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## REVIEW ARTICLE

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# Overview of nanobiotechnological perspectives and development of nano solutions in the fight against cancer

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### Abstract

It is a branch of science that deals with the nanoscale structures of biological systems, formed by the combination of biotechnology and nanotechnology main branches of science. Nano biotechnology science causes structural changes in biological systems by interacting with nanoscale materials and living molecules. Therefore, nanobiotechnology science has a great place in cancer treatment. With nanobiotechnology, more effective, efficient and safe treatment methods are developed through nano-sized materials used in cancer diagnosis and treatment. In this field, highly functional materials such as nanoparticles, nanocapsules and nanotubes are used. Nanoparticles, due to their size and surface properties, communicate with the signals of cancer cells and facilitate the delivery of the drug only to cancer cells. The role of nanobiotechnology in cancer treatment is based on the development of cancer cell targeted therapies. In addition, with the advantages offered by nanoscale materials, personalised treatment strategies can be applied in cancer treatment. Personalised cancer treatment allows the development of treatment regimens tailored to the genetic profile and biological structure of patients. Within the scope of this review, studies on what kind of perspectives and what kind of solutions can be brought in the fight against cancer from a general perspective of nanobiotechnology are mentioned. In this context, it is predicted that nanobiotechnology will play an important role in future cancer treatment and research in this field may contribute to the development of more specific and effective treatments.

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## 1. Introduction

Nanobiotechnology is a discipline that is a combination of biotechnology and nanotechnology. Nanotechnology is a field that investigates the interaction of biological systems with nanoscale structures. While the term "nano" refers to a reproduction of a billionth of a metre, "biotechnological" investigates the technological recording of biological systems and transforms them into commercial products. The aim of nano-biotechnology is to create new solutions by understanding biological systems at the nanoscale through the combination of these two fields [1]. This technology offers revolutionary developments in many fields such as health, environment and industry by directly using systems and molecules [2]. The first development of nano-biotechnology started in the late 1980s. Based on basic knowledge, this field has been exploring other applications of biotechnology for health from the road since the late 1990s. Especially useful applications such as cancer, genetic engineering and drug delivery systems are available. Recently, nano-biotechnology is becoming an important area of notification and commercialisation. Nano-biotechnology has great potential especially in cancer treatment. Cancer is one of the leading causes of death worldwide and the challenges to its treatment are often due to the damage done to the healthy and the continuous emergence of tumour suppressors. Conventional therapeutic treatments have difficulties in eliminating cancer and can damage healthy tissue [3]. Nanobiotechnology aims to improve this problem by utilising nano-sized features that can reach cancer. Devices such as nanoparticles, nanocapsules and nanosensors can target cancerous targets, ensuring that they are delivered to the right place and that the treatment is delivered specifically for treatment [4]. One of the contributions of nanobiotechnology to cancer treatment is the early detection of cancer. Nano biosensors and application monitoring systems can detect tumours early and initiate treatment early [5]. In addition, cancer treatment can be personalised using nanoparticles. Nanoparticles offer a unique and more effective therapeutic approach by targeting, developing and delivering products [1]. In this section, the role of nanobiotechnology in cancer treatment and current applications will be discussed. Nanobiotechnology has the potential to usher in a new era of cancer therapy by making treatment more effective, efficient and less invasive. Expanding the use of nanobiotechnology in cancer treatment can improve treatment outcomes and increase survival rates.

## 2. Fundamentals of nanotechnology and its impact on biotechnology

### 2.1. Basic introduction to nanobiotechnology

Nanotechnology is a sub-discipline that allows working with materials from 1 to 10 nanometres in size. The unit of nanometre size used in this field is expressed as 'nm.'. When nanometre-sized materials are examined, they show variable properties. As an example of this situation, although gold is a bright yellow metal, it can have different colours and properties when examined at nanometer size. For this reason, research at nano dimensions should be more sensitive [6], [7]. For this reason, precise studies should be carried out with nanoscale materials 'nanoparticles'. Nanoparticles are generally used as building materials;

- Metals: Gold, silver, titanium dioxide.
- Polymers: Plastic-based nanoparticles.
- Carbon: Carbon-based nanoparticles such as graphene, carbon nanotubes or fullerene.
- Ceramics: Ceramic nanoparticles such as silica or zirconia are used [8], [9], [10].
- These structures are carefully designed to be applied on biological systems. Nanoparticles that can directly interact with biological structures such as DNA, cells, proteins and enzymes provide precise and targeted work in the field of biotechnology. [11], [12], [13].

## 2.2. General Principles of Nanobiotechnology

Nanobiotechnology also aims to develop new materials, devices and methods that interact with biological structures at the nanoscale. Nanoparticles used in this branch of science are divided into types according to their intended use in treatment or diagnosis [1], [14], [15].

- **Nanoparticles:** These nano-sized particles have the ability to easily interact with biological molecules. They are especially used in nano-sized studies such as drug delivery to biological targets, providing catalyst function in biological and chemical reactions.

- **Nanocapsules:** They play a role in the safe delivery of drugs and genetic materials to target tissues. It facilitates treatments by passing biological barriers such as lipid membranes in cells [5], [16], [17].

- **Nanotubes and Nanofibres:** They are high conductivity structures used to reconstruct and repair damaged cellular structures, especially in the field of tissue engineering. In recent years, these materials have also been used to return nerve cells that do not normally have the ability to proliferate to their biologically active form.

- **Nanosensors:** These are structures that enable instant monitoring of biological processes and positive results in early diagnosis of diseases. These structures play an important role in the early diagnosis of diseases such as cancer by interacting with biomarkers in the body. With these structures, nanotechnology and biotechnology branches of science become interconnected with each other.

Materials used in nanobiotechnology interact physically and chemically with biological substances. Thanks to these properties, they play an important role in early diagnosis and disease treatment. In addition to these functions; the sensitivity offered by nanotechnology to science in areas such as drug delivery to target cells, gene therapy and biosensors offers effective and highly accurate solutions [6], [18], [19], [20], [21]. Substances such as nanoparticles, nanocapsules, nanotubes are powerful tools in the world of science in the diagnosis and treatment of diseases thanks to their properties. In this way, the door is now opened to revolutionary treatments [22].

## 2.3. Application areas of nanobiotechnology

One of the most widely used areas of nanobiotechnology is the biomedical field. Thanks to the devices and systems prepared at nano scales, a great degree of convenience and high success is now provided in the diagnosis and treatment of diseases. In the following headings, the general application areas of nanobiotechnology are mentioned more comprehensively [23], [24].

### 2.3.1. Drug transport systems

Conventional drug therapies are currently more widely used than nanobiotechnology. Drug forms such as enteric tablets, film-coated tablets, sugar-coated tablets, capsules and softgels have the ability to dissolve in target organs such as the mouth, stomach or small intestine. For example, drug forms designed to dissolve only in the small intestine have been developed. However, these drug forms can be metabolised outside the target tissue and cause side effects [25], [26]. Prevention of such unwanted side effects is provided by nanobiotechnology. By using nano-sized particles, targeted effect is achieved with maximum stability. For example, nanoparticles have the ability to direct drugs to specific cells or tissues. In this way, it increases the positive effects of treatments while reducing side effects [18], [25], [26], [27]. These nanoparticles, which are especially effective in cancer treatment, enable specific targeting of cancerous cells. There are also nanoparticles designed for use other than cancer treatment. Another disease that requires more application precision than cancer treatment is genetic diseases. In the next section, information about gene therapies is given.

### 2.3.2. Gene therapies

Gene therapy is a method that aims to treat disease by transferring genetic material directly into cells. Nanoparticles are used to provide direct interaction with cells. Thanks to nanoparticles, target genes are treated in a specific way [28], [29], [30], [31]. Thanks to these nanobiotechnological methods, the success rate in the treatment of inherited diseases is increasing. Gene diseases can occur in some people at an advanced age. An individual's susceptibility to genetic disease can be diagnosed by biomarkers in the body. Personalized treatments for individuals who are likely to develop a genetic disease are provided through early diagnosis methods.

#### *2.4. The role of nanobiotechnology in early diagnosis*

Early diagnosis of some genetic and immunological diseases is made with biomarkers. However, early diagnosis of some diseases is difficult because the diseases may not be able to create enough biomarkers. In addition, the stage of the disease sometimes makes early diagnosis applications difficult. Early diagnosis is very important in cancer, which is one of the most emphasised diseases. Because as cancer progresses, its treatment becomes more difficult. However, thanks to the early diagnosis methods used in nanobiotechnology, the disease status is determined in the early stages of cancer. Although traditional early detection methods are tried to be applied professionally, they have lagged behind compared to nanobiotechnological methods [17], [32]. At this stage, nanobiotechnology also shows its importance in early diagnosis where traditional medical practices are insufficient [33].

##### *2.4.1. Nanosensors and biosensors*

Nanotechnology increases the sensitivity of biosensors in early detection applications, enabling easy detection of biomarkers in blood [5], [17]. These biomarkers play a decisive role in the early stages of cardiovascular, cancer and hormonal diseases. Nanocarriers are able to detect biological changes in the body before the symptoms of the disease appear. In this way, early intervention against diseases is provided [34], [35].

##### *2.4.2. Imaging technologies*

Thanks to new imaging techniques developed with nanotechnology, cancerous cells can be easily visualised. For example, magnetic nanoparticles can be used with magnetic resonance imaging (MRI) devices to make small tumours visible in the body. Such techniques play an important role in early diagnosis [33].

#### *2.5. The role of nanobiotechnology in cancer treatment*

Nanotechnology in cancer treatment opens the door to groundbreaking new developments. Chemotherapy and radiotherapy treatments, which are traditional cancer treatment methods, can also damage healthy cells. Unlike traditional treatments, nanobiotechnology applications target regional treatment. With nanobiotechnology, more specific cancer treatments with minimal side effects become possible. Nanoparticles used in these treatment methods are selected according to the target tissue and carry cancer drugs [3], [11], [36], [37], [38], [39], [40]. In conventional cancer treatments; not only cancerous cells but also healthy cells are damaged due to organ loss, excessive radiation overload and especially due to the burning of cancerous cells with radiation at specific frequency band and specific intensity due to the non-homogenised distribution of cancerous cells. Sometimes the drugs used in chemotherapy can also have toxic effects on healthy tissues [7], [19]. Compared to traditional methods, target-oriented treatments are possible with nanobiotechnology. Nanoparticles used in cancer treatment are not immunogenic, remain stable in the circulatory system for a long time and do not collide with the entire surface of the target tissue thanks to their nano size are important advantages of nanoparticles. They can also establish a specific interaction with hereditary materials in cell nuclei. In addition to these treatment methods, photothermal therapy is also used [7], [39], [40].

