Introduction

Nanotechnology has emerged as one of the most promising frontiers in modern medicine, offering innovative strategies to improve cancer treatment. Nanotechnology research currently includes liposomal drug delivery systems, polymeric nanoparticles, gold nanoparticles for photothermal therapy, and extracellular vesicles (EVs). EVs are being studied as therapeutic agents and biomarkers[15]. This paper will discuss five main areas: The role of nanoparticles in medicine, extracellular vesicles in cancer diagnosis and treatment, the application of nano systems in lung cancer therapy, current clinical trials involving nanotechnology, future applications and ethical considerations. Nanotechnology has the potential to revolutionize personalized medicine and targeted therapy. While nanotechnology holds great potential to shape the future of personalized and targeted medicine, unresolved issues remain regarding possible toxicity, immune reactions, and the need for careful regulatory oversight.

I. Overview of Nanotechnology in Medicine

Nanoparticles are one of many types of nanomaterials. They are classified as zero-dimensional nanomaterials. The nanomaterials in this class have all three dimensions in the nanoscale range. However in the zero dimension the electron movement is restricted in all three spatial directions. This results in discrete energy level. They can be any shape therefore they are defined as particles that are 1-100 nanometers in diameter. Due to their size they have different physical and chemical properties than larger particles. These properties allow them to be manipulated differently and be used in different ways in medicine, electronics and material science. They are widely used in healthcare, usually for drug delivery, imaging and regenerative medicine[1]. There are different types of nanoparticles that have been developed for medical applications. Nanoparticles are further divided into 3 classes: organic, carbon-based, and inorganic. Each class has unique advantages and applications in medicine.

Organic nanoparticles are are made from proteins, carbohydrates, lipids, polymers or any other organic compounds. In this class the common ones found are liposome and dendrimers. Liposomes are hollow spheres of lipids that drugs diffuse into, protecting them until they reach target cells. This allows the liposomes to safely carry the drugs into the target cells and release it. This improves drug safety, bioavailability, and targeting ability. Lipid-based nanoparticles can be further classified into 5 categories, and they are dependent on the fabrication method as well as the physicochemical properties of the formulations. The 5 categories are liposomes, niosomes, transfersomes, solid lipid nanoparticles (SLN) and nanostructured lipid centers (NLC)[2]. Lipid based nanoparticles carriers reduce systemic toxicity, improve drug stability, and enhance targeted delivery. However, their lack of penetrating ability in the stratum corneum affects the application of liposomes in dermal delivery. They also have weak storage stability due to drug leakage in the media. Clinically, Doxil, also known as liposomal doxorubicin, is frequently used to treat breast cancer that has spread to other parts of the body. This has shown to reduce cardiotoxicity and improve anticancer ability compared to Doxil by itself. It is usually common to have blood tests or an electrocardiogram and echocardiogram before starting Doxil.

Another one of the subdivisions in Organic nanoparticles are dendrimers. Dendrimers are also commonly used in drug delivery. Dendrimers have the look of a branching tree. They have symmetrical structures with defined shapes and specificity. Dendrimers have the ability to act as a sort of Christmas tree where the dendrimer is the Christmas tree, and the ornaments would be the drug molecules or targeting agents on the outer branches. Their architecture allows multiple functional groups to attach to the outer branches, increasing therapeutic effectiveness. Dendrimers are classified broadly into two categories: medical and non-medical. There are two different ways that dendrimers deliver drugs. The first way is formuulation where drugs are held inside the dendrimer cavities or attached by weak forces such as hydrogen bonds or hydrophobic interactions. This is especially helpful with hydrophobic drugs

