

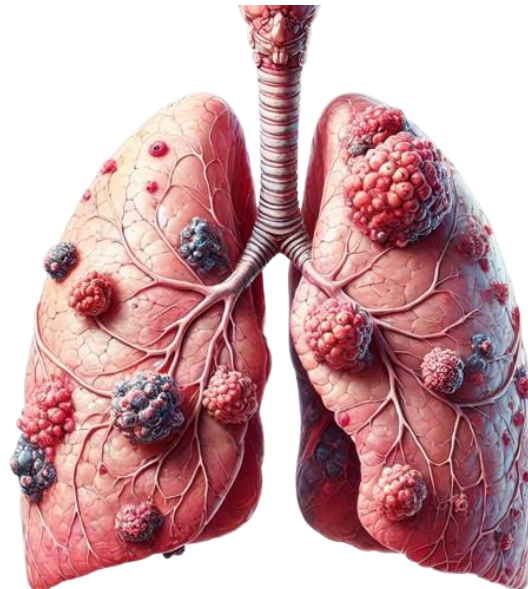


**TECNOLOGIA  
SETÚBAL**

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POLITÉCNICO SETÚBAL

LUÍS CORREIA 202200162  
RAQUEL CLEMENTE 202200102

**NANOTECHONOLOGIES FOR LUNG  
CANCER TREATMENT USING  
GOLD NANOPARTICLES**



Degree Report  
Nanotechnologies in Biomedicine

**DOCENT**

Professor Catarina Santos

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## TEAM



Luís Correia

Nº 202200162

LTB – 2024/2025



Raquel Clemente

Nº 202200102

LTB – 2024/2025

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Next, we would like to thank everyone who has helped us, directly or indirectly, to better understand, develop and enrich the subject of cancer, more specifically lung cancer and its complications, as well as its solutions, and our learning process.

## ABSTRACT

In this report, as already discussed in its title, we will talk about nanotechnologies for the treatment of lung cancer.

They are redefining the horizons of modern medicine, presenting numerous innovative solutions to some of the biggest challenges in oncology, namely with regard to lung cancer, which is one of the most aggressive and lethal forms of cancer worldwide. Through the manipulation of materials on the nanometer scale, it is possible to create therapeutic systems with unprecedented precision, capable of selectively locating and attacking tumors, minimizing the side effects of conventional treatments, such as chemotherapy.

Nanotechnologies also pave the way for earlier diagnoses, sharper tumor imaging, and advanced therapies that combine multiple approaches. In a scenario where the need for innovation is critical, nanotechnology offers new hope in the fight against lung cancer, promising to revolutionize the future of oncology medicine.

Lung cancer is a type of cancer that originates in the lungs, as the name mentions, usually in the cells that line the airways. It can also be said that this is characterized by the uncontrolled growth of abnormal cells in the lungs, which form so-called tumors. When left untreated, the cancer can spread to other parts of the body (metastasize), thereby compromising vital organs.

It can also be said that there are two types of lung cancer, which are, namely: Non-small cell carcinoma (NSCLC) and small cell carcinoma (SCLC).

**Keywords:** Nanotechnologies, Biomedical, Gold Nanoparticles, Cancer, Lung, among others.

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## **LIST OG ACRONYMS AND ABBREVIATIONS**

AuNPs - Gold Nanoparticles

PDT - Photodynamic therapy



## **Chapter 1**

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This chapter aims to introduce the theme of this project. We will indicate our objectives, present the logo, explain the reason for it and the name, and finally, the structure of our work.

### **1. Introduction**

#### **1.1. Motivation**

In the Nanotechnologies course, the students were asked to carry out a research project and produce a poster.

This topic was chosen because of its relevance and transformative potential in modern medicine.

Lung cancer is one of the most aggressive forms of cancer with the highest mortality rate in the world, and conventional treatments such as chemotherapy often have significant limitations, such as serious side effects and reduced effectiveness in advanced stages.

Nanotechnology, on the other hand, has emerged as an innovative approach, offering more precise and effective solutions, from targeted drug delivery to early diagnosis. This promising field has the potential to revolutionise oncology, and addressing this topic allows us to explore the future of personalised and more efficient treatments in the fight against cancer.

#### **1.2. Objective**

For a better understanding of the report, we can start by saying that we will be looking at nanotechnologies for the treatment of cancer, specifically lung cancer.

As such, the aim of this work is to give a detailed account of the knowledge we have acquired on this subject, according to the research carried out.

#### **1.3. Website Logo – CANCER NANOTECHONOLOGIES**

According to, Figure 1 the logo created by us is as follows.



*Figure 1 - Cancer Nanotechnologies logo*

### **1.3.1. Reason for choosing the name and logo**

The name was chosen based on the disease covered, with the aim of being eye-catching and appealing to people.

The logo was chosen based on the white ribbon that signifies lung cancer.

### **1.4. Work Structure**

This work is divided into five distinct chapters and among them the respective subchapters.

In the first chapter, we talk about the motivation, the objective, the reason for the name of the logo, as well as the structure of the work.

In the second chapter, the historical contextualization of nanotechnologies in the world is addressed, what lung cancer is, what types of lung cancer exist, the risk factors, their symptoms, the diagnoses that can be reached, as well as their treatments.

Regarding the third chapter, it emphasizes the biomedical applications that these nanotechnologies can have, emphasizes their toxicity, emphasizes the properties, as well as the production methods of nanotechnologies, which are the ones that are talked about in the work.

In the fourth chapter, the same topics are emphasized, but they are related to gold nanoparticles.

Finally, in the fifth chapter, a brief conclusion of all this research work is obtained.

## Chapter 2

This chapter is dedicated to a brief explanation of lung cancer, where we will explain its definition, what types there are, symptoms, risk factors, diagnosis and treatment, stages and prevention.

### 2. Lung Cancer in Context

#### 2.1. Lung Cancer

Lung cancer is a disease characterised by the uncontrolled growth of abnormal cells in the lungs. These cells can form tumours that impair the functioning of the lung and can spread to other parts of the body, a process known as metastasis.