2.5.1. photothermal therapy

Photothermal therapy, which is a part of thermal therapies, is an effective method using nanobiotechnological methods. Photothermal therapy aims to specifically destroy cancer cells by using the heat generated from the absorption of light [41], [42] This treatment method is based on the principle of inhibition of these cells by thermal ablation (heat treatment) by creating a hyperthermic effect on cancerous cells selected as targets [24], [37], [43]. In the next section, the development of nanobiotechnology is discussed.

2.6. Clinical applications and future of nanobiotechnology

The development of nanobiotechnological methods takes place in the clinical laboratories of R&D centres. There are large investments in studies in this field. Although this treatment method is not widely applied today, it is expected to replace traditional treatment applications in the near future. As seen as a result of preclinical and clinical studies, nanobiotechnological methods are a treatment method with great potential. The nanobiotechnology method, which provides high sensitivity towards the target, is becoming more widespread as time progresses. As an example of this application, Figure 1 below shows the effects of nanobiotechnology on cancerous cells, disruption of the division process [37], [43], [44].

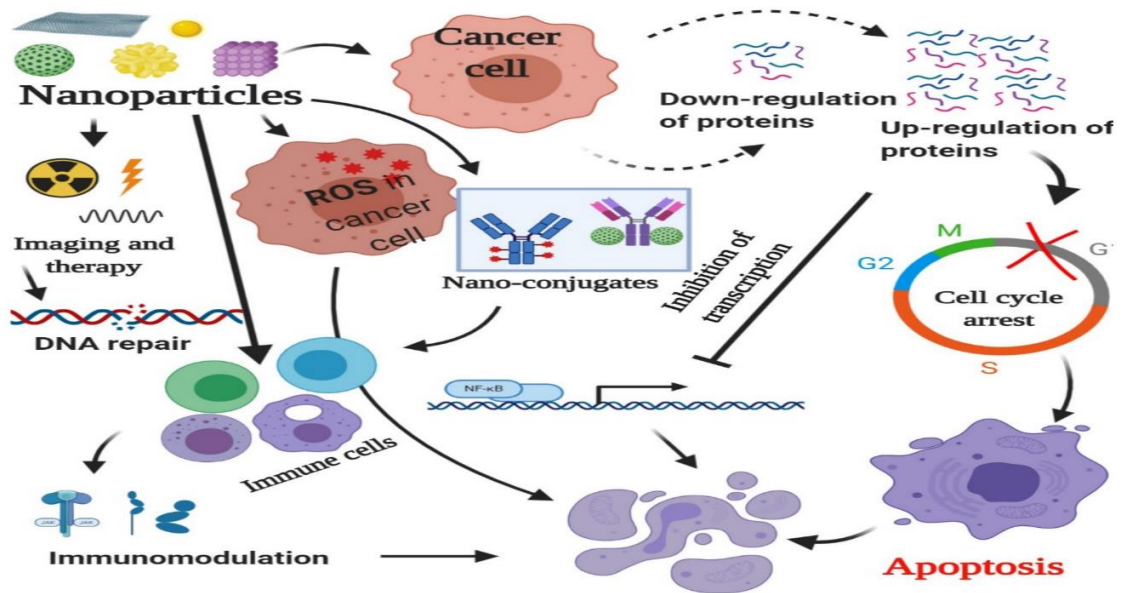


Fig 1. Disruption of cancer cell division by nanoparticles [45], reprinted with permission from MDPI.

2.6.1. Personalised treatment

Personalised therapy, which is a subject being studied in the field of nanobiotechnology, provides treatment specific to the genetic structure of the patient. In this field; treatments specific to the genetic profile and biomolecular structure of patients are designed. For example; genetic profiles of patients can be monitored instantly with nanocensors. Thus, optimum doses of treatment can be provided to patients instantly [40], [46], [47]. Nanobiosensors used in this

treatment enable instantaneous monitoring of metabolic processes of patients. As a result, the most appropriate treatment method can be designed with instant monitoring of chronic diseases.

### *2.6.2. Treatment of chronic diseases*

Chronic diseases such as cancer have been a major problem for humanity for centuries. Unless these diseases are left untreated, they can cause severe damage or fatal consequences. In the scientific world, studies are being carried out for the treatment of these severe diseases. However, traditional methods are losing their popularity in these complex treatment processes [24], [32], [48]. Examples of nanobiotechnology in the treatment of chronic diseases include insulin transport systems developed for diabetic patients. With nanobiosensors, it is possible to instantly determine the amount of insulin required by the body [7], [11].

### *2.6.3. Treatment of infectious diseases*

Another disease area whose treatment is facilitated by nanobiotechnology methods is infections. Traditional methods are no longer sufficient against many infectious diseases, especially infectious diseases such as influenza and Covid-19. It is undesirable that some drugs take a long time to treat and side effects occur. Now, in such diseases, targeted drug delivery can be performed by utilising the ability of nanoparticles to pass directly through the membrane of infected cells. Especially in the fight against antibiotic resistance, nanobiotechnology offers the most effective solutions [24], [49].

### *2.7. Future applications and potential of nanobiotechnology*

Nanobiotechnology branch offers effective drug delivery systems and diagnostic methods especially against many severe and complex diseases. Especially thanks to specific treatments, it offers miraculous treatment methods for patients and doctors, with less side effects against other organs and tissues and easier application [19], [49]. Recently, as the subject of some nanobiotechnological projects, genetic maps, family tree analyses and metabolic activities of individuals can be examined, and with the help of various markers, treatment can be designed according to the disease before the disease occurs, and preventive measures can be taken against these diseases [25], [44], [50].

## **3. Application areas of nanobiotechnology**

The application areas of nanobiotechnology have a wide range. This technology creates a great impact with applications in different industries. Especially in the health, environment, agriculture, textile, textile, construction, animal and food sectors, significant contributions are provided.

### *3.1. Nanobiotechnology applications in healthcare*

Nanobiotechnology plays a very important role in the health sector. In particular, it has an important place in early diagnosis, treatment and instant monitoring of diseases. Nanoparticles, biomolecules and nanorobots are used in various medical applications.

#### *3.1.1. Nanobiotechnology in cancer treatment*

The development of treatment methods specifically targeted to cancer cells is enabled by nanobiotechnology. By utilising the stimulating effect of DNA molecules on the immune system, DNA-targeted drugs are now being designed. By preventing damage to healthy cells during treatment, treatment that focuses only on cancerous cells and has fewer

side effects becomes possible. In addition, nanotechnological materials make the treatment process more effective by targeting cancer cells with stimuli such as light, heat or magnetic fields [29], [51].

### 3.1.2. Early diagnosis and imaging

Another important application area of nanobiotechnology is early diagnosis of diseases. Nanoparticles make early diagnosis possible by interacting with biomarkers from diseases. These nanoparticles allow diseases to be detected even in the early stages after being injected into the body. In addition, nanotechnological materials increase the sensitivity of medical imaging techniques, allowing tumours or infected cells to be seen more clearly [18].

### 3.1.3. Drug transport systems

Nanobiotechnological methods are used in the development of systems that provide controlled release of drugs into the body. The carriers produced in nano dimensions enable the delivery of drugs to the desired target tissue by crossing the blood-brain barrier and biological barriers in the skin. As shown in Figure 2, nanoparticles not only provide better distribution in biological structures that are difficult to pass in the body, but also increase the dissolution power of drugs with low dissolution ability [29], [51], [52], [53].

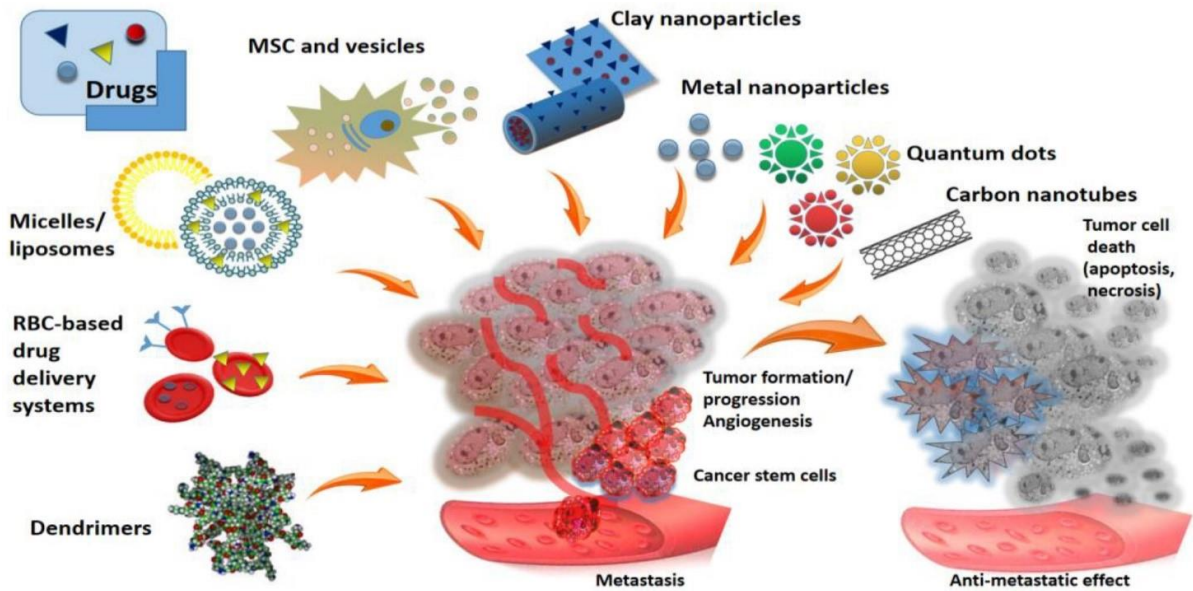


Fig 2. Drug delivery by nanoparticles into the cancer structure is shown [45], reprinted with permission of MDPI.

## 3.2. Nanobiotechnology applications in environment

Nanobiotechnology has an important place in the field of environmental protection and sustainability. This technology offers innovative solutions in reducing environmental pollution, water treatment applications and waste management.

### 3.2.1. Water treatment and pollution control

The availability of nanobiotechnology in the field of water treatment allows the development of new methods for water purification. Nanoparticles can absorb toxic substances, heavy metals and pathogens that mix in water. Furthermore, nanofiltration technology is an efficient method that can be used in water treatment.

### *3.2.2. Waste management and bioremediation*

Nanobiotechnology is used in environmental waste treatment and bioremediation processes. Nanomaterials are used in the separation of organic and inorganic pollutants, in biodegradation and as an effective tool. Bioremediation is the destruction of pollutants by microorganisms by natural means.

### *3.3. Nanobiotechnology applications in agriculture*

In the agricultural sector, nanobiotechnology is used to increase productivity and reduce harmful environmental impacts. Nanobiotechnological methods are used in fields such as plant protection products, fertilizers and biosensors.

#### *3.3.1. Pesticide and fertiliser transport*

The materials used in nanobiotechnological methods provide more efficient transport of pesticides and fertilisers to plants. Nanoparticles can increase the effectiveness of chemicals by carrying these chemicals directly to the roots or leaves of plants. Thus, more efficient agriculture can be carried out with less chemical use. Nanoparticles help to greatly reduce environmental pollution by preventing pesticides from leaching into soil or water.