in which attaching them to the dendrimers can improve their solubility. The second type of dendrimer drug delivery system is nano construct. This is where drugs are chemically bonded to the surface of the dendrimers. This is usually more stable than formulation and allows the drug to be released in a more controlled fashion. However, drugs can also be encapsulated in dendrimers. There are three main ways that drugs can be carried in dendrimers, those being physical encapsulation, electrostatic interactions and covalent conjugation. In physical encapsulation the drug molecules are trapped inside the internal cavities of dendrimers. This can be done through hydrophobic forces, hydrogen bonding or shape complementarity. An example of this type of drug encapsulation is Adriamycin or Doxorubicin. As well as previously mentioned, this can help improve the solubility of anticancer drugs which are usually water insoluble. In electrostatic interactions dendrimers with charged groups such as amino functional groups or carboxylic acid groups are able to bind to ionizable drugs. Polyamidoamine (PAMAM) dendrimers are a good example of this. They are "a versatile and reproducible type of nanocarrier that can be loaded with drugs and modified by attaching target-specific ligands that recognize receptors that are over-expressed on cancer cells… [and] can preserve the nucleic acids from degradation" [3]. This method is used to enhance bioavailability by surface complexation. Lastly Covalent conjugation is where drugs are chemically bonded to the dendrimer surface. In this form drugs can be attached by spacers or linkers. These can be polyethylene glycol p-aminobenzoic acid, p-aminohippuric acid and lauryl chains. The spacers or linkers help the stability and kinetics of the drug become enhanced. This can be seen in penicillin V, venlafaxine, 5-aminosalicylic acid, naproxen and propranolol conjugated with PAMAM dendrimers[4].

Gold nanoparticles are a type of inorganic nanoparticles that can be used in cancer therapy. These particles are small, non-toxic and non-immunogenic, which is ideal for targeted delivery systems. Gold nanoparticles can be engineered with lung targeting ligands or drugs for precision delivery with reduced

side effects. Gold nanoparticles are composed of a gold metallic core. Since the core is highly reactive there are ways, it can be functionalized or stabilized by various molecules. These stabilizers include citrate ions which give the molecule a negatively charged surface, Thiols which create a very strong gold sulfur bond and then form self-assembled monolayers, or polymers like (PEG) polyethylene glycolic which help with steric stability and biocompatibility. Because of these surface modifications gold nanoparticles are excellent nanoplatforms for attaching drugs, antibodies or nucleic acids. The gold atoms arrange into a face centered cubic (FCC) crystal lattice. This lattice structure allows for a high stability along with a unique surface plasmon resonance (SPR). "Gold nanoparticles exhibit unique physicochemical properties including surface plasmon resonance (SPR) and the ability to bind amine and thiol groups, allowing surface modification and use in biomedical applications" [5]. There are different shapes that can be made including nanospheres, nanorods, nano shells etc. These shapes alter light absorption or scattering properties. Because of the metallic gold lattice conduction electrons oscillate collectively when exposed to light. This is the basis of their strong optical absorption/scatter which is used in photothermal therapy and imagining.

Polymeric nanoparticles are flexible carriers due to their ability to deliver a wide array of therapeutic agents with controlled release profiles. This enhances the drug's efficacy and reduces side effects as well. Different polymers, along with shape, surface charge, and drug-loading capacity, affect nanoparticle behavior in biological systems. There are methods that have been used to fabricate and characterize polymeric nanoparticles that are crucial for ensuring targeting capability and drug release performance. These methods include controlling the size of the nanoparticle, charge and morphology. Polymeric nanoparticles face key barriers such as toxicity concerns, formulation stability, scalability and regulatory issues. Regardless of these barriers Smart polymeric nanoparticles can help improve solubility stability and tumor specific release for poorly soluble drugs such as paclitaxel or cisplatin.

This could be adapted for inhalation delivery where thermo responsive or pH sensitive polymeric nanoparticles can help reduce systemic exposure.

II. Advantages of Nanotechnology in Medicine

Nanotechnology has several advantages over traditional therapies. Some advantages include Enhanced drug availability, reduced toxicity, targeting and personalized medicine. With enhanced drug bioavailability nanoparticles are very good solutions, as mentioned previously, to poorly soluble drugs. They help improve solubility and are able to protect drugs from degradation which is very helpful for biomolecules such as peptides or proteins. One example of this is "Polymeric nanoparticles allow encapsulation of bioactive molecules and protect them against enzymatic and hydrolytic degradation. For instance, it has been found that insulin-loaded nanoparticles have preserved insulin activity and produced blood glucose reduction in diabetic rats for up to 14 days following the oral administration."[6] Their small size and high surface area allows absorption and penetration to be improved across biological barriers which also boosts systemic bioavailability.