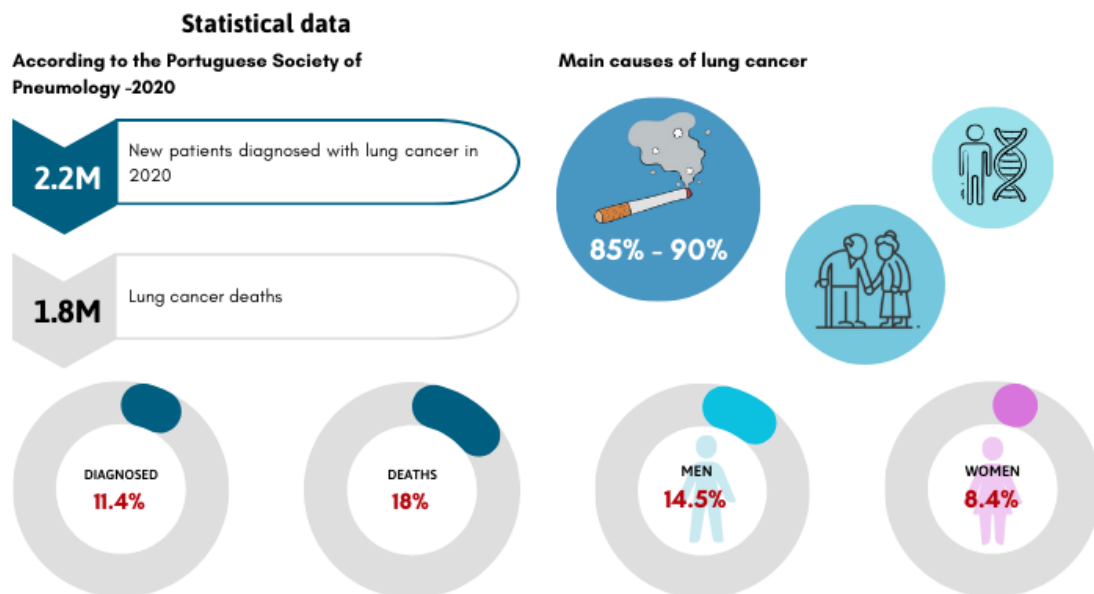


Figure 2 - Statistical Data (according to the Portuguese Society of Pneumology - 2020)

## **2.2. Types of Lung Cancer**

For a better understanding of lung cancer, it's important to note that there are two types of lung cancer: non-small cell lung cancer and small cell lung cancer.

- ☞ Small cell lung cancer - A more aggressive type, often associated with smoking.
- ☞ Non-small cell lung cancer - The most common type, accounting for around 85 per cent of cases, with subtypes such as adenocarcinoma and carcinoma.

Non-small cell lung cancer, which normally accounts for 85% of lung cancer cases and grows and metastasises more slowly, can be classified into three distinct subtypes, such as:

- ☞ Adenocarcinoma - this is the most common malignant epithelial tumour of lung cancer, accounting for 30-50% of cases. It is more common in women and non-smokers and is therefore less associated with a history of smoking.
- ☞ Squamous cell carcinomas – squamous cell, epidermoid or squamous cell – represent around 25-30% of all lung tumours and occur mostly in men. It is strongly related a history of smoking. However, although smoking habits have not changed considerably, the incidence of this type of cancer has been decreasing in relation to adenocarcinoma, probably due to changes in the constituents of tobacco.
- ☞ Large cell carcinomas - rarer, accounting for 3% of cases.

Small cell lung cancer is strongly associated with smoking. This type of cancer occurs both in the periphery of the lungs and in the large bronchi.

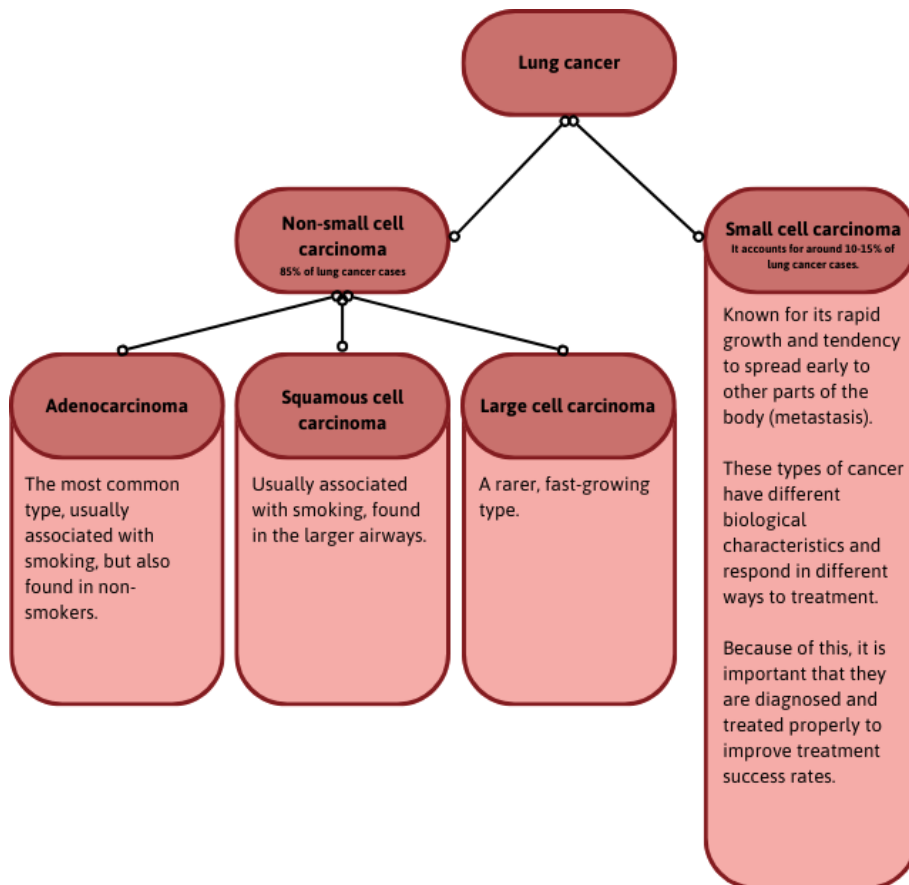


Figure 3 - Types of Lung Cancer

### 2.3. Risk Factors

The main risk factor for lung cancer is smoking, which accounts for approximately 85 per cent of cases. Smoking causes the inhalation of carcinogenic substances that damage lung cells over time. Other risk factors can be seen in Figure 4.

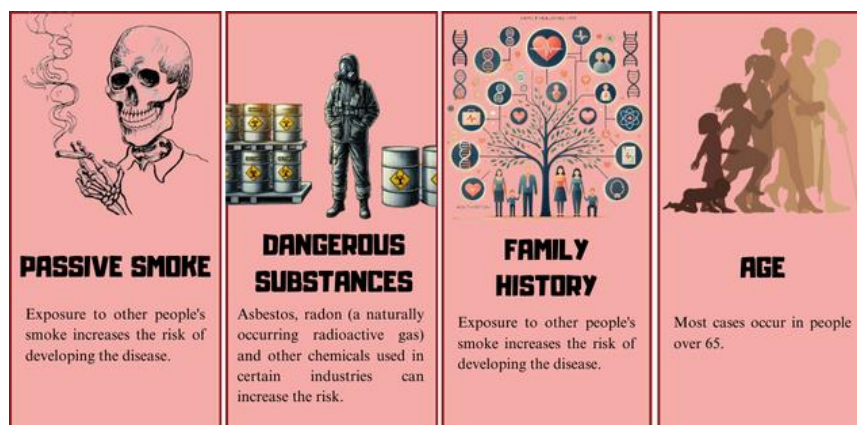


Figure 4 - Risk Factors

## 2.4. Symptoms

The symptoms of lung cancer may not be evident in the early stages, which makes early diagnosis difficult. However, the most common signs are shown in Figure 5.