#### *3.3.2. Early detection and treatment of plant diseases*

In particular, plant viruses and bacterial infections can be detected more precisely using nanomaterials. Nanotechnological sensors can quickly recognise these pathogens. In this way, they allow the correct treatment methods to be applied. Biosensors can quickly detect the presence of microorganisms, harmful agents and plant diseases.

#### *3.3.3. Nanobiotechnological fertilisers*

Nanotechnology offers solutions that enable fertilisers to be applied to plants more efficiently. Nanoparticles transport nutrients to the roots of the plant. In this way, the efficiency of fertilisers increases. Another advantage of nanobiotechnological fertilisers is that they have a longer release time compared to normal fertilisers. In other words, with slow release, the fertiliser supplementation period can be spread over longer intervals.

### *3.4. Nanobiotechnology applications in food industry*

In the food sector, nanobiotechnology offers advantages in food safety and processing. There are nanotechnological solutions for increasing the quality of food products and extending their shelf life.

#### *3.4.1. Food safety and monitoring*

Nanobiotechnology provides advanced monitoring and detection systems to ensure the safety of food products. This technology enables the rapid detection of harmful microorganisms, pathogens and toxins in food. Thus, products can be monitored throughout the food supply chain and if a risk of contamination is detected, it allows rapid



intervention. Nanomaterials provide great advantages in the quality control of food products thanks to these properties.

#### 3.4.2. Food Packaging

Nanotechnology improves the properties of materials used in food packaging. Nanomaterials allow safe packaging methods such as preventing oxidation of food products, reducing moisture loss and preventing the growth of microorganisms. They also play a role in reducing the risk of microbial contamination of food packaging by using nanomaterials with antibacterial properties [54].

#### 3.4.3. Nutritional value enhancement and enrichment

Nanobiotechnological methods can also be used to increase the nutritional value of food products. Especially in plant foods, nutrients carried by nano materials are transferred to plants and contribute to the formation of new products with rich nutrient content.

#### 3.4.4. Effective and targeted distribution of food additives

Nanobiotechnology enables efficient and controlled delivery of food additives. Nanomaterials enable more efficient diffusion of active ingredients in food.

#### 3.4.5. Food identification and tracking systems

Nanobiotechnology can also be used to solve the problems of authorisations to place food products on the market under false identity. Nanotechnological labels and nanosensors are used to verify and track the authenticity of food products.

#### 3.4.6. Effects of nanobiotechnology on food consumer health

Nanobiotechnology can also be used to improve the health of food consumers. For example; substances to be applied to food products with nano materials can prevent food-borne health problems.

#### 3.4.7. Food processing

Nanobiotechnology is also used to improve food processing. Nanotechnological tools can enable foodstuffs to be processed more homogeneously and have a higher nutritional value.

### 3.5. Nanobiotechnology applications in energy sector

Nanobiotechnology science also plays an important role in energy production and efficiency. Nanotechnological solutions are also used in the use of renewable energy sources and the development of energy storage systems. By taking advantage of the potential of nanobiotechnology to solve problems related to energy production and consumption, environmentally friendly and economical solutions are provided.

#### 3.5.1. Biological energy production (bioenergy)

Nanobiotechnology can be used to increase the efficiency of biological energy sources such as biomass and biogas production. Nanoparticles are used to optimise the biological processes of microorganisms. Thus, more energy can be obtained from organic wastes.

### *3.6. Biotechnology in animal nutrition and nanobiotechnology applications in animal husbandry*

The livestock sector has a critical importance in terms of food production, economic development and environmental sustainability, increasing feed utilisation, desired product quality and disease control worldwide. In recent years, the use of advanced sciences such as nanobiotechnology in animal husbandry has led to significant developments in the sector. These technologies have an important role in improving the health rate of animals and increasing production efficiency. While many enzymes, probiotics, prebiotics and organic acids are used as feed additives, genetically modified organisms are also used as feed sources. Nanoparticles are supported in these areas [55].

#### *3.6.1. Genetic improvement and cloning*

Nanobiotechnology is used in animal husbandry to obtain efficient and healthy organisms. Genetic improvement and cloning techniques appear as a very effective method. The sustainable and ethical use of these technologies is also used within ethical frameworks to improve the genetic characteristics of animals, increase productivity and create disease-resistant breeds [56], [57]

#### *3.6.2. Biological supplements and probiotics*

Nanobiotechnology provides healthier and more efficient animal husbandry practices by improving biological supplements used in animal nutrition. Such biological supplements provide great benefits, especially in organic and sustainable livestock farms. For example; techniques such as nanoencapsulation increase the bioavailability of probiotics and nutritional supplements.

#### *3.6.3. Early detection and treatment of diseases*

Nanobiotechnology also plays an important role in protecting animal health. In particular, biosensors are used for the rapid detection and treatment of pathogens. The rapid and sensitive diagnostic properties of nanobiotechnology in this field contribute greatly to the prevention and treatment of diseases before they spread.

#### *3.6.4. Nanotechnological drug delivery systems for animals*

Nanotechnology is also influencing and improving the way drugs are administered to animals. Nano-drug delivery systems enable drugs to reach target cells directly, reducing side effects in animals and making treatment more effective and safer.

#### *3.6.5. Reducing environmental impact in animal husbandry*

Nanobiotechnology can also contribute to reducing environmental impacts in the livestock sector. In particular, nanotechnological solutions are used in the processing of animal waste. It leads to the reduction of environmental impacts by using biogas from animal wastes and recovering water. Such technologies can make a significant difference, especially in large-scale livestock enterprises.

### *3.7. Environmental sustainability and energy efficiency*

Nanotechnology is also used to reduce the environmental impact of building materials and improve energy efficiency.

### 3.8. Comparison of traditional cancer treatment methods with nanobiotechnological methods

Comparing the strengths and weaknesses of traditional cancer treatment methods and nanobiotechnological treatment methods requires us to focus on the different features and effective situations of both approaches.

#### 3.8.1. Strengths of traditional cancer treatment methods

**Comprehensive Treatment:** Chemotherapy and radiotherapy can be effective on many types of cancer.

**Clinical Background:** These are treatment modalities that have been proven by many years of research and clinical experience.

**Accessibility and Widespread Use:** Traditional treatment methods usually include surgery, chemotherapy and radiotherapy. It can be easily applied in most hospitals and is widely used.

#### 3.8.2. Weaknesses of traditional cancer treatment methods

**Side Effects:** Chemotherapy and radiotherapy can damage healthy cells. This leads to side effects such as nausea, hair loss, immune system collapse and breathing difficulties in most patients.

**Treatment Limitations:** Not every type of cancer shows the same effect in every patient. Some cancers may be resistant to treatment. This situation creates a more challenging and intensive process for the patient.

**Late Recovery:** These treatment methods make it possible for the resistant cancer not to heal faster and create a risk of recurrence.

#### 3.8.3. Strengths of nanobiotechnological cancer treatment methods

**Targeted Therapy:** Cancer cells can be directly targeted using nanoparticles. In this way, it destroys cancer cells more easily without damaging healthy cells.

**Less Side Effects:** Nanotechnology allows treatment agents to be used in lower doses and in a targeted manner. In this way, it reduces side effects at a high rate.

**Advanced Technology and Specialised Applications:** Innovative approaches such as biosensors and controlled release of therapeutic agents are used in nanobiotechnology. It prioritises the use of new and specialised methods in cancer treatment and makes it possible to apply it in every field.

**Early Diagnosis and Monitoring:** Thanks to nanotechnological sensors, cancer can be detected at earlier stages. It makes the treatment process more effective and lighter.

#### 3.8.4. Weaknesses of nanobiotechnological cancer treatment methods

**Lack of Clinical Experience:** Nanotechnological treatment methods are still under development. More research on safety is needed to establish long-term efficacy.

**High Cost:** Nanobiotechnological treatments can be more expensive than traditional methods. This may limit access to treatment and the next stages.

## 4. Early diagnosis methods with nanobiotechnology

### 4.1. What is early diagnosis?

It means identifying and diagnosing diseases at an early stage, often before symptoms become severe. Detecting cancer early when tumours are smaller and localised increases the chances of successful treatment with less invasive

procedures and side effects. For example, early detection of cancers such as breast, colorectal or cervical cancer not only improves survival rates but also reduces treatment costs [58], [59]. The World Health Organisation (WHO) emphasises that early detection is crucial to reduce cancer mortality and the cost of the disease [57]. In summary, early detection provides the best treatment outcomes, saving lives and reducing healthcare costs.

#### *4.2. Use of nanobiotechnology in the diagnosis and treatment of cancer*

Nanotechnology plays an active role in both the diagnosis and treatment of cancer. Cancer detection, which traditionally relies on imaging methods such as MRI, CT and PET, can be significantly improved by nanotechnology [56], [60]. Since nanoparticles are small in size (between 10 and 100 nanometres), they can target cancer cells more effectively than the techniques we use today. For example, nanoparticles such as gold, liposomes or magnetic particles can be designed to bind to tumour markers, making it easier to find and identify cancer cells in their early stages. This approach not only helps to detect tumours earlier, but also helps to advance treatment by providing real-time feedback [10], [18], [61]. Nanotechnology is also revolutionising cancer treatment by facilitating targeted drug delivery. Nanoparticles can be designed to deliver chemotherapy drugs directly to cancer cells, minimising damage to surrounding healthy tissue and reducing side effects. Nanomaterials have been found to have intrinsic anticancer properties. In this way, nanoparticles increase the effectiveness of treatments by controlling the release of drugs and provide a more effective and localised treatment.

##### *4.2.1. Early diagnosis methods and applications*

Nanobiotechnology offers revolutionary advances in this field, making early diagnosis methods more sensitive, fast and effective. Below, early diagnosis methods and the information of these methods in the field of health are examined and shared in detail [62].

##### *4.2.2. Nanoparticle based diagnostic methods (nanoparticle based diagnostic methods)*

Nanoparticles are one of the cornerstones of nanotechnology and help to detect diseases at a very early stage by communicating with biological systems. Nanoparticles are an important tool in the recognition of diseases with their ability to transport, orient biomolecules and form bonds with specific molecules [39], [63].

Applications:

- Gold Nanoparticles: Can be used to detect cancer characteristics by binding to biomarkers. These nanoparticles can be combined with imaging techniques such as MRI and PET, allowing more sensitive imaging of cancerous tissues.
- Magnetic Nanoparticles: Can be used to eliminate the possibility of cancer. This method can detect the early stages of cancer cells thanks to liquid antibiotics by looking at the blood samples of patients [63].

##### *4.2.3. Biosensors*

Biosensors enable the detection of cancer in its early stages. By designing with nanomaterials (e.g. nanoparticles or nanotubes), dispersed milk biomarkers can be detected at very low concentrations.