Nanoparticles are also able to enhance therapeutic efficacy while reducing adverse effects because they allow control and sustained drug release, and it therefore limits systemic drug exposure. "Liposomes are defined by a unique structure that is similar to cellular membranes, and they are considered to be more biocompatible than other synthetic materials. These characteristics make them highly valuable for drug transport systems, and they are being developed as nanocarriers."[7]

As mentioned previously nanoparticles allow for site targeting. Surface modifications play a critical role in enabling nanoparticles to selectively target tumors while sparing healthy tissues. Site specific targeting for tumors is possible because of surface modifications. Surface modifications can be done with poly(ethylene glycol) and this "may lead to an increased presence in the circulation by avoiding

recognition and phagocytosis by the mononuclear phagocytic system."[7] Antibodies are also an option to be attached to the "nanoparticle surface and this may allow for a more specific immune-directed targeting of the particles to certain cells or organs."[7] Passive targeting through the enhanced permeability and retention (EPR) effect in tumors enables nanoparticles to accumulate more effectively in cancerous tissues. In gold nanoparticles the surface can be functionalized with different ligands "such as peptides, proteins, or DNA… Due to this property, the surface of these nanoparticles can be easily modified or conjugated with functional biomolecules or other materials" [7]. Moreover, bio interfaces such as antibodies, biopolymers, and collagen layers further enhance compatibility and precision, since "in order to interact with biological targets, a biological or molecular coating or layer acting as a bioinorganic interface should be attached to the nanoparticle. Examples of biological coatings may include antibodies, biopolymers like collagen, or monolayers of small molecules that make the nanoparticles biocompatible" [8].

Personalized medicine potential is one of the most promising aspects of nanotech. The treatment can be tailored to the unique genetic molecular and immune characteristics of each individual patient. The issue with the current standard of care is the lack of specificity in chemotherapies and systemic treatments. This can lead to widespread toxicity and variable outcomes across patient populations. Smart nanocarriers are engineered to incorporate stimulus-responsive mechanisms. Responsive mechanisms include pH, temperature, or enzyme sensitive release systems. The therapeutic agent will only be released in the diseased microenvironment and when these conditions are met. This minimizes exposure to healthy tissues. "By exploiting these hallmarks, nanoparticles can be programmed to release their payload specifically within tumor sites, thus aligning treatment with the patient's molecular profile" [3]. Extracellular vesicles (EVs) offer another promising dimension of personalization. Since EVs are derived from the patient's own cells, they carry low immunogenicity and high compatibility. EVs can be

engineered and loaded with chemotherapeutics, immunomodulators, or nucleic acids and then reinfused into the same patient, functioning as an autologous nanomedicine system. In addition, EVs circulating in patient blood samples can be analyzed as "liquid biopsies" to determine tumor-specific molecular markers in real time, guiding the design of tailored nano therapies[5]. Nano carriers and EVs interact with the body at a molecular level, and the repercussions or long-term effects are not well known. There could be issues such as bioaccumulation, off-target toxicity, and unpredictable immune responses raise ethical concerns about patient safety[3]. Although a helpful personalized therapy the issue of EV based therapies not having a standardized method for isolation, purification and large-scale production pose a risk. Inconsistent preparations may lead to variable efficacy or unintended risks[5]. Therefore, it is difficult for regulatory bodies such as the FDA and EMA to approve this treatment because they require reproducibility, quality assurance and clear safety data for biologics.

III. Extracellular Vesicles (EVs) in Cancer Diagnosis and Therapy

Extracellular vesicles (EVs) are nano-sized, lipid-bound particles that are released by cells. They contain proteins, nucleic acids, metabolites, and lipids, and are found in various body fluids including blood, saliva, sputum, and pleural effusions[5]. There are different subtypes, the main three being exosomes (30–150 nm), microvesicles (100–1000 nm), and apoptotic bodies (1–5 μm). Their biological function centers on intercellular communication. As Kato et al. noted, "In the context of lung cancer, emerging evidence implicates EV involvement during various stages of tumor development and progression, including angiogenesis, epithelial to mesenchymal transformation, immune system suppression, metastasis and drug resistance" [5]. EVs are also highly attractive as liquid biopsy biomarkers and drug delivery systems because the lipid bilayer encapsulation provides stability to their molecular cargo[5].