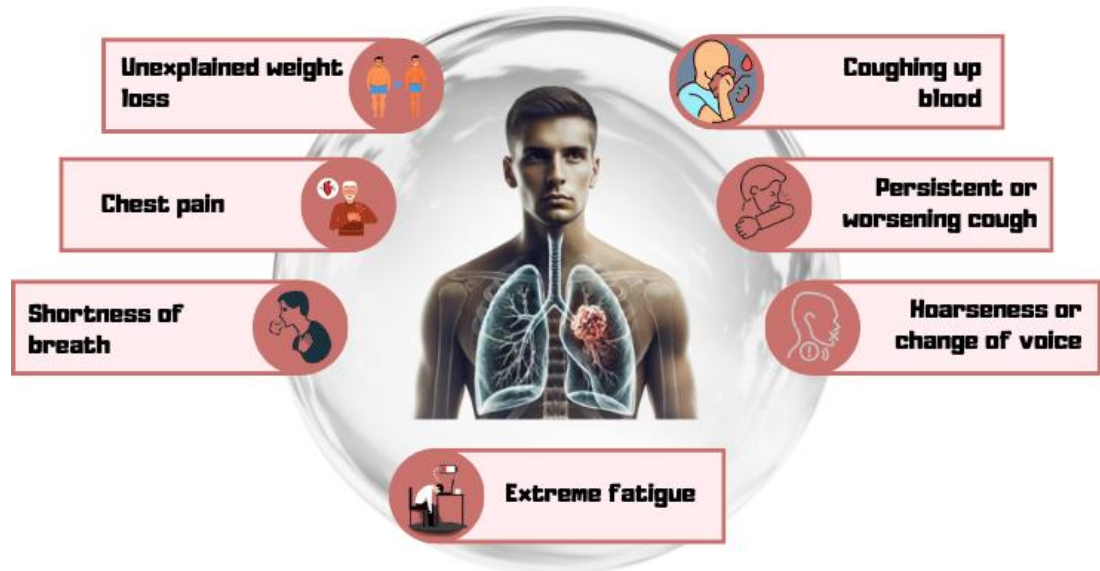


Figure 5 - Symptoms

## 2.5. Diagnostics

The diagnosis of lung cancer involves a series of tests to confirm the presence and extent of the disease. The main methods are shown in Figure 6.

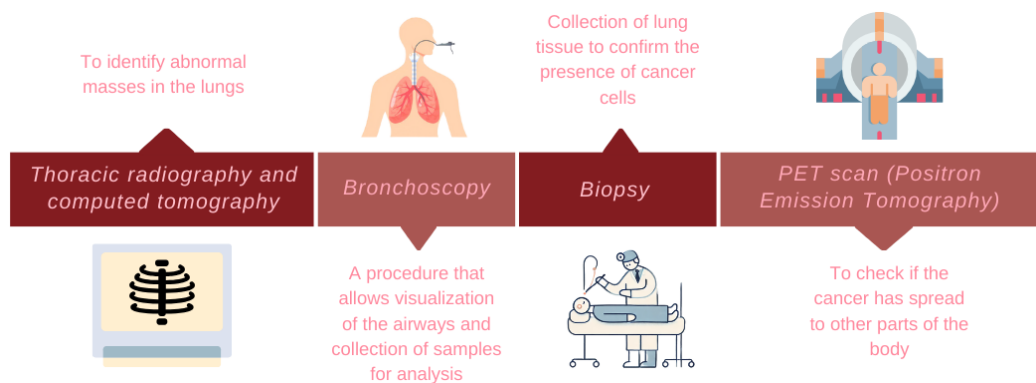


Figure 6 - Diagnostics

## 2.6. Stages

Lung cancer is categorised into different stages based on its extent and spread.

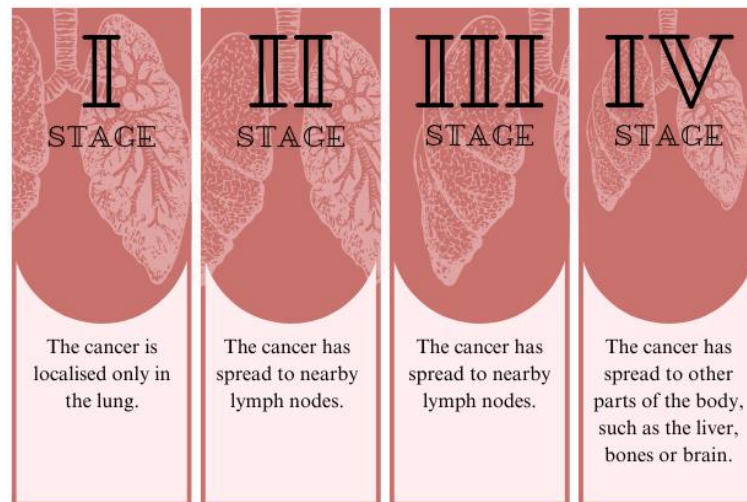


Figure 7 - Stages

## 2.7. Treatments

The treatment of lung cancer depends on the type, stage and general condition of the patient. Treatment is often multidisciplinary, involving various therapies to improve results. The main options are shown in Figure 8.

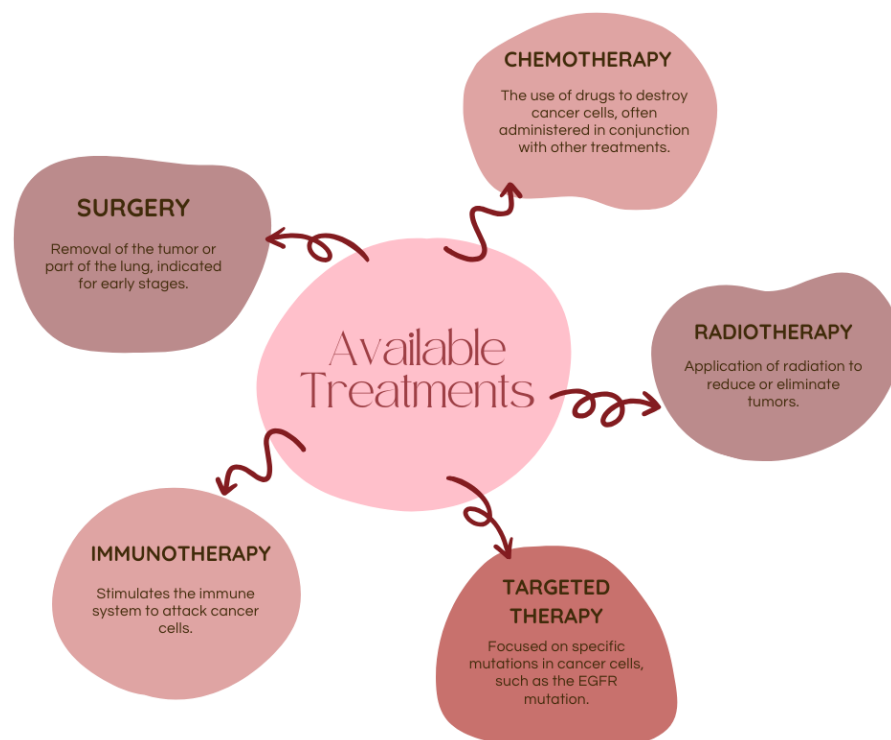


Figure 8 - Treatments

## **2.8. Prevention**

There are ways to try to prevent lung cancer. Some of these are shown in Figure 9.