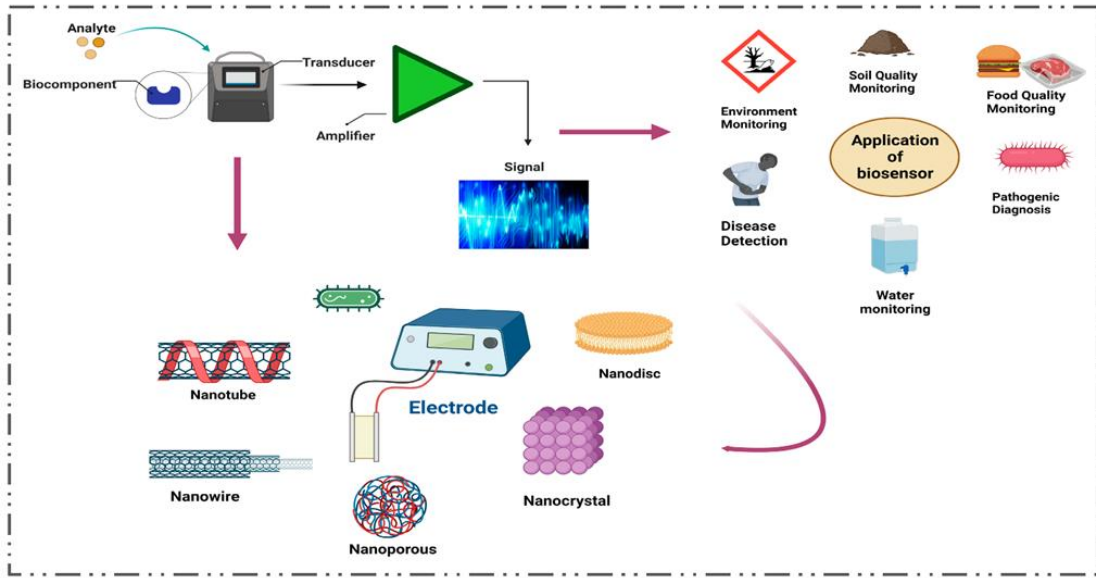


Fig 3. Applications of the biosensor mechanism [64], reprinted with permission from MDPI.

**Applications:**

- **Cancer Biosensors:** Contributes to the separation analysis of cancer cells or cancer-modifiable biomarkers using nanoparticles.
- **Infectious Disease Biosensors:** Gold nanoparticles or quantum dots are widely used to detect viruses. These sensors provide fast and accurate results for early detection of latent or viral systems [27], [65].

**4.2.4. Molecular imaging**

Molecular imaging allows very precise imaging of biological particles. Nanoparticles interact with biomarkers specific to cancer appearance, improving this appearance detection.

**Applications:**

- **Nanoparticle-Enhanced PET and MR Imaging:** Monitoring imaging modalities such as PET (Positron Emission Tomography) and MR (Magnetic Resonance Imaging) can more precisely visualise cancerous areas that are supplemented with nanoparticles. For example, gold nanoparticles or magnetic nanoparticles can be deposited around cancer cells, providing clearer images to reveal these details [65].

**4.2.5. Polymerase chain reaction (pcr) and nanodiagnosics**

Nanotechnology increases the sensitivity of traditional genetic tests such as PCR (Polymerase Chain Reaction). Nanomaterials in PCR tests for early detection of genetic changes, faster and more precise replication of genetic material, as well as the integration of nanomaterials into PCR tests enables easier and faster detection of rare genetics.

**Applications:**

- **Quantum Dots:** Quantum dots used in PCR tests label the genetic material, allowing faster and more sensitive detection of DNA sequences. This enables genetic diseases to be recognised at an early stage.

- Carbon Nanotubes: Carbon nanotubes increase the accuracy of genetic tests, enabling more precise detection [17], [42].

#### 4.2.6. Early detection of infections

Nanotechnological tools have an important role in the early detection of systems. Nanoparticles make it easier to detect microbes by combining them [5], [58], [59].

Applications:

- Rapid Diagnostic Tests: By obtaining rapid diagnosis with nanotechnology, viruses are detected with superior performance in early stages.
- Nanodiagnosics: Using nanomaterials in blood samples, comprehensive and viral pathogens can be detected quickly and accurately, which can lead to early treatment possibilities.

#### 4.3. Areas of use in early diagnosis of diseases

Advances in the fields of nanotechnology and biotechnology offer new areas of use in the early diagnosis of disease. These technologies enable the early detection of various formations and improve the distribution of process treatments and overall health characteristics [40], [66].

##### 4.3.1. Cancer diagnosis

Nanotechnology offers highly sensitive and useful tools to detect cancer in its early stages, making treatment easier. By targeting biomarkers specific to cancerogenesis, it provides a general baseline of knowledge [66].

Applications:

- Nanoparticles and Biosensors: Nanoparticles enable the detection of cancer in its early stages by recognising cancer-specific molecules. For example, gold nanoparticles make it possible to obtain clear results in methods such as PET and MR by binding to cancerous methods.
- Liquid Bacteria: Nanotechnology is enabling the emergence of biosensors that can capture cancer cells. This is a non-invasive treatment method for the early diagnosis of cancer [58], [66].

##### 4.3.2. Early diagnosis of cardiovascular diseases (early diagnosis of cardiovascular diseases)

Cardiovascular diseases increase the mortality rates in the world in large numbers. By detecting this infection in the early stages, the treatment process becomes much more successful.

Applications:

- Biomarker Detection with Nanoparticles: Nanoparticles are used in the recognition of cardiovascular diseases by separating into specific biomarkers in blood serum. These biomarkers can provide early warning signs of emergencies, especially heart attacks.
- Rapid Diagnostic Devices: These devices facilitate recovery by rapidly detecting biomarkers from blood samples [19].

##### 4.3.3. Early diagnosis of genetic diseases

Nanotechnology is improving the accuracy and reduction of genetic testing, enabling more sensitive recognition of altered genetics at early stages [29], [67].

Applications:

- DNA Error and Genetic Analyses: Nanotechnology increases the sensitivity of PCR (Polymerase Chain Reaction) tests used for the early diagnosis of genetic diseases. Nanomaterials such as carbon nanotubes provide signal amplification during the distribution of genetic materials [17].
- Genetic Screening with Nanotubes: It is used to detect DNA sequences quickly and precisely. Therefore, genetic diseases (cystic fibrosis, muscular dystrophy) can be diagnosed in the early stages with the help of scans [16].

#### 4.3.4. Early diagnosis of neurological diseases

Neurological diseases (such as Alzheimer's and Parkinson's) are usually detected in advanced stages. Nanobiotechnology used in the early diagnosis of these diseases offers a new and effective future [68].

Applications:

- Brain Imaging with Nanoparticles: Nanobiotechnology is used to determine brain imaging techniques. Nanoparticles can detect early stages of Alzheimer's or Parkinson's diseases by finding abnormal distortions in the brain [68], [69].
- Detection of Neurological Biomarkers: Nanobiosensors are used to detect biomarkers that can be permanently stored. These sensors enable earlier interventions by observing flowering patterns [68].

#### 4.4. Benefits of early diagnosis of diseases

The benefits of early disease diagnosis are multifaceted, with advantages not only for individual patients but also for the wider health system [66].

##### 4.4.1. Treatment success rate

Early diagnosis significantly increases the success rate of treatments. When diseases such as cancer are diagnosed early, there are many treatment options [58].

##### 4.4.2. Cost savings

Treating diseases at an early stage provides a better opportunity in terms of cost. Early-stage cancer treatments may only require surgery or local treatment, while late-stage treatments are often expensive. It may require chemotherapy, radiotherapy, and long-term hospital stays.

##### 4.4.3. Improving quality of life

Early diagnosis prevents the progression of the disease and ensures timely intervention. In this way, patients can maintain a higher quality of life during the treatment process. Early diagnosis in individuals with diabetes or heart disease provides a healthier and higher quality of life in the long term.

##### 4.4.4. Procedure process

Early diagnosis is usually done with simpler tests. In early-stage cancers, biopsy methods or blood tests can confirm the diagnosis without requiring major surgery. Early detection can facilitate the entire treatment process, making it less complex and more manageable [70].

#### 4.5. Advantages and disadvantages

Although the use of nanobiotechnologies provides various advantages in terms of both health and economics, it also includes some disadvantages [40], [66].

#### 4.5.1. Early treatment results

Thanks to early diagnostics with nanotechnology, it is possible to detect the initial stages of the disease. In this way, treatment can be started earlier and success rates increase [57].

#### 4.5.2. Reduced treatment costs

A high increase in costs is observed due to the continuation of the treatment process with early diagnosis. In the late stages of diseases such as cancer, treatment is generally more expensive and difficult. Early detection reduces interruptions such as long-term treatment [71].

#### 4.5.3. Fast and precise diagnosis

Nanotechnological devices and biosensors can detect diseases more precisely and accurately. Thanks to these devices, biomarkers can target and recognise the disease at an early stage. For example, it offers more reliable diagnostic methods by finding solutions at very low rates with nanoparticles.

#### 4.5.4. Long regulation and approval processes

Nanotechnological devices and biosensors undergo rigorous testing and are approved by monitoring bodies before they are used in healthcare. These processes can take a long time, which can delay the introduction of new treatment and diagnostic methods to the market.

#### 4.5.5. Incorrect results

Although nanotechnological tests offer high sensitivity, they can sometimes give false results (diagnosing a disease in a healthy person). In this case, treatment may start and progress incorrectly [50], [70], [72].

### 4.6. Future potential

Nanobiotechnology has a great potential in the field of early diagnosis. In the following processes, it is thought that it can ensure that health results are more sensitive, fast and effective. The development of these technologies offers opportunities to revolutionise both the differences in the early stages of growth and comprehensive treatments [71], [74].

#### 4.6.1. Personalised medical practices

One of the greatest potentials of nanotechnology is personalised medical applications. Nanotechnological devices, which are designed with genetic and biological considerations in mind, make it possible to develop customised treatment plans according to the individual characteristics of the person. Personalised treatment methods provide better treatment by accurately detecting diseases and increase success rates [28], [65], [73], [74].

- Genetic Profiling: Nanotechnology can improve the distribution and robustness of genetic analyses. By detecting genetic predispositions and biomarkers, it allows for clear identification of disease and improved personalised treatment.



- Biomarker Disruptions: Disruption of new biomarkers and the production of specialised nanotechnological sensors are improving earlier detection and identification of personalised treatment pathways.

#### 4.6.2. Early diagnosis and treatment of infections

Microorganisms need to be identified more quickly and accurately. Nanotechnological methods are used especially in the treatment of antibiotic resistant bacteria [75], [76].

- Nanobiosensors: Nanobiotechnology enables the development of biosensors that detect pathogens in the early stages of diseases. These sensors are able to recognise braided and viral vessels very quickly. Thus, it can start the treatment process in a shorter time [5].