In the context of cancer, tumor-derived EVs (TDEs) are increasingly recognized as key regulators of tumor biology. They influence angiogenesis by transporting oncogenic microRNAs and growth factors. For example, exosomal miR-21 is taken up by stromal and endothelial cells, where it upregulates vascular endothelial growth factor (VEGF). This stimulates the formation of new blood vessels that supply oxygen and nutrients to the tumor, accelerating growth and providing routes for metastasis. Additionally, exosomal miR-21 facilitates epithelial-to-mesenchymal transition (EMT), enabling cancer cells to migrate and invade distant tissues[5]. EVs also carry molecules such as PD-L1 and EGFR that modulate the immune microenvironment. By promoting regulatory T cells (Tregs) and suppressing cytotoxic T-cell activity, TDEs create an immunosuppressive niche that allows cancer to evade host defenses. Furthermore, TDEs contribute to therapy resistance by transferring resistance-associated proteins and RNAs, such as miR-21 and miR-222-3p, which activate pathways (e.g., Akt) that diminish chemotherapy sensitivity[5]. They can also physically sequester or expel drugs, further limiting therapeutic efficacy[5]. Because TDEs mediate these harmful processes, they can be exploited as biomarkers—since their cargo reflects tumor activity—or as therapeutic targets, where blocking their release or modifying their contents may reduce tumor progression.

EVs also have promising applications as non-invasive biomarkers. Because EVs encapsulate cargo reflective of their cell of origin, they serve as “molecular snapshots” of tumor biology[5]. Their cargo includes DNA fragments, various RNA species (including mRNA, microRNAs, and lncRNAs), proteins, and lipid signatures that provide highly specific information about oncogenic pathways active in the tumor. As EVs circulate in diverse biofluids, they are accessible for diagnostic sampling, and compared to traditional tissue biopsies, EV-based liquid biopsies are less invasive and can detect malignancies at earlier stages[5]. Studies have shown that exosomal integrins, miRNAs, and surface proteins can serve as indicators of tumor origin, metastatic potential, and treatment response. Unlike free circulating nucleic

acids, EV cargo is encapsulated within a lipid bilayer, which protects against degradation and ensures greater stability for downstream analysis[5].

In addition to diagnostic potential, EVs are being explored as therapeutic tools. For example, when EVs are modified with targeting ligands they are able to deliver drugs directly to tumor cells while limiting exposure to healthy tissues[5]. One key aspect of EVs is their biocompatibility. They are naturally immunogenic, biodegradable and mimic the membrane structures of cells. This lowers the risk of rejection in comparison to synthetic carriers such as liposomes or polymeric nanoparticles. Since EVs are also derived from immune cells they have been investigated as anti-cancer vaccines. The reason being is that they retain antigen presenting properties that can activate tumor specific immune responses[5]. As previously mentioned, there are still issues that come along with this treatment such as not being able to produce EVs on a large scale, standardizing methods of isolation, and being able to achieve consistent and efficient cargo loading. However, even with these challenges, preclinical and clinical research still highlights EV based therapies as a promising direction in cancer treatment.

3.1 FDA-Approved Nanomedicine for Lung Cancer

Though there are many nano systems being researched, only a few have received approval from the FDA for clinical use. One key example is Abraxane. Abraxane is an albumin bound form of paclitaxel. The difference between paclitaxel and Abraxane is that Abraxane has shown improved pharmacokinetics along with lower hypersensitivity reactions. This makes Abraxane a better option in treatment for non-small cell lung cancer (NSCLC) treatment. There have been clinical trials indicating that when combined with carboplatin, Abraxane produces better response rates than older solvent-based paclitaxel regimens[3]. Another therapy that has been approved by the FDA is Genexol-PM. This therapy uses polymeric micelles to deliver paclitaxel. This design improves drug solubility and allows for higher

doses without relying on toxic solvents like Cremophor EL. In early clinical studies results have shown that Genexol-PM is more tolerable and effective in lung cancer patients. However further safety monitoring is still needed. Both of these examples show how FDA-approved nanomedicines can transition successfully from clinical practice into real-world treatment even though the number of approved options is still very small in comparison to the many systems under research[3].