*Figure 9 - Prevention*



## **Chapter 3**

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This chapter addresses the created project for the medical device created, its components and materials, its operation, the design of the prototype, its characterization as equipment, and its advantages and disadvantages.

### **3. Contextualisation of Nanotechnologies in the Treatment of Lung Cancer**

Nanotechnologies applied to the treatment of lung cancer represent transformative and promising areas of modern medicine, as previously mentioned. This field, which has evolved significantly over the last few decades, reflects advances in vast disciplines, including chemistry, biology, and physics, with a direct impact on oncology. The development of technologies capable of manipulating materials on a nanometric scale has brought new solutions to complex challenges in the treatment of lung tumours, one of the most lethal and aggressive forms of cancer.

For a better understanding of this report, we will look at the history of nanotechnology.

The idea of nanotechnology was first proposed in 1959 by Richard Feynman, a physicist, during a lecture entitled ‘There's a lot of space down there’. He predicted that in the future it would be possible to control atoms and molecules to create structures and technologies.

This visionary concept only began to be realised in the 1980s and 1990s, with the development of tools such as the scanning probe microscope, which allowed scientists to manipulate matter at extremely small levels.

Then, in the 1990s, nanotechnology was applied to medicine, especially in the development of drug delivery systems.

Then there were the first attempts to use nanotechnology in cancer treatments, with nanoparticles made from liposomes and biodegradable polymers, which were only approved in 1995.

In the 2000s and 2010s, nanoparticles were applied for the first time in pre-clinical studies for the selective delivery of chemotherapy drugs. With this sophisticated advance

in nanoparticles, they began to be used, enabling the controlled release of drugs and the combined use of chemotherapy and radiotherapy.

With regard to the future, it can be said that in recent years nanotechnologies have been applied in immunotherapy, helping to direct the immune system against cancer cells. In addition, liquid biopsy techniques make it possible to detect tumour markers in the blood, which consequently makes it possible to make earlier and, above all, less invasive diagnoses.

The future of these small-scale technologies therefore promises increasingly significant advances, with the development of programmable nanoparticles and nano robots that will be able to deliver drugs ultra precisely, ultimately personalising treatment based on the genetic profile of the tumour. In the 2000s and 2010s, nanoparticles were applied for the first time in pre-clinical studies for the selective delivery of chemotherapy drugs. With this sophisticated advance in nanoparticles, they began to be used to enable the controlled release of drugs and the combined use of chemotherapy and radiotherapy.

Regarding the future, it can be said that in recent years nanotechnologies have been applied to immunotherapy, helping to direct the immune system against cancer cells. In addition, liquid biopsy techniques make it possible to detect tumour markers in the blood, which consequently makes it possible to make earlier and, above all, less invasive diagnoses.

The future of these small-scale technologies therefore promises increasingly significant advances, with the development of programmable nanoparticles and nano robots that will be able to deliver drugs ultra precisely, ultimately personalising treatment based on the genetic profile of the tumour. These innovations bring longer life expectancy, fewer side effects and better results for all patients.[1], [2], [3]

### **3.1. Properties**

As in many other areas, there are specific properties for nanotechnologies in the treatment of cancer, particularly lung cancer. These are essential for understanding how it works and are also very promising. The main properties of nanoparticles can be found in the Figure 10.[4]

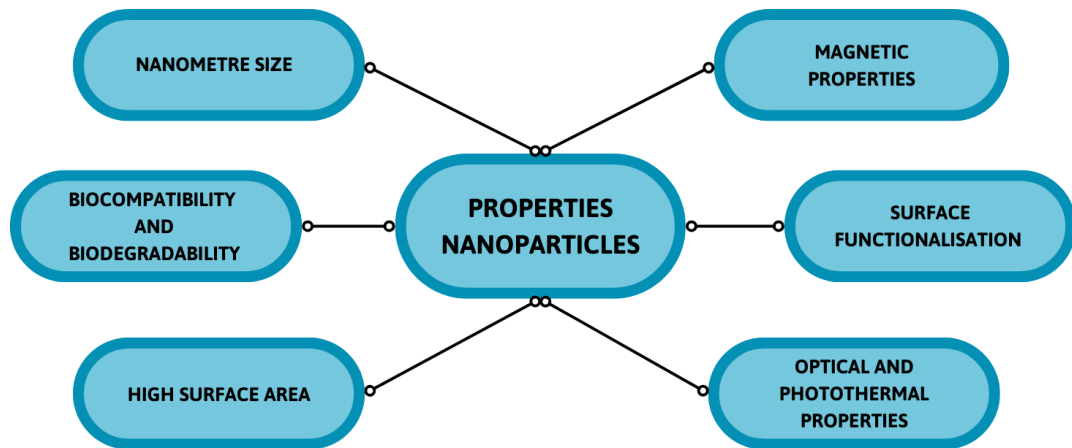


Figure 10 - Nanoparticle properties

### 3.2. Biomedical Applications

Nanotechnologies have revolutionised the treatment of lung cancer through remarkable advances in the development of targeted drug delivery systems.

These systems, using nanoparticles, allow chemotherapy drugs to be transported directly to cancer cells, reducing the impact on healthy tissue. This minimises the side effects of conventional treatments and increases efficacy by improving the absorption of drugs by tumour cells.[4]