- Antibiotic Option: Nanotechnology can develop new methods for the treatment of antibiotic-resistant diseases. Nanoparticles can directly interfere with the cell walls of pathogens, enabling the destruction of microorganisms that are resistant to treatment [8].

#### 4.6.3. Portable and Easy to Use Diagnostic Devices

Nanotechnological diagnostic devices provide faster access to health services. These devices enable rapid detection at home or in a health institution.

- Home Health Monitoring Devices: These devices can detect the early stages of many conditions such as cancer, diabetes, infectious diseases and provide immediate feedback.

- Advanced Biosensors: Emerging biosensors are enabling faster access to healthcare, enabling medical intervention to be initiated at an early stage. This is thanks to devices that continuously monitor patients' health.

#### 4.6.4. Global health improvement and access

Nanotechnology has the potential to increase accessibility to and accessibility of improved health services. These technologies offer solutions with easier methods and treatment [77].

- Low Probability Methods: Nanotechnology can provide easy access to healthcare services by enabling the development of low-income, portable and rapid diagnostic devices.

- Global Health Monitoring: Nanotechnological sensors can make worldwide health monitoring systems more effective. This can be used for disease monitoring and early intervention in health crises.

## 5. The role of nanobiotechnology in cancer treatment

### 5.1. Basic biology of cancer

Cancer is defined as a disease caused by the uncontrolled growth and proliferation of cells. Normal cells go through certain stages that regulate their growth and division processes. This cycle includes G1, S, G2 and M stages. Unlike normal cells, cancer cells become insensitive to growth signals and continue to proliferate by bypassing apoptosis. Cancer cells attack the surrounding tissues and can reach other parts of the body through the bloodstream. Cancer usually develops in several stages, classified as abnormalisation of cells, tumour formation, invasion and metastasis. Tumours form new blood vessels and develop their own blood supply to provide oxygen and nutrients for growth. There are two types of cancer; hard tumours and haematological cancers. Hard tumours are solid tumours, such as breast, lung and colon cancer. Haematological cancers are cancers of the blood and bone marrow, such as leukaemia and lymphoma. The body uses the immune system to recognise and destroy cancer cells. However, cancer cells develop various strategies to evade the immune system. The basic biology of cancer is critical to understanding the disease and developing treatment methods [33].

### 5.1.1 Development and spread of cancer

Cancer is caused by changes in genetic material. These changes can occur in oncogenes and tumour suppressor genes. Overactivation of oncogenes or inactivation of tumour suppressor genes leads to uncontrolled growth of cells. Changes in gene expression without changes in DNA sequence play a role in cancer development. Epigenetic factors can influence the behaviour of cells. The process of transformation of normal cells into cancer cells usually starts with the "pre-malignant" stage. In this stage, the cells become abnormal, but are not yet able to form a cancerous tumour. Initially, benign tumours can form. Over time, however, malignant tumours can develop. Malignant tumours have the potential to invade and metastasise to surrounding tissues. Cancer cells can form tumours in new areas by attacking and spreading to surrounding healthy tissues. This process involves cells crossing the basement membrane and entering neighbouring tissues. Cancer cells can spread to other parts of the body through blood or lymph vessels. This process occurs when cancer cells detach from the primary tumour, move through the circulatory system and attach to a new location. During metastasis, cancer cells can settle in a new environment and form new tumours there. These metastatic tumours usually have the same characteristics as the primary tumour. The cells, blood vessels and connective tissue surrounding the cancer cells are important factors that influence the growth and spread of the tumour. The development and spread of cancer is a complex process and is shaped by the interaction of many factors. This understanding is critical for the development of strategies to prevent and treat cancer [17], [29], [30], [31], [38], [78].

### 5.1.2. Current cancer treatment methods

Cancer treatment varies depending on the type and stage of the disease and the general health status of the patient [79].

- Surgical treatment: These are operations to remove cancerous tissue. This method is usually effective in early stage cancers.
- Radiotherapy: High-energy rays are used to kill cancer cells or stop their growth. External radiotherapy is given from outside the body, while internal radiotherapy is administered by placing radioactive substances directly into the tumour.
- Chemotherapy: Systemic treatment of drugs used to kill cancer cells or stop their growth. It is usually administered by mouth or intravenously. Side effects of chemotherapy include nausea, hair loss and a weakened immune system.
- Targeted Therapy: Drugs designed for specific targets in cancer cells are used. These drugs target specific pathways that affect the growth of cells.
- Immunotherapies: Treatments that enable the body to fight against cancer cells by activating the immune system. Checkpoint Inhibitors; treatment methods that enable the immune system to recognise cancer cells.
- Hormonal Therapy: Some types of cancer grow depending on hormone levels. Hormonal treatment prevents the growth of cancer by reducing the effect of these hormones. For example; It is used in the treatment of breast and prostate cancer.
- Stem Cell Transplantation: Reconstitutes the bone marrow after chemotherapy or radiotherapy and after high-dose treatment to produce healthy blood cells. Own stem cells or stem cells from a compatible donor can be used [79].

## 5.2. Applications of nanobiotechnology in cancer treatment

### 5.2.1. Targeted drug transport

Targeted drug delivery is a method developed to deliver drugs directly to specific cells or tissues in the body. It plays a particularly important role in cancer treatment as it targets cancer cells and prevents damage to healthy cells. A more detailed visual explanation is given in the image below [18], [19].

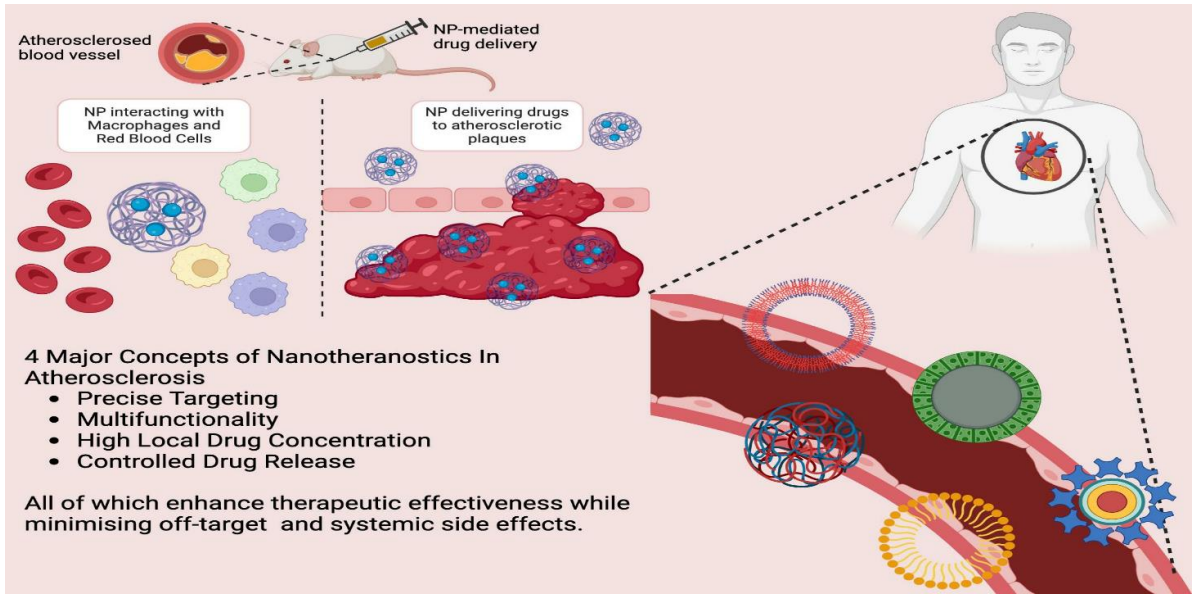


Fig 4. Drug delivery system [80], reprinted with permission from MDPI.

### 5.2.2. Utilisation of nanoparticles

Nanoparticles act as drug carriers. These small structures ensure that drugs are directed to specific targets in the body. By adding cancer cell-specific biomarkers and drugs to the surface of nanoparticles, targeted accuracy is increased [9].

### 5.2.3. Advantages

- **Reduced Side Effects:** Targeted drug delivery reduces damage to healthy cells and side effects of chemotherapy.
- **Increased Efficacy:** The ability of drugs to reach cancer cells directly increases the effectiveness of treatment. In this way, more effective results can be achieved with lower doses.

### 5.2.4. Application areas

Targeted drug delivery is particularly used in cancer therapy, immunotherapy and gene therapy. This method has the potential to treat not only cancer but also other diseases.

### 5.2.5. Developments and research

Research into targeted drug delivery aims to develop new nanoparticle systems and improve existing therapies. Clinical trials are examining the outcomes of patients treated with this method and enabling the development of new strategies [81].

### 5.2.6. Nanoparticles and drug delivery systems

Nanoparticles are defined as nanostructures ranging in size from 1 to 100 nanometres. Since these small sizes change the physical and chemical properties of nanoparticles, they play an important role in the biomedical field, especially in drug carrier and release systems [9], [82], [83].

#### 5.2.7. Properties of nanoparticles

Surface area; The large surface area of nanoparticles enables drugs to be loaded and transported to target cells more effectively. Controlled release; nanoparticles improve treatment processes by enabling the release of drugs at a certain speed and time [9].

#### 5.2.8. Drug release systems

- Sustained Release Systems; the drug is released at a constant rate over a certain period of time. This ensures that a constant level of drug is maintained throughout the treatment period.
- Smart Release Systems; drug release is controlled in response to physical or chemical stimuli (pH change, temperature, biomolecules). These regimens can provide specific responses to treatment [46].

#### 5.2.9. Advantages of nanoparticles in drug delivery

- Targeting; nanoparticles enable drugs to be directed to specific cells or tissues. This allows cancer cells to be targeted while helping to protect healthy cells.
- Stability; nanoparticles can increase the stability of drugs, allowing them to stay in the body longer [77], [84].

#### 5.2.10. Application areas

- Cancer treatment; nanoparticles increase the effectiveness of treatment by enabling cancer drugs to reach directly to tumour sites.
- Gene therapy; genetic material can be transferred to target cells by using nanoparticle. They contribute to the development of more effective and targeted therapeutic approaches and are an important part of modern medicine [5].

### 4.3. Nanocapsules and nanotubes

Nanocapsules and nanotubes are used in biomedical applications, especially in drug delivery and release systems, and are important building blocks of nanotechnology.

#### 5.3.1. Nanocapsules

Nanocapsules are capsules, typically 1 to 100 nanometers in size, that form around drugs or biomolecules. These capsules allow drugs to be encapsulated in a protective layer. The outer part contains a protective layer while the inner part contains the drug. Nanocapsules can provide targeted release of drugs. It allows drugs to remain in the body for a longer period. Nanocapsules provide treatment without harming healthy cells and reduce the effects of drugs before reaching the target cells [39].