3.2 Challenges in Nano system Development

While nano systems show strong potential there are still several challenges that continue to limit their use in lung cancer treatment. One major issue is that many systems have low drug encapsulation efficiency. This means they are not able to carry enough of the therapeutic agent in order to be fully effective[3]. Even when drugs are successfully loaded some of the nano systems struggle to keep them stable either during circulation or storage. This can cause the drug to be released too early or degrade before reaching the tumor.

Another issue is the risk of immune rejection. Since the body might mistakenly recognize nanoparticles as foreign, they can be removed quickly therefore shortening the time they remain in circulation and also lowering their therapeutic effect. This issue may be resolved though through modifications such as PEGylation in order to extend circulation time, but repeated dosing can still lead to immune reactions and faster clearance[1]. There are also concerns on long term safety. There could be a possibility of chronic toxicity or organ damage since nanoparticles have the possibility of building up in organs like the liver, spleen, or kidneys. Genetic and tumor variability makes it more difficult to design a once size fits all therapy which points to the need for a more personalized approach[5]. In order to overcome these barriers, next generation carriers are being developed where drugs would only be released when triggered by conditions such as pH, temperature or specific enzymes in the tumor environment. Others

are exploring nanoparticles that are able to deliver gene-editing tools such as CRISPR. These advances aim to improve drug stability and targeting while reducing side effects[3].

IV. Clinical Trials in Nanotechnology and Medicine

Currently there are clinical trials that are exploring the use of nanotechnology for cancer therapy and diagnostics. Nanoparticle based immunotherapies are promising as they are designed to improve immune activation against tumors. “One of the most promising solutions would be the development of immunotherapies… novel formulations, such as combinations of drug-loaded nanoparticles and immune checkpoint inhibitors (ICIs)” [3]. Similarly, there has been a close focus on a new radioenhancer nanoparticle named Nanobiotix. The company is also focusing on nanoparticle enhanced radiotherapy in combination with immunotherapy. They have a phase 1 clinical trial that is evaluating the safety and early efficacy of radioenhancer known as NBTXR3. The radiotracer NBTXR3 is activated by radiotherapy and then followed by anti-PD-1 treatment. This is currently being used in patients with advanced cancers. Preliminary results are indicating that this combination is being well tolerated[19]. Another focus currently under clinical investigation is extracellular vesicle based liquid biopsies. EV’s are proving to be stable carriers of tumor derived molecules. They can be isolated from multiple body fluids. “Exosomes occur in virtually all body fluids…making them ideal for liquid biopsies” [5]. This method would allow for the identification of tumor specific molecular signatures in real time which would in turn improve early diagnosis and personalized treatment strategies. Even though they seem promising researchers emphasize that EV isolation methods and standardizing this method would be challenging as well as slow in clinical adaptation[16] [17].

Lastly another focus in the nanotechnology clinical trial area involves CRISPR-loaded nanoparticles for gene therapy. There have been other clinical successes that have highlighted the translational potential

of nanomedicine. Two liposome-based chemotherapies already approved by the FDA and widely used in oncology are Doxil and Abraxane. Abraxane "proved to be effective as part of the lung cancer cure, showing milder adverse effects and great tolerability when administered alone as a chemotherapeutic agent or in conjunction with other traditional drugs" [3]. CRISPR/Cas9 can efficiently be delivered by lipid nanoparticles to tumor sites. This shows therapeutic potential however in models of head and neck squamous cell carcinoma[18]. These studies show how nanosystems are able to reduce toxicity while improving therapeutic outcomes. One of the most pressing concerns, despite having encouraging trial results, is long term safety.