#### Clinical Applications of Nanotechnologies

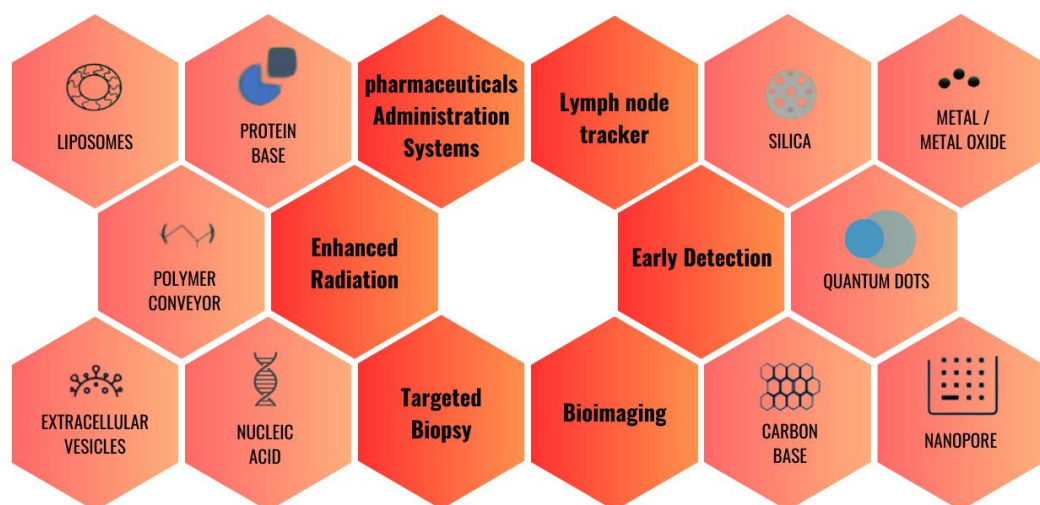
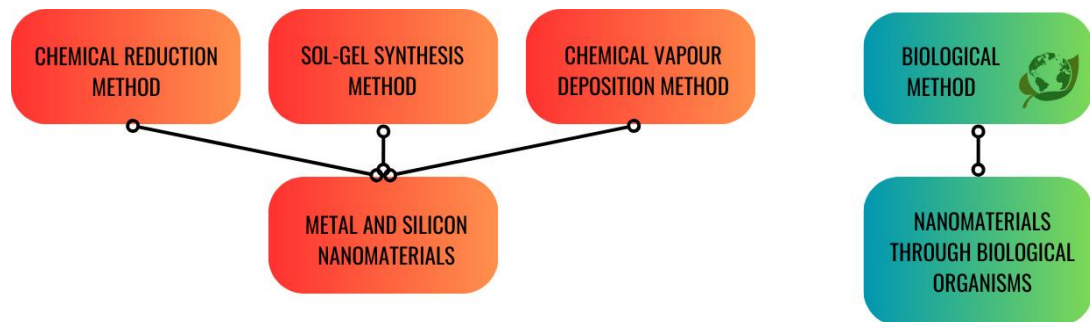


Figure 11 - Biomedical Applications

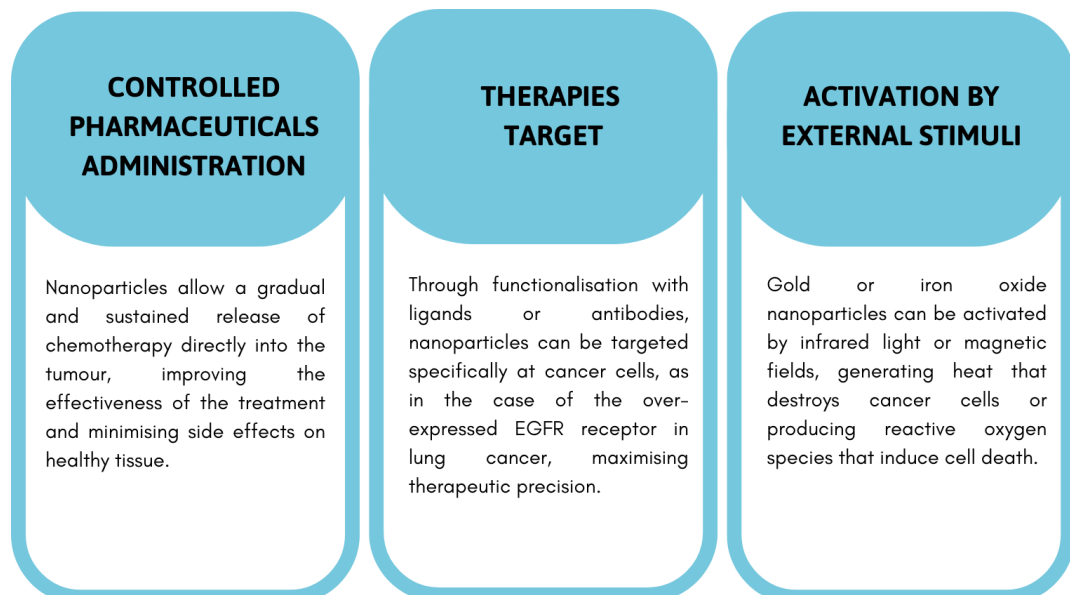
### 3.3. Production of Nanomaterials



### 3.4. Action Mechanisms

Nanotechnology's mechanisms of action in the treatment of lung cancer involve a highly sophisticated approach aimed at increasing therapeutic efficacy, improving selectivity and minimising the side effects associated with traditional therapies.

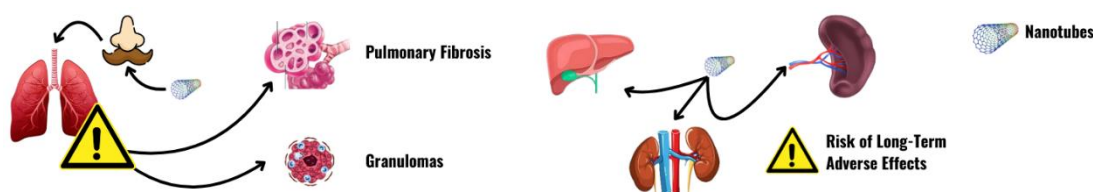
Nanotechnology offers the possibility of using nanoscale materials to improve drug delivery, tumour cell destruction and immune system modulation, among other advances. The main mechanisms of action of nanotechnologies in the treatment of lung cancer are presented below:[4]



*Figure 12 - Action Mechanisms*

### 3.5. Toxicity

Although nanoparticles offer significant benefits in the treatment of lung cancer, their toxicity represents a crucial challenge. Studies show that metallic nanoparticles, such as silver and iron oxide, can induce cell toxicity through the generation of reactive oxygen species (ROS), leading to oxidative stress and chronic inflammation in the lungs. In particular, carbon nanotubes can cause pulmonary fibrosis and granulomas when inhaled, increasing the risk of tissue damage. In addition, the accumulation of nanoparticles in organs such as the liver, spleen and kidneys can cause long-term adverse effects. Non-biodegradable nanoparticles tend to accumulate, enhancing cytotoxicity. Strict dosage control and appropriate functionalisation of nanoparticles are essential to mitigate these effects and guarantee their biocompatibility.[5]



## Chapter 4

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Chapter 4 aims to address nanotechnologies and gold nanoparticles.

### 4. Nanotechnologies and Gold Nanoparticles

#### 4.1. Biomedical Application

The biomedical applications of nanotechnologies in the treatment of lung cancer have shown enormous potential to transform the clinical approach to this disease, one of the most lethal globally. The development of specific nanomaterials for the treatment of lung cancer aims to overcome the limitations of traditional therapies, such as chemotherapy and radiotherapy, which often lack selectivity and can cause significant side effects.

Of the many biomedical applications that exist for this type of cancer, the one that stands out the most is targeted drug delivery. This is achieved through the engineering of nanoparticles, such as liposomes, gold nanoparticles and polymeric nanoparticles. These aim to carry chemotherapeutic agents in a controlled manner and release them directly into tumour cells.

The nanoparticles can be functionalised with ligands that recognise the receptors expressed on the lung cancer cells in the case, minimising the exposure of healthy tissues to the drug. This increases therapeutic efficacy while reducing adverse reactions, which improves systemic chemotherapy somewhat.

However, as mentioned above, this is only the biomedical application that stands out most in this type of cancer, as there are many others such as being used for diagnostics and theragnostic, for advanced therapies such as photothermal therapy, for RNA-based therapies, and for overcoming biological barriers.

