. Yew, and C.L. Poh, *Nanovaccines against Viral Infectious Diseases*. Pharmaceutics, 2022. **14**(12).
20. Cui, J., et al., *Circular RNAs: Biomarkers of cancer*. Cancer Innov, 2022. **1**(3): p. 197-206.
21. Zhao, W., et al., *Circular RNAs: A novel target among non-coding RNAs with potential roles in malignant tumors (Review)*. Mol Med Rep, 2019. **20**(4): p. 3463-3474.
22. Bollman, B., et al., *An optimized messenger RNA vaccine candidate protects non-human primates from Zika virus infection*. NPJ Vaccines, 2023. **8**(1): p. 58.
23. Yang, Y., et al., *Extensive translation of circular RNAs driven by N6-methyladenosine*. Cell Research, 2017. **27**(5): p. 626-641.
24. Legnini, I., et al., *Circ-ZNF609 Is a Circular RNA that Can Be Translated and Functions in Myogenesis*. Mol Cell, 2017. **66**(1): p. 22-37.e9.
25. de Alwis, R., et al., *A single dose of self-transcribing and replicating RNA-based SARS-CoV-2 vaccine produces protective adaptive immunity in mice*. Mol Ther, 2021. **29**(6): p. 1970-1983.
26. Essink, B., et al., *The safety and immunogenicity of two Zika virus mRNA vaccine candidates in healthy flavivirus baseline seropositive and seronegative adults: the results of two randomised, placebo-controlled, dose-ranging, phase 1 clinical trials*. Lancet Infect Dis, 2023. **23**(5): p. 621-633.
27. Cordeiro, A.S., et al. *Nanovaccine Delivery Approaches and Advanced Delivery Systems for the Prevention of Viral Infections: From Development to Clinical Application*. Pharmaceutics, 2021. **13**, DOI: 10.3390/pharmaceutics13122091.
28. Chenthamara, D., et al., *Therapeutic efficacy of nanoparticles and routes of administration*. Biomaterials Research, 2019. **23**(1): p. 20.
29. Jeevanandam, J., et al., *Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations*. Beilstein Journal of Nanotechnology, 2018. **9**: p. 1050-1074.
30. Gomes, A.C., M. Mohsen, and M.F. Bachmann, *Harnessing Nanoparticles for Immunomodulation and Vaccines*. Vaccines (Basel), 2017. **5**(1).
31. Oyewumi, M.O., A. Kumar, and Z. Cui, *Nano-microparticles as immune adjuvants: correlating particle sizes and the resultant immune responses*. Expert Rev Vaccines, 2010. **9**(9): p. 1095-107.
32. Xiang, S.D., et al., *Pathogen recognition and development of particulate vaccines: does size matter?* Methods, 2006. **40**(1): p. 1-9.

33. Genito, C.J., et al., *Considerations for Size, Surface Charge, Polymer Degradation, Co-Delivery, and Manufacturability in the Development of Polymeric Particle Vaccines for Infectious Diseases*. Advanced NanoBiomed Research, 2021. **1**(3): p. 2000041.
34. Bachmann, M.F. and G.T. Jennings, *Vaccine delivery: a matter of size, geometry, kinetics and molecular patterns*. Nat Rev Immunol, 2010. **10**(11): p. 787-96.
35. Reddy, S.T., et al., *In vivo targeting of dendritic cells in lymph nodes with poly(propylene sulfide) nanoparticles*. J Control Release, 2006. **112**(1): p. 26-34.
36. Raval, N., et al., *Chapter 17 - Surface Modifications of Biomaterials and Their Implication on Biocompatibility*, in *Biomaterials and Bionanotechnology*, R.K. Tekade, Editor. 2019, Academic Press. p. 639-674.
37. Hu, X., et al., *Surface modifications of biomaterials in different applied fields*. RSC Advances, 2023. **13**(30): p. 20495-20511.
38. Murphy, W.L., T.C. McDevitt, and A.J. Engler, *Materials as stem cell regulators*. Nat Mater, 2014. **13**(6): p. 547-57.
39. Benčina, M., et al. *Use of Plasma Technologies for Antibacterial Surface Properties of Metals*. Molecules, 2021. **26**, DOI: 10.3390/molecules26051418.
40. Xiang, E., et al. *Nanosurface Texturing for Enhancing the Antibacterial Effect of Biodegradable Metal Zinc: Surface Modifications*. Nanomaterials, 2023. **13**, DOI: 10.3390/nano13132022.