#### 5.3.2. Nanotubes

Nanotubes are tubes with a cylindrical structure that are nanometre-sized. They usually consist of materials such as carbon nanotubes. They can be used to deliver drugs to target cells by placing the drugs in these tubes. Nanotubes can load more drugs because they have a large surface area. It enables the drugs to reach the target cells effectively, thus increasing the effectiveness of the treatment [8]. Nanocapsules and nanotubes are innovative tools provided by nanotechnology and have important applications in biomedicine. These structures increase the effectiveness of drugs and help the treatment processes to be targeted and effective. However, more research is needed on the safety and long-term effects of these techniques [7], [8].

#### 5.4. The role of nanotechnology in early diagnosis

Nanotechnology offers revolutionary innovations in the early detection of diseases such as cancer. The use of nanoparticles and nanomaterials can greatly improve the detection and monitoring of diseases. As shown in Figure 4, these pre-treatment imaging methods are the most important stage before the creation of a treatment plan [57].

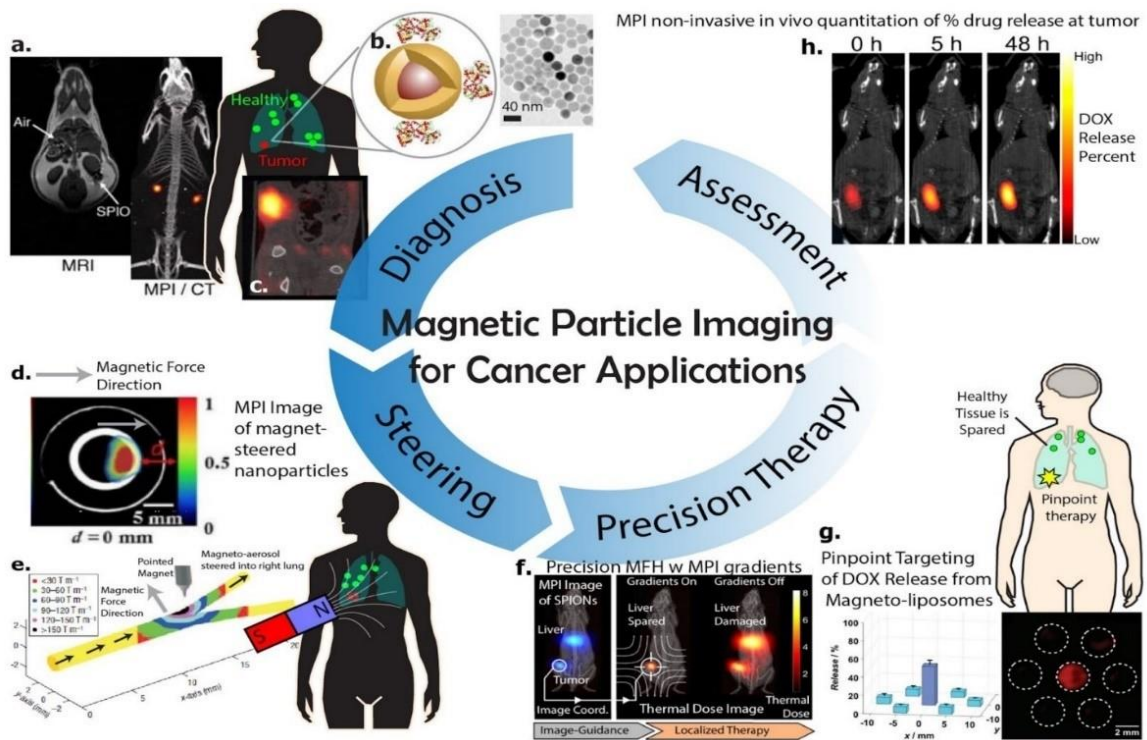


Fig 5. Magnetic particle imaging for cancer therapy applications [85], reprinted with permission from MDPI.

##### 5.4.1. Targeted biomarker recognition

Biomarkers; nanoparticles can be used to identify biomarkers specific to cancer cells. This allows the disease to be detected in the early stages. High sensitivity; nanomaterials can detect cancer cells even at very low concentrations by interacting with biomarkers on the cell surface [9].

#### 5.4.2. Advanced imaging techniques

Contrast agents; nanoparticles can be used as contrast agents in imaging techniques such as PET (Positron Emission Tomography) or MR (Magnetic Resonance). This allows tumours to be seen more clearly and distinctly. Fluorescent nanoparticles; such nanoparticles help to identify specific cells or tissues and provide high sensitivity during imaging [12].

#### 5.4.3. Early diagnosis tests

- Blood tests; tests developed using nanotechnology can rapidly and accurately detect cancer-related biomarkers in blood samples. In this way, early diagnosis is possible without the need for surgical methods.
- Rapid diagnostic methods; nanotechnology applications accelerate diagnostic processes and facilitate patients to receive treatment at an early stage [20].

#### 5.4.4. Multidisciplinary approaches

- Combination technologies; nanotechnology, combined with genetic analysis, enable the development of more comprehensive diagnostic methods. This enables personalised diagnostic approaches based on the genetic profile of patients.
- Multiple test systems; nanoparticles allow multiple biomarkers to be detected simultaneously, making diagnosis more effective [86].

#### 5.4.5. Low cost and easy operation

- Portable devices; nanotechnology enables the development of portable diagnostic devices. This facilitates early diagnosis, especially in developing regions.
- Ease of use; the ability to use nanotechnological systems outside the laboratory environment accelerates diagnostic processes.

#### 5.5. Imaging methods: enhanced visualisation using nanoparticles

Advanced visualisation using nanoparticles is finding important applications especially in forensic and biomedical fields. This method enables invisible or difficult objects to be seen more clearly by utilising the properties of nanoparticles [9], [33].

##### 5.5.1. Properties of nanoparticles

Nanoparticles provide more reactivity and interaction thanks to their large surface areas. This feature enables them to be used effectively on various surfaces. Optical properties; nanoparticles can exhibit different optical properties due to quantum effects. For example, their ability to absorb or emit light at certain wavelengths provides advantages in imaging applications [9], [87].

##### 5.5.2. Application areas

- Forensic science uses nanoparticles such as silica nanoparticles to visualise fingerprints. These nanoparticles play an important role in crime scene investigations by making fingerprints clearly visible. Silica nanoparticles are preferred because they provide effective visibility on various surfaces.
- Biomedical applications; nanoparticles are also used in the imaging of cells and biomolecules. For example, some nanoparticles can be used in targeted imaging techniques to detect cancer cells [28], [88].

### 5.5.3. Visualisation methods

- Chemical and physical methods; nanoparticles can be applied to surfaces by various chemical and physical methods to increase the visibility of target objects.
- Optical techniques; The optical properties of nanoparticles, combined with lasers and other light sources, enable higher resolution imaging [10].

## 6. Clinical applications and future of nanobiotechnology

In recent years, nanobiotechnology has gained significant importance in clinical applications and has been recognised as a technology that could revolutionise the health sector thanks to its future potential [50].

### 6.1. Clinical application areas of nanobiotechnology

Nanobiotechnology has begun to be used in many clinical areas, leading to important developments in areas such as diagnosis, treatment, cellular engineering, tissue engineering and drug delivery systems. These applications have great potential for earlier detection of diseases, more effective treatment methods and the development of personalised treatment approaches. As shown in Figure 5, there are some topics targeted by nanobiotechnology that allow us to look hopefully to the ever-developing future [89].

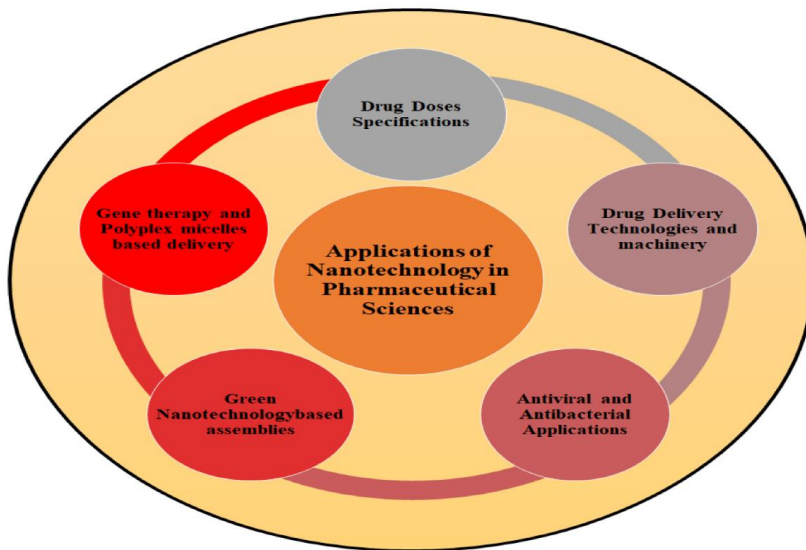


Fig 6. Applications of nanotechnology in pharmaceutical sciences [89], reprinted with permission from MDPI.

## 6.2. Use in diagnostic methods

The use of nanobiotechnology in diagnostic methods is as follows.

### 6.2.1. Targeted diagnosis with nanoparticles

Nanoparticles can be used to detect biomarkers and diseases with their ability to recognise biological molecules. These nanoparticles usually bind biomolecules (e.g. antibodies or DNA sequences) to their surfaces, enabling specific binding to targeted cells or tissues [18], [19].

- **Cancer Diagnostics:** Nanoparticles are used to recognise specific biomarkers on the surface of cancer cells. For example, gold nanoparticles can provide early diagnosis of cancer by binding to certain proteins on cancer cells.
- **Viral and Bacterial Infections:** Nanoparticles have the ability to recognise the surface proteins of pathogens (viruses or bacteria). In this way, they allow infections to be identified more quickly [76], [90], [91], [92].
- **Immunological Diagnosis:** Nanoparticles can be labelled with antibodies or other immune system molecules and used to diagnose diseases such as infections, autoimmune diseases and cancer [53].

### 6.2.2. Nano-imaging techniques

Nanotechnology is used in various imaging techniques, especially for the detection and monitoring of biomolecules. These techniques provide greater resolution and accuracy in the detection of diseases.

- **Magnetic Nanoparticles:** Magnetic nanoparticles can be used in magnetic resonance imaging (MRI) techniques. These nanoparticles bind to target cells, making MR images more sensitive and distinct. This technique is being developed for the detection of cancerous cells [92].
- **Fluorescent Nanoparticles:** Fluorescent nanoparticles glow under light, enabling biomolecules to be monitored. This is particularly useful for the detection of cancer cells and other diseases. Fluorescent labelling is used to detect and locate cancerous cells [93].
- **Optical Imaging:** Nanoparticles can be used in optical imaging techniques by interacting with light. This is particularly useful in the development of rapid and low-cost diagnostic methods in the biological environment.

### 6.3. Nano-Biosensors

Nanotechnology benefits the development of biosensors that can detect biomolecules. Nano-biosensors can recognise biomarkers at low levels and analyse them with high sensitivity to identify diseases [5].