In the image below, we can see numerous applications that have been discussed and not yet talked about:[4], [6]



Figure 13 - Biomedical Applications (Gold)

## 4.2. Properties

There are several properties of gold nanoparticles, but these have been emphasised:

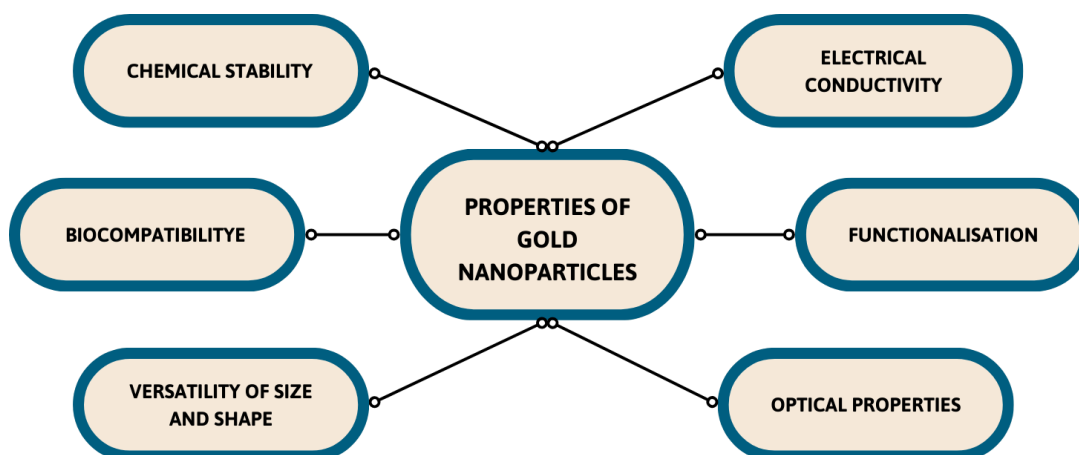


Figure 14 - Properties (Gold)

## 4.3. Production of Gold Nanoparticles

The production of gold nanoparticles (AuNPs) for the treatment of lung cancer involves a series of complex processes, with the aim of creating particles that are safe, effective and suitable for therapeutic and diagnostic applications. AuNPs are valued in nanomedicine due to their biocompatibility, stability and ability to functionalise with a variety of molecules, which allows for great versatility in cancer therapy. To be effective in the treatment of lung cancer, AuNPs must be carefully synthesised and prepared to ensure that they have the necessary characteristics to target tumour tissue precisely and safely.

The first step in producing AuNPs is choosing the synthesis method, which can be physical, chemical or biological. Chemical methods are the most common and use reducing agents to transform gold salts (such as gold chloride) into gold nanoparticles. In this process, the addition of stabilising agents is essential to control the size and shape of the nanoparticles and prevent them from aggregating. Chemical synthesis methods have the advantage of being fast and controllable, allowing the production of AuNPs with specific sizes and shapes, such as spheres, rods or stars, each with unique properties. Physical methods, such as evaporation and condensation, are less common due to high costs and the need for specialised equipment, but can be used to produce AuNPs of high purity.

One promising approach is biological synthesis, which uses living organisms such as bacteria, fungi and plants to reduce gold salts and produce AuNPs. This method is considered more sustainable and less toxic, as it avoids the use of potentially dangerous chemical agents. In addition, AuNPs produced by biological methods tend to be biocompatible, a desirable characteristic for applications in medicine. However, control over the size and shape of the nanoparticles in this method is more difficult to achieve, which may limit their use in some specific applications.

After synthesis, the AuNPs are functionalised to confer specific properties that improve their efficiency in the treatment of lung cancer. Functionalisation consists of adding bioactive molecules, such as drugs, antibodies or peptides, to the surface of the nanoparticles. This step is crucial as it allows the AuNPs to recognise and bind specifically to cancer cells, maximising the effectiveness of the treatment and minimising damage to healthy tissues. Functionalisation with polyethylene glycol (PEG), for example, is often used to increase the biocompatibility of AuNPs and prolong their circulation in the body, avoiding early recognition by the immune system.

Furthermore, the production of AuNPs for cancer treatment involves rigorous testing to guarantee the stability and safety of the nanoparticles. The characterisation of AuNPs, including analysis of their size, shape, surface charge and stability, is essential to confirm that they have the desired properties. Techniques such as electron microscopy, UV-vis spectroscopy and dynamic light scattering are often used to carry out these analyses. In vitro and in vivo tests are also needed to assess the effectiveness



of AuNPs in eliminating cancer cells, their ability to penetrate tumour tissue and their toxicity to healthy cells.

In short, the production of gold nanoparticles for the treatment of lung cancer is a process that requires precision and control over multiple stages, from synthesis to functionalisation and final characterisation. The ability to adjust the size, shape and surface of AuNPs makes it possible to adapt these particles to different therapeutic strategies, such as photothermal therapy and controlled drug release. With advances in production techniques and growing knowledge about the toxicity and biocompatibility of AuNPs, this approach represents a promising alternative for the treatment of lung cancer, with the potential to offer more effective, selective and less invasive treatments.[4], [5], [6]

#### **TOP-DOWN METHOD**



*Figure 15 - Production of Gold Nanoparticles*

#### **4.4. Actions Mechanisms**

Gold nanoparticles (AuNPs) have several mechanisms of action that make them promising tools in the treatment of lung cancer, offering high specificity and efficacy when interacting with tumour cells. Among the main mechanisms are photothermal therapy, photodynamic therapy, controlled drug release, immunotherapy and gene therapy, as well as the possibility of theranostic applications, which combine diagnosis and treatment.

Photothermal therapy (PTT) takes advantage of AuNPs' ability to absorb light at near-infrared (NIR) wavelengths and convert it into heat. This localised heating, resulting from exposure to NIR lasers, destroys tumour cells by damaging proteins

and nucleic acids, leading to cell death through necrosis or apoptosis. This method is especially advantageous due to its selectivity, as it preferentially targets tumour cells and preserves surrounding healthy tissue, making it an effective approach for treating solid lung tumours.

Photodynamic therapy (PDT) involves the functionalisation of AuNPs with photosensitising molecules which, when activated by light, produce reactive oxygen species (ROS) capable of oxidising essential cell structures, promoting the death of tumour cells. This method is useful for tumours that are resistant to conventional treatments, since ROS act independently of the signalling pathways that may be altered in cancer.

Another relevant mechanism is the controlled release of drugs. AuNPs, functionalised with chemotherapy drugs, act as vectors for the targeted and gradual transport of the drugs to the tumour. This selective delivery allows the controlled release of the drugs in response to the acidic pH of the tumour microenvironment, concentrating the therapeutic action on the cancer cells and reducing side effects. In this way, AuNPs make it possible to maintain an effective concentration of the drug in the tumour over time, increasing the effectiveness of the treatment.