41. Gautam, S., et al., *Recent advancements in nanomaterials for biomedical implants*. Biomedical Engineering Advances, 2022. **3**: p. 100029.
42. Wang, D.-Y., et al., *Beyond surface modification strategies to control infections associated with implanted biomaterials and devices - Addressing the opportunities offered by nanotechnology*. Biomaterials, 2024. **308**: p. 122576.
43. Abaszadeh, F., et al., *Nanotechnology development in surgical applications: recent trends and developments*. European Journal of Medical Research, 2023. **28**(1): p. 537.
44. Yi, C., et al., *Gold Nanoparticles Promote Osteogenic Differentiation of Mesenchymal Stem Cells through p38 MAPK Pathway*. ACS Nano, 2010. **4**(11): p. 6439-6448.
45. Bapat, R.A., et al., *Recent advances of gold nanoparticles as biomaterial in dentistry*. International Journal of Pharmaceutics, 2020. **586**: p. 119596.
46. Chakraborty, N., et al., *Nanobiotics against antimicrobial resistance: harnessing the power of nanoscale materials and technologies*. Journal of Nanobiotechnology, 2022. **20**(1): p. 375.
47. Eleraky, N.E., et al., *Nanomedicine Fight against Antibacterial Resistance: An Overview of the Recent Pharmaceutical Innovations*. Pharmaceutics, 2020. **12**(2).
48. Shabatina, T., et al., *Nanoparticles of Bioactive Metals/Metal Oxides and Their Nanocomposites with Antibacterial Drugs for Biomedical Applications*. Materials (Basel), 2022. **15**(10).
49. Gupta, A., et al., *Combatting antibiotic-resistant bacteria using nanomaterials*. Chemical Society Reviews, 2019. **48**(2): p. 415-427.
50. Lu, X., et al., *Enhanced antibacterial activity through the controlled alignment of graphene oxide nanosheets*. Proc Natl Acad Sci U S A, 2017. **114**(46): p. E9793-e9801.
51. Hamal, D.B., et al., *A multifunctional biocide/sporicide and photocatalyst based on titanium dioxide (TiO₂) codoped with silver, carbon, and sulfur*. Langmuir, 2010. **26**(4): p. 2805-10.
52. Ilhami, F.B., S.-Y. Huang, and C.-C. Cheng, *Multi-Biofunctional Silver-Containing Metallosupramolecular Nanogels for Efficient Antibacterial Treatment and Selective Anticancer Therapy*. Acta Biomaterialia, 2022. **151**: p. 576-587.

53. Dąbrowska, A.K., et al., *The relationship between skin function, barrier properties, and body-dependent factors*. *Skin Res Technol*, 2018. **24**(2): p. 165-174.
54. Kushwaha, A., L. Goswami, and B.S. Kim, *Nanomaterial-Based Therapy for Wound Healing*. *Nanomaterials* (Basel), 2022. **12**(4).
55. Berthet, M., et al., *Nanoparticle-Based Dressing: The Future of Wound Treatment?* *Trends Biotechnol*, 2017. **35**(8): p. 770-784.
56. Wu, C.-Y., et al. *Conductive Supramolecular Polymer Nanocomposites with Tunable Properties to Manipulate Cell Growth and Functions*. *International Journal of Molecular Sciences*, 2022. **23**, DOI: 10.3390/ijms23084332.
57. Xie, Z., et al., *Dual growth factor releasing multi-functional nanofibers for wound healing*. *Acta Biomaterialia*, 2013. **9**(12): p. 9351-9359.
58. Sangnim, T., et al., *Nanomaterials in the Wound Healing Process: New Insights and Advancements*. *Pharmaceutics*, 2024. **16**(3).
59. Chopra, H., et al., *Bacterial Nanocellulose based Wound Dressings: Current and Future Prospects*. *Curr Pharm Des*, 2022. **28**(7): p. 570-580.
60. Monteiro, N., et al., *Antibacterial activity of chitosan nanofiber meshes with liposomes immobilized releasing gentamicin*. *Acta Biomater*, 2015. **18**: p. 196-205.
61. Thapa, R.K., K.L. Kiick, and M.O. Sullivan, *Encapsulation of collagen mimetic peptide-tethered vancomycin liposomes in collagen-based scaffolds for infection control in wounds*. *Acta Biomater*, 2020. **103**: p. 115-128.
62. Patel, K.K., et al., *Antibiofilm Potential of Silver Sulfadiazine-Loaded Nanoparticle Formulations: A Study on the Effect of DNase-I on Microbial Biofilm and Wound Healing Activity*. *Mol Pharm*, 2019. **16**(9): p. 3916-3925.