- **Electronic Biosensors:** Nanomaterials are used in sensors that can detect electron transfer of biological molecules. It allows diseases such as cancer, heart disease or infections to be detected before they progress [5].
- **PDA (Polydopamine) and Graphene-based Biosensors:** Such sensors have been developed for the detection of cancer cells and offer fast and reliable results.
- **Immunosensors:** Nanotechnological immunosensors can detect biomarkers by antigen-antibody reactions. These sensors have an important role in the diagnosis of diseases such as cancer and HIV.

### 6.4. DNA and genetic diagnosis

Nanobiotechnology also has an important role in areas such as genetic disease detection and genetic profiling. Nanoparticles are useful in directing genetic material to specific regions.

- **DNA Nanobiosensors:** Nanoparticles with DNA targeting and recognition can be used in the diagnosis of genetic diseases. Nanoparticles that interact with DNA sequences can provide sensitive results in detecting genetic changes [5], [17].



- Polymerase Chain Reaction (PCR) Assisted Diagnosis: Nanotechnological tools can make PCR technology faster and more efficient. Nanoparticles accelerate DNA amplification and provide more sensitive results for the detection of genetic diseases [1].

### 6.5. Drug transport systems

Drug Delivery Systems (DDS) are systems designed to ensure effective delivery of drugs to targeted sites. These systems are being developed to increase the bioavailability of drugs, reduce side effects and improve treatment efficacy. Nanotechnology has an important role in the evolution of drug delivery systems. Nanoparticles and nanomaterials offer a more precise and more effective approach to treatment by enabling specific delivery of drugs to target cells or tissues.

#### 6.5.1. Basic properties of drug transport systems

Biocompatibility and Biodegradability: Drug delivery systems should not harm the body and should dissolve safely in the biological environment. The biodegradability of nanomaterials increases the safety of such systems [18], [61].

- Targeted Delivery: Nanoparticles can be created to direct drugs only to specific cells or tissues. This increases the effectiveness of the treatment by preventing damage to healthy cells.
- Controlled Release: Drug delivery systems can control the release of the drug. This allows medicines to be administered in continuous low doses, ensuring a longer duration of treatment.

#### 6.5.2. Types of drug transport systems

##### 6.5.2.1. Nanoparticles (NPS)

Nanoparticles are micro and nano-sized transport systems that usually have dimensions between 1-100 nm and are targeted transport in biological systems. Nanoparticles are usually made of lipid, polymer or inorganic materials [9], [94], [95].

- Lipomas: They are nanoparticles composed of lipid layers and can load both hydrophobic and hydrophilic drugs. They are frequently used in cancer treatment.
- Polymeric Nanoparticles: Polymers can be used to form the structure of drug delivery systems. These nanoparticles can provide controlled release by carrying drugs in encapsulated or dissolved form.
- Gold Nanoparticles: It is used in targeted treatment systems for cancer cells. Gold nanoparticles are widely used for cell-specific transport and photothermal therapy, especially in cancer treatment [42], [96].

##### 6.5.2.2. Nanotubes

Carbon nanotubes are used in drug transport systems due to their hollow structure. These nanotubes are generally recognised as effective vehicles for carrying drugs and delivering them to target cells [16], [20].

- Carbon Nanotubes (CNTs): Carbon nanotubes have large surface areas, enabling the drug to be transported in higher quantities. They also have the ability to cross cell membranes, making them highly valuable in areas such as gene therapy and neurological treatment.

##### 6.5.2.3. Nanocellular systems

Nanoparticles are often assembled with biological structures created for cell-specific transport. These systems can transport drugs directly to target cells or tissues.

- Dendrimers: Dendrimers, which are versatile polymeric structures, are nanomolecules that carry drugs and have advanced targeting properties. They are used in the treatment of genetic diseases and cancer treatment.
- Liposomes: Microscopic capsules composed of lipid bilayer. By keeping the drugs inside, they provide cell-specific transport and enable targeted therapy.

#### 6.5.2.4. Nanospheres

Nanospheres are drug-carrying nanocapsules and can be used to control the release rate of drugs. These systems can be used to accumulate drugs and then deliver them towards target cells.

#### 6.5.2.5. Genetic and DNA based systems

Nanotechnology is used in the field of gene therapy. Drug delivery systems can have a transport role to deliver genetic material to cells [17], [97]. Gene delivery systems: Nanoparticles are used in the treatment of genetic diseases by carrying DNA or RNA molecules. These therapies are envisaged as a promising approach, especially for cancer and hereditary diseases [29], [67], [68], [97], [98].

#### 6.5.3. Usage areas of drug transport systems

Cancer Therapy: Nanoparticles provide targeted drug delivery to cancer cells, providing more effective treatment and fewer side effects. In cancer treatment, nanoparticles can carry drugs specific to cancer cells or photothermal therapy (killing cancer cells by laser heating) can be provided. Gene Therapy: Nanotechnology provides new ways of treatment by using gene transport systems in the treatment of genetic diseases. Genetic therapy can be applied by transporting DNA or RNA molecules to target cells with the help of nanoparticles. Neurological Diseases: Nanotechnology can transport drugs directly to the brain by crossing the blood-brain barrier. Nanoparticles can be used as an effective treatment method in the treatment of neurological diseases such as Alzheimer's and Parkinson's. Antibacterial Treatment: Nanoparticles have antibacterial properties and can also provide direct targeted treatment against bacteria. This can increase the effectiveness of antibiotics and prevent antibiotic resistance.

#### 6.5.4. Advantages of drug transport systems

- High Efficacy: Drugs can be delivered in higher concentrations to targeted areas.
- Reduced Side Effects: The risk of damage to healthy cells is reduced because the drug is only effective in the target cells.
- Controlled Release: Drugs can be released at specific intervals, which increases the effectiveness of the treatment [9], [26], [83].

#### 6.6. Tissue engineering and cellular therapies

Tissue engineering and cellular therapies are two important factors that have revolutionised biotechnology and medicine. These fields combine biological, chemical and engineering approaches to repair and regenerate damaged or lost tissues and organs. New technologies such as nanotechnology and genetic engineering have an important role in making tissue engineering and cellular therapy applications more effective [99], [100].

##### 6.6.1. Tissue engineering

Tissue engineering is the process of artificially creating or repairing biological tissues and organs. The main goal in this field is the functional regeneration of damaged or lost tissues. Tissue engineering combines factors such as cell biology, materials science, genetic engineering, nanotechnology and mechanical engineering.

#### 6.6.1.1. Basic components

**Cells** The most important components in tissue engineering are cells that are usually taken from the body or produced by biotechnological methods. These cells are used to create artificial tissues and organs. **Biomimetic Materials:** They are biological materials that provide a suitable environment for the growth and proliferation of cells. These materials have similar properties to the properties of natural tissues. For example, polymeric, hydrogel or biological materials are widely used in this field. **Bioreactors and 3D Printing Technology:** Bioreactors are used for the growth of cells in tissue engineering. In addition, 3D bioprinting technology shows great potential for tissue and organ production in tissue engineering [20], [101].

#### 6.6.1.2. Application areas

**Bone and Cartilage Repair:** Tissue engineering offers alternative treatments for bone fractures, joint diseases and cartilage damage using biomaterials and cellular therapies. Personalised bone implants can be produced with 3D printing.

**Skin Wound Healing:** For burn treatment or skin diseases, tissue engineering can enable the proliferation and regeneration of skin cells with cellular therapies.

**Liver, Kidney and Heart Repair:** Bioengineering approaches that can be used for organ transplantation achieve functional recovery or reconstruction of organs. Alternative solutions are being developed especially for patients waiting for organ transplantation [99].

#### 6.6.1.3. Challenges and future perspectives

Tissue engineering is associated with significant challenges such as cell growth, adequate vascularisation and tissue integration. To overcome these problems, disciplines such as bioengineering, genetic engineering and nanotechnology are progressing with greater integration.

#### 6.6.2. Cellular therapies

Cellular therapy is an approach that uses cells to treat certain diseases. This type of treatment aims to heal by transplanting new or modified cells into diseased areas of the body. Cellular therapies have shown promising results in the treatment of various medical conditions such as genetic diseases, cancer, cardiovascular diseases and neurological disorders.

##### 6.6.2.1. Types of cellular therapy

- **Stem Cell Therapy:** Stem cells are cells that can transform into various cell types in the body and have regenerative properties. Stem cell therapy is particularly used to treat tissue and organ damage.
  - **Embryonic Stem Cells:** Stem cells that can differentiate into various cell types.
  - **Adult Stem Cells:** Stem cells that can be found in various parts of the body and transform into a limited number of cell types. Haematopoietic stem cells are used in blood diseases.
  - **Induced Pluripotent Stem Cells (iPS Cells):** They are cells formed by making adult cells pluripotent by genetic modification. These cells have an important potential in the treatment of genetic diseases.

- Cellular Therapies in Cancer Treatment: Cellular therapies are also used in cancer treatment. Immune cells or modified T cells are often used to target and destroy cancer cells.
- CAR-T Cell Therapy: This treatment takes patients' T cells and genetically modifies them to make them more effective against cancer cells. It is recognised as a major step forward in cancer treatment [34], [48].
- Cell Based Vaccines: It is a treatment method used to create a specific immune response to cancer cells.
- Neurological Diseases and Cellular Therapies: In the treatment of neurological diseases, stem cell therapies can help regenerate damaged brain tissue. Cellular therapies are used in the treatment of diseases such as Parkinson's, Alzheimer's and spinal cord injuries [20], [48], [101].
- Genetic Diseases: Stem cell therapies are used in the treatment of genetic diseases, replacing diseased cells with healthy cells [29].

### 6.6.3. The role of nanotechnology in tissue engineering and cellular therapies

Nanomaterials are used in areas such as the production of biomimetic materials that support the growth of cells, the development of drug or gene delivery systems, and the improvement of tissues [19], [99].

- Nanotubes and Nanoparticles: Nanotubes can be used as efficient transport systems that carry drugs or genetic material into cells. Nanoparticles enable cellular therapies to be applied more effectively.
- Biomimetic Surfaces: Nanotechnology enables cells to adhere, proliferate and differentiate by creating biomimetic surfaces and matrices.
- Nanobiosensors: Can be used to monitor the health of cells and tissues [86], [102].

### 6.7. Biosensors and Microfluidic Systems

Biosensors and microfluidic systems are tools that can perform fast, sensitive and low-cost analyses. These technologies are used to monitor various biological and chemical parameters, diagnose diseases and guide treatment processes.