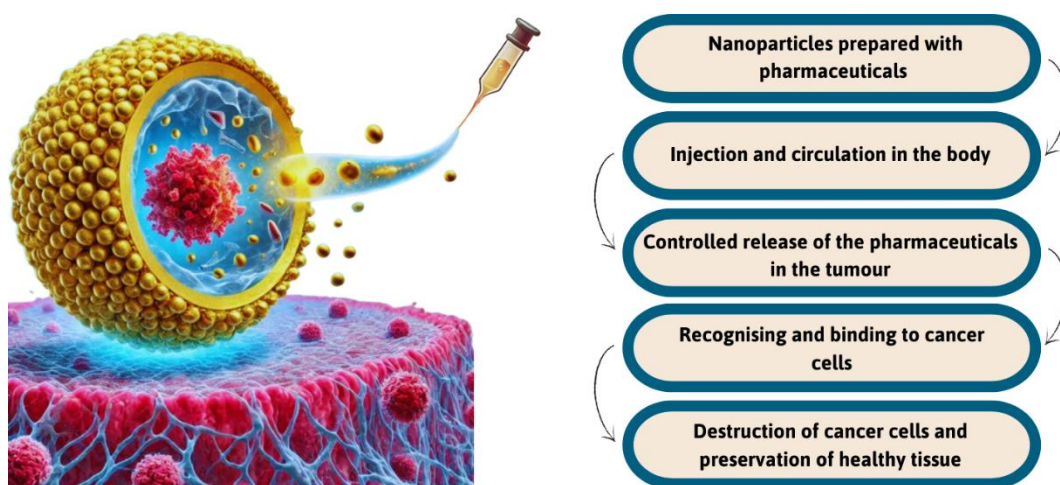
AuNPs also have promising applications in immunotherapy, as they are functionalized with immunomodulatory molecules that stimulate the immune system to attack cancer cells. The nanoparticles can carry tumour antigens that ‘teach’ the immune system to identify and destroy malignant cells. In the case of lung cancer, this approach aims to combat the immunosuppression characteristic of the tumour environment by activating an effective anti-tumour immune response.

Another significant advance is the use of AuNPs in genetic therapies, such as the transport of interference RNA (siRNA) or DNA, aimed at silencing oncogenic genes or activating specific tumour suppressor genes. This mechanism allows for a personalised approach, with precise modification of gene expression in cancer cells, promoting cell death or inhibiting tumour progression in a targeted manner.

In addition, AuNPs offer the possibility of theranostic application, integrating diagnosis and therapy in a single system. Functionalised with fluorescent or radioactive molecules, AuNPs can be used for real-time monitoring of the tumour, making it easier to follow the response to treatment and providing more precise

therapeutic planning. Because they accumulate preferentially in the tumour, AuNPs provide information on the location and size of the tumour, allowing treatment to be adjusted as necessary.

In summary, the mechanisms of action of AuNPs for the treatment of lung cancer encompass highly selective therapeutic and diagnostic methods, with the potential to improve treatment efficacy and reduce adverse effects. These approaches represent an important step forward in the development of safer and more personalised therapies, with promising prospects for the fight against lung cancer.[4]



*Figure 16 - Actions Mechanisms (Gold)*

#### **4.5. Functionalisation/Bioconjugation**

The functionalisation and bioconjugation of gold nanoparticles (AuNPs) have been prominent in the development of advanced therapies for the treatment of lung cancer, exploiting the unique properties of these particles, such as high stability, biocompatibility and energy conversion capacity. These modifications make AuNPs promising for the selective delivery of drugs and other therapies into the tumour environment, as well as offering less invasive and more effective therapeutic options.

The functionalisation process involves modifying the surface of nanoparticles to allow controlled interaction with cancer cells, ensuring specific and efficient delivery. Functionalisation strategies include the binding of specific molecules, such as antibodies and peptides, which recognise and bind to biomarkers expressed on lung

cancer cells. This results in high selectivity, targeting treatment directly to tumour cells and reducing side effects on healthy tissue. Outra abordagem é a modificação da superfície das AuNPs com quimioterápicos, como doxorrubicina ou paclitaxel, que são libertados diretamente nas células cancerígenas, aumentando a eficácia terapêutica e diminuindo a toxicidade geral.

In addition, coating the nanoparticles with biocompatible polymers, such as polyethylene glycol (PEG), can increase the stability of the nanoparticles in the body and improve their blood circulation, prolonging their time of action.

Bioconjugation, meanwhile, is the process of binding biomolecules such as proteins, nucleic acids or antibodies to the surface of AuNPs, facilitating their interaction with specific biological targets in the body. In the case of lung cancer, antibody bioconjugation allows the nanoparticles to identify and bind to specific membrane proteins of the cancer cells, facilitating the precise delivery of the therapy to the tumour. Similarly, bioconjugation with DNA or RNA opens possibilities for genetic therapies that target specific mutations or gene silencing in cancer cells. Bioactive peptides are also frequently conjugated with AuNPs, enhancing the therapeutic effect, as some of these peptides have intrinsic anti-tumour properties.

These functionalized and bioconjugated nanoparticles have been used in innovative approaches to treat lung cancer. Photothermal therapy (PTT) is one such strategy, in which AuNPs, when exposed to infrared laser light, convert this energy into heat and induce the destruction of tumour cells through hyperthermia.

In short, the functionalisation and bioconjugation of gold nanoparticles represent significant advances in the search for more specific and effective treatments against lung cancer, making it possible to develop therapeutic approaches that combine innovation with less impact on the patient's general health.[4]

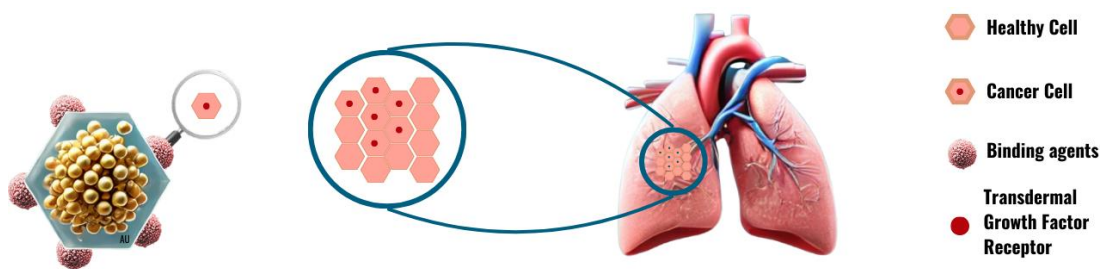


Figure 17 - Functionalisation/Bioconjugation (Gold)

#### **4.6. Toxicity**

Gold nanoparticles (AuNPs) offer significant potential for the treatment of lung cancer, but their toxicity is a crucial aspect that needs to be carefully managed to ensure the safety and efficacy of the treatment. The toxicity of AuNPs depends on several factors, including size, shape, dose, surface functionalisation and exposure time. The size and shape of AuNPs influence their biodistribution and toxicity: smaller particles, with a diameter of less than 10 nm, tend to accumulate in organs such as the liver, spleen and kidneys, where elimination is more difficult and can cause toxic effects. In addition, AuNPs with spherical shapes generally have lower toxicity compared to those with other shapes, such as rods or stars, which makes it essential to develop AuNPs with optimised sizes and shapes to reduce toxicity and improve therapeutic efficacy.