There are several clinical trials that highlight nanomedicine's translation from the lab to real world cancer care. As previously mentioned, liposomes based chemotherapies doxil and Abraxane are one of the firsts to receive FDA approval and remain milestones in this field. Formulations such as these indicate that nanosystems are able to make chemotherapy both more effective and less toxic. "Abraxane proved to be effective as part of the lung cancer cure, showing milder adverse effects and great tolerability when administered alone as a chemotherapeutic agent or in conjunction with other traditional drugs" [3]. These therapies show that liposomes and albumin bound nanoparticles as the foundation for modern nanomedicine in oncology. As previously mentioned NBTXR3 nanoparticles are being used to enhance radiotherapy. It has advanced to late-phase clinical trials and has shown the ability to amplify the radiation's impact on tumors while also minimizing damage to the healthy tissue. This also demonstrates how nanotech can work in combination with cancer treatments[20].

Another approach uses gold nanoparticles for photothermal therapy (PTT). Gold nanoparticles can precisely target and destroy tumors by converting near-infrared light into heat. An "elegant and encouraging solution… was proposed in which Fe3O4 super particles would encapsulate and carry immune-adjuvant drugs to a magnetic-targeted site, using complementary photothermal therapy (PTT)"

[3]. There have been recent advances in nanoparticle mediated gene editing that are opening up new possibilities in cancer treatment. CRISPR/Cas9 technology has the potential to become an important tool in lung cancer therapy[3]. It has been shown that lipid nanoparticles can successfully deliver CRISPR/Cas9 which offers a non-viral method that appears both safer as well as more precise for gene editing in living systems[18]. These developments demonstrate how nanomedicine is expanding cancer therapy, strengthening traditional options like chemotherapy as well as radiotherapy while also driving forward new strategies such as photothermal therapy and CRISPR-based therapies.

V. Future Applications and Ethical Considerations in Nanomedicine

Smart nanocarriers are systems that can respond to biological or environmental cues. These cues range from pH, temperature, enzymes, light or ultrasound. The carriers are then designed to only release drugs at the target site which is also the disease site. This reduces toxicity and improves precision. “The most vital aspects of nanotechnology are the development of a proper synthesizing method that can reduce toxicity, surface modifications, and the therapeutic design of nanoparticle-based formulations in cancer” [3]. Systems based on stimulus response are showing that they could significantly improve tumor targeting all while minimizing side effects[12] [13].

Currently artificial intelligence (AI) is also shaping how nanocarriers are designed. Machine learning models are being used to optimize nanoparticle size, shape, and surface chemistry, tailoring them to the molecular profiles of individual patients. AI along with machine learning models suggest that the next generation of nanocarriers will be smarter as well as highly personalized because of blending computational design with biomedical innovation[3] [14] [15].

Nanomedicine is quickly advancing and making promising innovations however they also raise important ethical concerns. One of these concerns is about long-term patient safety. Nanoparticles can

accumulate in organs such as the spleen, liver and kidneys. This can increase the risk of chronic effects that currently short-term studies are not fully able to capture. Long term safety studies are very much needed before nanomedicine can be fully and widely adopted. Another concern is equal accessibility. Nanotherapies are not cheap. They are expensive to develop, test and manufacture. This could limit their availability to patients in low resource regions. A major obstacle that is still hard to overcome is high expenses. These high expenses highlight the importance and need for cost effective solutions along with fair distribution strategies in order to ensure that all patients are able to benefit from these technologies[11].

However, there are also still questions about ethical genetic manipulation. One of these technologies is CRISPR delivered via nanoparticles. This method shows the most significant potential for correcting genetic mutations, but it also poses risks of unintended alterations as well as possible misuse[3]. This is a part of nanomedicine that once it advances will need more stringent oversight in order to make sure that the progress in therapy is matched with ethical responsibility.