63. Shah, M.R., et al., *Morphological analysis of the antimicrobial action of silver and gold nanoparticles stabilized with ceftriaxone on Escherichia coli using atomic force microscopy*. *New Journal of Chemistry*, 2014. **38**(11): p. 5633-5640.
64. Zhang, Y., et al., *Functional carbohydrate-based hydrogels for diabetic wound therapy*. *Carbohydr Polym*, 2023. **312**: p. 120823.
65. Rezvani Ghomi, E., M. Niazi, and S. Ramakrishna, *The evolution of wound dressings: From traditional to smart dressings*. *Polymers for Advanced Technologies*, 2023. **34**(2): p. 520-530.
66. Shi, J., et al., *Cancer nanomedicine: progress, challenges and opportunities*. *Nat Rev Cancer*, 2017. **17**(1): p. 20-37.
67. Su, X., et al., *Advances in the application of nanotechnology in reducing cardiotoxicity induced by cancer chemotherapy*. *Semin Cancer Biol*, 2022. **86**(Pt 2): p. 929-942.
68. Wei, G., et al., *Recent progress in nanomedicine for enhanced cancer chemotherapy*. *Theranostics*, 2021. **11**(13): p. 6370-6392.
69. Wu, W., Y. Pu, and J. Shi, *Nanomedicine-enabled chemotherapy-based synergetic cancer treatments*. *Journal of Nanobiotechnology*, 2022. **20**(1): p. 4.
70. Rashidi, N., et al., *Nanoparticles in cancer diagnosis and treatment: Progress, challenges, and opportunities*. *Journal of Drug Delivery Science and Technology*, 2024. **95**: p. 105599.
71. Fan, W.-L., et al., *Hydrogen-bonded cytosine-endowed supramolecular polymeric nanogels: Highly efficient cancer cell targeting and enhanced therapeutic efficacy*. *Journal of Colloid and Interface Science*, 2024. **665**: p. 329-344.
72. Kaymaz, S.V., et al., *Nanomaterial surface modification toolkit: Principles, components, recipes, and applications*. *Advances in Colloid and Interface Science*, 2023. **322**: p. 103035.

73. Ilhami, F.B., E.A. Bayle, and C.-C. Cheng, *Complementary Nucleobase Interactions Drive Co-Assembly of Drugs and Nanocarriers for Selective Cancer Chemotherapy*. *Pharmaceutics*, 2021. **13**(11).
74. Ilhami, F.B., et al., *Hydrogen Bond Strength-Mediated Self-Assembly of Supramolecular Nanogels for Selective and Effective Cancer Treatment*. *Biomacromolecules*, 2021. **22**(10): p. 4446-4457.
75. Ilhami, F.B., et al., *Self-assembled nanoparticles formed via complementary nucleobase pair interactions between drugs and nanocarriers for highly efficient tumor-selective chemotherapy*. *Materials Chemistry Frontiers*, 2021.
76. Hassanzadeganroudsari, M., et al., *Targeted nano-drug delivery system for glioblastoma therapy: In vitro and in vivo study*. *Journal of Drug Delivery Science and Technology*, 2020. **60**: p. 102039.
77. Ahlawat, J., et al., *Nanocarriers as Potential Drug Delivery Candidates for Overcoming the Blood–Brain Barrier: Challenges and Possibilities*. *ACS Omega*, 2020. **5**(22): p. 12583-12595.
78. Durymanov, M.O., A.A. Rosenkranz, and A.S. Sobolev, *Current Approaches for Improving Intratumoral Accumulation and Distribution of Nanomedicines*. *Theranostics*, 2015. **5**(9): p. 1007-1020.
79. Pérez-Herrero, E. and A. Fernández-Medarde, *Advanced targeted therapies in cancer: Drug nanocarriers, the future of chemotherapy*. *European Journal of Pharmaceutics and Biopharmaceutics*, 2015. **93**: p. 52-79.
80. Gawne, P.J., et al., *New opportunities and old challenges in the clinical translation of nanotheranostics*. *Nature Reviews Materials*, 2023. **8**(12): p. 783-798.
81. Khan, I., K. Saeed, and I. Khan, *Nanoparticles: Properties, applications and toxicities*. *Arabian Journal of Chemistry*, 2019. **12**(7): p. 908-931.
82. Zhang, Y., et al., *Nanotechnology in cancer diagnosis: progress, challenges and opportunities*. *Journal of Hematology & Oncology*, 2019. **12**(1): p. 137.