Another important factor is the functionalized surface of AuNPs. These are often modified with biocompatible molecules such as polyethylene glycol (PEG), which helps to reduce toxicity by preventing particle aggregation and decreasing recognition by the immune system. In contrast, AuNPs with negative or positive surface charges can interact more aggressively with the cell membrane, increasing toxicity. Therefore, careful functionalisation is essential to control toxicity, ensuring safer and more effective distribution in the body.

The dose of AuNPs is one of the main determinants of toxicity. Higher doses can cause oxidative damage to cells, promoting the production of reactive oxygen species (ROS) that cause oxidative stress, leading to cell death in both cancerous and healthy cells. Adjusting the dose and applying it gradually or locally helps to reduce these toxic effects, increasing the safety of the treatment.

The biodistribution and elimination of AuNPs also influence the level of toxicity. When administered, AuNPs tend to accumulate mainly in the liver and spleen, the main organs responsible for filtering and eliminating foreign particles. This retention can cause long-term damage, such as immunotoxic effects and chronic inflammation. For the treatment of lung cancer, the development of AuNPs with modifications that favour rapid elimination by the kidneys could be an effective strategy for reducing accumulated toxicity.

Chronic toxicity is another important concern, since prolonged exposure to AuNPs can lead to subclinical effects such as alterations in liver function and the

immune system, as well as a potential risk of genotoxic effects. Studies indicate that AuNPs can penetrate cells and interfere with DNA, depending on their characteristics, making long-term clinical trials essential to assess long-term safety. The development of biocompatible AuNPs, controlled release strategies and the customisation of nanoparticles based on the specific characteristics of each patient and tumour type are promising solutions for controlling toxicity and ensuring safer treatments.

In summary, although AuNPs are promising in the treatment of lung cancer, their toxicity must be carefully managed. Optimisation of parameters such as size, shape, functionalised surface and dose, as well as in-depth studies on long-term effects, are essential to develop safer and more effective therapies. With continued advances in nanomedicine and detailed clinical trials, it will be possible to improve safety and personalise the use of AuNPs in the treatment of lung cancer.[6]

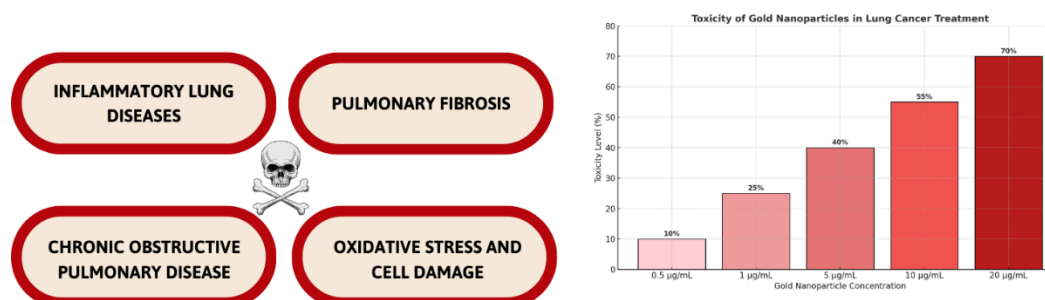


Figure 18 - Gold Toxicity



## Chapter 5

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Chapter 5 aims to conclude the theme of this project.

### 5. Conclusion

Lung cancer is one of the main causes of cancer mortality worldwide, characterised by its aggressiveness and difficulties in early diagnosis, which often results in unfavourable prognoses. Conventional therapies such as chemotherapy, radiotherapy and surgery, although effective in many cases, are associated with high side effects, low specificity and resistance acquired by tumour cells. In this context, nanotechnology has emerged as a revolutionary approach to the treatment of lung cancer, offering new possibilities to overcome the limitations of traditional treatments. Nanotechnology in the treatment of lung cancer offers several advantages, highlighted by its ability to deliver drugs directly to tumour cells, minimising the impact on healthy tissues and significantly reducing side effects. Due to their nanoscale size, nanoparticles are able to cross complex biological barriers and accumulate preferentially in tumour tissues, promoting more efficient distribution of therapeutic agents. In addition, the development of nanoparticles functionalized with specific ligands allows for active targeting of lung cancer cells, increasing treatment efficacy and improving therapeutic selectivity.

In addition, nanotechnologies allow multiple functions to be incorporated into a single platform, such as the transport of drugs and imaging agents, facilitating not only treatment but also the monitoring of disease progression in real time through advanced imaging techniques. Innovative therapies such as photothermal therapy and magnetic hyperthermia are particularly promising for destroying lung tumour cells without affecting the surrounding tissues. Finally, the application of nanotechnology in immunotherapy represents another significant advance, as it allows for the enhancement of immune responses against lung tumour cells. Despite huge challenges, such as the potential toxicity of certain nanomaterials and the complexity of producing them on a large scale, progress in research and development indicates that nanotechnologies could redefine lung cancer treatment, offering more effective, personalised and less invasive alternatives, with the potential to significantly improve prognoses and patients' quality of life.

## References

- [1] Leena Latonen and Pekka Ruusuvuori, “Building a central repository landmarks a new era for artificial intelligence-assisted digital pathology development in Europe,” doi: 10.1016/j.ejca.2021.03.018. Accessed: Oct. 27, 2024. [Online]. Available: <https://pubmed.ncbi.nlm.nih.gov/33892405/>
- [2] Brian Bolto, Jianhua Zhang, Xing Wu, and Zonglie Xie, “A Review on Current Development of Membranes for Oil Removal from Wastewaters,” doi: 10.3390/membranes10040065. Accessed: Oct. 27, 2024. [Online]. Available: <https://pubmed.ncbi.nlm.nih.gov/32272650/>
- [3] Firas Faisal, Manon Bertram, Corinna Stumm, Fabian Waidhas, Olaf Brummel, and Jörg Libuda, “Preparation of complex model electrocatalysts in ultra-high vacuum and transfer into the electrolyte for electrochemical IR spectroscopy and other techniques,” doi: 10.1063/1.5047056. Accessed: Oct. 27, 2024. [Online]. Available: <https://pubmed.ncbi.nlm.nih.gov/30501282/>
- [4] Piao Jiang *et al.*, “New insights into nanosystems for non-small-cell lung cancer: diagnosis and treatment,” doi: 10.1039/d3ra03099g. Accessed: Oct. 27, 2024. [Online]. Available: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10300523/>
- [5] A. Guinart, H. L. Perry, J. D. E. T. Wilton-Ely, and T. D. Tetley, “Gold nanomaterials in the management of lung cancer,” Dec. 01, 2021, *Portland Press Ltd.* doi: 10.1042/ETLS20200332.
- [6] P. Kesharwani *et al.*, “Gold nanoparticles and gold nanorods in the landscape of cancer therapy,” Dec. 01, 2023, *BioMed Central Ltd.* doi: 10.1186/s12943-023-01798-8.