#### 6.7.1. Biosensors

Biosensors are devices that detect and measure biological and chemical parameters and convert this measurement into an electrical, optical or mechanical signal. They basically consist of three main components:

- Biological Sensing Element: Works with biological substances such as enzymes, antibodies, nucleic acids or cells. This element provides specific interaction with the target molecule [103].
- Transducer: It converts the biological signal received from the sensing element into electrical, optical or mechanical signals. For example, an electrode can detect the signal and this can be converted into a digital display.
- Processing and Reading Unit: It analyses the data measured by the biosensors and provides an output to the user. This output is usually displayed in a digital format [5], [17].

##### 6.7.1.1. Usage areas of biosensors

- Diagnosis and Monitoring: Biosensors are used in the early diagnosis of conditions such as cancer, infections, heart diseases. For example, special biosensors are being developed for cancer biomarkers.
- Food and Water Security: Biosensors can be used for the detection of pathogens and contaminants in the food industry.
- Environmental Monitoring: Biosensors can be used effectively in air and water quality monitoring [5].

##### 6.7.2. Microfluidic systems

Microfluidic systems are used to manage and process small-scale fluids. These systems, which usually consist of microchannels, pumps and valves, aim to perform laboratory-scale processes faster and at low cost. The main advantages of microfluidic systems are:

- **Low Sample Quantity:** Microfluidic systems can analyse using only a few microlitres of liquid.
- **High Precision and Speed:** Microscopic reduction of various biochemical reactions is aimed at faster and more sensitive analyses.
- **Integrated Laboratory Systems:** A microfluidic platform can be integrated with biosensors to become lab-on-a-chip (LOC) devices.

#### 6.7.2.1. Application areas of microfluidic systems

**Biotechnology and Clinical Diagnosis:** Microfluidic systems can be used to analyse biomolecules, rapidly perform blood tests and perform genetic tests.

- **Cell Analysis:** Microfluidic platforms are used in the analysis of cancer cells or immune system cells, as they study the behaviour and properties of cells.
- **Multiple Biomarker Analysis:** More comprehensive diagnoses can be made by using microfluidic systems for simultaneous monitoring of multiple biomarkers.

#### 6.7.3. Integration of biosensors and microfluidic systems

Biosensors and microfluidic systems are complementary technologies. Microfluidic systems enable biosensors to perform fast and accurate measurements on a large number of samples. This integration enables the development of "lab-on-a-chip" platforms. For example, it is possible to rapidly detect various biomarkers in blood samples using biosensors in microfluidic channels. Furthermore, the combination of microfluidic systems and biosensors can automate clinical diagnostics and make laboratory analyses more portable [5], [104], [105].

##### 6.7.3.1. Integrated application areas

- **Clinical Diagnosis:** Processes such as rapid blood tests and biomarker analysis can be performed in an integrated manner on microfluidic-biosensor platforms.
- **Multiple Parameter Monitoring:** Biosensors, when combined in microfluidic systems, have the capacity to monitor multiple biological parameters simultaneously.

As a result, biosensors and microfluidic systems offer great advantages, especially in the fields of diagnosis, treatment and disease monitoring. Thanks to microfluidic systems, biosensors can operate faster, more precisely and more efficiently. In the future, the integration of these two technologies will allow the development of systems that are more portable, user-friendly and capable of performing rapid tests [4].

#### 6.8. Advantages in clinical applications of nanobiotechnology

Some advantages of nanobiotechnology in clinical applications [31], [57].

- **Early Diagnosis and High Sensitivity Tests:** Nanotechnological devices enable more sensitive detection of biomarkers. Nanoparticles and nanomaterials can detect markers in the early stages of diseases such as cancer and initiate faster and more effective treatment. For example, nanoparticles can bind to cancer cells and target biomarkers that will enable early diagnosis of the disease [18].
- **Drug Delivery and Targeted Therapy:** Nanoparticles can provide more effective delivery of drugs to targeted areas. This is especially important in the treatment of diseases such as cancer. Nanoparticles provide treatment without

damaging surrounding tissues by carrying drugs directly to tumour cells. Such targeted treatment methods minimise side effects by reducing damage to healthy cells during treatment [18], [19].

- **Biosensors and Sensing Systems:** Nanobiotechnological sensors show very high sensitivity in biological and chemical analysis. It detects pathogens, cancer cells and other biomolecules, especially in blood, urine or other biological fluids. These sensors enable monitoring of diseases and treatment responses.
- **Genetic Therapy and Personalised Treatment:** Nanoparticles enable effective transport of genetic material to target cells in gene therapy applications. They also have an important role in the development of personalised treatment methods based on individual genetic characteristics [47], [65], [73], [74], [106].
- **High Effect at Low Dose:** Nanotechnology enables drugs to show high effect with low doses. Nanoparticles enable drugs to be more effectively distributed in the biological system and reach their targets. In this way, the duration of treatment is shortened, side effects are reduced and the cost of the treatment process is reduced.
- **Tissue Repair and Regenerative Medicine:** Nanoparticles can promote the growth and differentiation of cells and accelerate the repair of damaged tissues. In addition, nanomaterials can be used in the production of artificial organs.
- **Antibacterial and Antiviral Effects:** Nanoparticles can show antibacterial or antiviral properties by interacting directly with microorganisms. This offers an important innovation in the treatment of infection, aiming to prevent bacteria and viruses from rapidly evolving and becoming resistant to drugs.

### 6.9. The future of nanobiotechnology

Nanobiotechnology is a rapidly developing field in recent years and has the ability to create important revolutions in many fields such as health, environment, energy and industry in the future. In the future, nanobiotechnology is expected to make significant progress in some of the following areas [50], [70].

#### 6.9.1. Personalised medicine and genetic therapy

One of the most promising applications of nanobiotechnology is personalised medicine. By combining genetic engineering and nanotechnology, customised treatment methods can be developed based on the genetic structure of each individual. Nanoparticles can increase the effectiveness of gene therapy applications by carrying genetic material to target cells [73], [74].

#### 6.9.2. Intelligent medication systems

Nanotechnological systems can optimise the targeted transport and release of drugs. In the future, "smart drugs" may become more widespread. Thanks to nanoparticles, these drugs can be designed to be released only at the required time and in the required amount to specific cell types or diseased areas. This approach can increase the efficacy of drugs while minimising side effects [55], [107], [108].

#### 6.9.3. Early diagnosis and nanobiosensors

Nanobiotechnology can develop much more sensitive biosensors to help detect diseases in their early stages. These sensors can recognise various diseases such as cancer, heart disease, neurological disorders at the molecular level [17].

#### 6.9.4. Targeted cancer therapies

Nanoparticles prevent damage to healthy cells during treatment by carrying drugs directly to cancer cells. In addition, nanoparticles can inhibit the growth of tumours by disrupting the metabolic functions of cancer cells. In the

future, it is expected to develop more effective, less side-effective and more targeted treatment methods in cancer treatment.

#### *6.9.5. Tissue engineering and regenerative medicine*

Nanomaterials can enable the healing of damaged tissues in the body. Especially in areas such as organ transplantation and tissue regeneration, new treatment options can be foreseen for the repair of damaged tissues by using nanotechnological methods. In addition, biological implants and artificial organs can be produced using nanotechnology.

#### *6.9.6. Antibiotic resistance and infection treatment*

Nanotechnology can offer new treatment options against bacteria that develop resistance to antibiotics. Nanoparticles can be effective against resistant bacteria by targeting the cell membranes of microorganisms and increasing the effectiveness of antibiotics. In addition, antiviral agents developed with nanobiotechnology can prevent viruses from rapidly evolving and developing resistance to treatments [75].

#### *6.9.7. Environmental and biotechnological applications*

Nanomaterials can offer environmentally friendly solutions such as water purification, air purification and waste management. They can also develop more efficient and sustainable methods in biological production processes (e.g., biofuel production or food processing) [109], [110].

## **7. Conclusion**

Recently, nanobiotechnology has led to revolutionary breakthroughs in various fields, including health, agriculture, environment, energy, construction, textiles, animal husbandry, and food. Due to scientific and engineering advancements, this technology allows for unprecedented solutions, particularly in the health industry. With many diagnoses, treatments and applications, it is becoming a more rigorous and innovative source of technology. Nanotechnology refers to the use of matter on an atomic and molecular scale to construct structures of extremely small size. While these phenomenon, also the interaction of these structures with biological systems, has played a significant role in generating a lot of potential in the health sector. In this regard, clinical implementations of nanotechnology are significantly crucial in describing more sensitive diagnostic approaches as well as treatment options for individualized treatment forms and early-stage interventions. Unfortunately, the clinical approval processes that will guarantee the applicability of nanotechnology within the framework of health is a very complex and long-lasting procedure. The translation of nanotechnological products into the clinical setting frequently struggles with the challenges associated with the specific and unpredictable nature of their interactions with living systems. The nanoparticles that have several benefits including their size and surface properties can greatly affect their functioning in the body and targeting of critical cells. As a result, the usual tests do not suffice and the development of unique tests is necessary for safety and efficacy. Nanotechnological products are built over a series of steps from the preclinical test to the clinical trial. The process is long, it can take years. The safety of these products need to be approved by regulatory bodies that have to carefully evaluate the biological effects of the products. But the very nature of nanotechnology is more intricate by virtue of the fact that international standards on regulating it have not yet been established. Such uncertainties render the approval process longer and tedious. After entering the market, nanotechnological products also require long-term safety monitoring of their consumer risks. This is done methodically to evaluate the enduring impacts of the products on population health. Nanotechnology shows tremendous potential, particularly in the area of cancer therapy. One major obstacle in the treatment of cancer is that

there is no single treatment of cancer that does not harm the healthy cells along with the cancerous ones. Nanoparticles allow drugs to be targeted and delivered to the cancerous cells as they are able to identify and bind to specific biomarkers on the surface of the cancer cells. Nanoparticles reduce the exposure of the healthy cell membrane while also allowing drugs to deliver to cancerous cells as the treatment progresses. Nanobiotechnology also shows great promise for the early diagnosis and prevention of diseases. With nanotechnological sensors and biomarkers, the diseases can be diagnosed much earlier, allowing for faster and more efficient interventions. Genetic-level interventions provide treatment-specific solutions along with avoiding damages to healthy cells as well as makes the treatment process more effective. Nanobiotechnology: Advantages in Treatment The specific effects and application advantages of this technique ensure better effectiveness while avoiding damages during the treatment process. Also, the use of this technology helps a lot in terms of energy efficiency and resource utilisation in the medical science due to the environmentally friendly solutions and sustainability. Nanotechnology's increased efficiency in the health sector leads to lower treatment costs while producing better results. Nonetheless, the long-term impact and safety concerns regarding nanobiotechnology need to be addressed and analyzed thoroughly. Studies are needed prior to widespread use in health field due to the unknown long-term effects of these nanoparticles in biological systems. The significant step in overcoming technical and ethical barriers in this area allows the efficient implementation of nanotechnology in the health industry. To summarise, nanobiotechnology has the capacity to transform the healthcare industry, yet careful assessment of these technologies is necessary for safe and effective application. Nanobiotechnology can make faster, more precise and unique health solutions contributing to a healthier society.

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