Key regulatory challenges must be addressed in order for nanomedicine to advance into routine clinical practice. Multifunctional nanosystems do not fall into a typical or traditional category. Therefore, currently the pathways the FDA and the EMA provide are often rigorous in terms of safety and in efficacy[3]. Doxil and Abraxane set important benchmarks; however, for more sophisticated nanoparticles it can be challenging to assess. Especially if they combine therapeutic diagnostic and immune modulating functions.

Extracellular vehicle (EV)-based therapies are one of those particles that illustrate these properties. Although they are able to diagnose and treat, they lack standardization as well as protocols for isolation, safety assessments, and quality control. Without internationally harmonized procedures, the approval and clinical integration of EV-based therapies may face significant delays[5] [16] [17].

Lastly, there is an urgent need for safety evaluations specifically designed for nanomaterials. Currently, traditional toxicology safety methods often lack the ability to identify risks unique to nanoparticles. These issues range from immune clearance, tissue accumulation, or long-term biodegradation. Regulatory agencies have been improving and trying to address these issues, but significant gaps are still remaining. Once these gaps and issues are adequately addressed, nanomedicine can grow safely and effectively from the lab to the clinic.

Conclusion

Overall nanotechnology provides a reasonable approach from the current standard of care for lung cancer. Current lung cancer chemotherapies are harmful and have debilitating side effects meanwhile nanotechnology focuses on more precise targeted approaches. There are various types of nanocarrier systems that have been explained, such as liposomes and albumin-bound particles in drug delivery systems that allow for safer drug delivery. As well as polymeric carriers that are able to release the medication in a controlled manner or because of certain stimulus conditions. As well as gold nanoparticles for photothermal therapy or the use of extracellular vesicles that are used for both drug delivery and diagnostics. All of these strategies are focusing on one goal which is being able to increase drug concentration specifically at the tumor site while minimizing the harmful side effects on the rest of the body. Clinical trials already show that nanoscale formulation is able to enhance both efficacy and tolerability. These nanocarrier systems are able to increase payload, release kinetics, and route of administration. This could be through inhalation-based strategies or combinations with radiotherapy or immune checkpoint inhibitors.

Lung cancer has certain biological hallmark features that nanocarriers are able to exploit. Lung tumors often develop leaky, irregular blood vessels. Nanoparticles can easily pass through these gaps more

easily than normal tissue. This is known as enhanced permeability and retention effect. Extracellular vesicles these are tiny vesicles that are naturally released by cancer cells; they carry DNA, RNA and protein and are able to show what is happening inside the tumor. By collecting these EV's doctors can monitor tumor activity in real time without having to continuously do invasive tissue biopsies. This can also help detect whether a medication is working against the tumor or not. Lastly AI, CRISPR based delivery systems and theranostic platforms are future directions that nanomedicine is heading in. AI might be able to help design the perfect nanoparticle based on the patient's needs. CRISPR based delivery systems can allow nanoparticles to deliver CRISPR/ Cas9 gene editing tools directly to lung cancer cells and this can potentially correct cancer driving mutations. Lastly, theranostic platforms are multifunctional nanoparticles that are able to combine therapies and diagnostics in one system, and it is able to provide a personalized all-in-one cancer management tool. This vision will be achievable if three areas are met. Rigorous safety science tailored to nanoparticles has to be met. Because traditional toxicology tests are not always enough for medicine, there are concerns that need to be addressed. This includes immune clearance, organ accumulation, and biodegradation. Without specialized safety testing, regulatory agencies will be less likely to approve widespread clinical use. In regard to EVs, they need harmonization standards. These include isolation methods since different labs use different methods, characterization methods in terms of size, contents and purity, and ensuring quality control across all batches. These need to be harmonized in order to obtain results that are consistent. Once this is achieved, it will be helpful to streamline EV-based treatments and tests into practice. Lastly, equal access strategies. Nanoparticles are expensive to manufacture and develop. If there are no strategies in place to make them affordable, it becomes a treatment that is only available to wealthy and high resource countries. This then requires pricing models that help keep treatments affordable, international distribution frameworks in order to reach patients globally and cost-efficient manufacturing methods.

With these foundations, nanotechnology will move from a concept to a clinical reality and will be able to make an impact throughout modern lung cancer therapy.

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