GENE THERAPY AND NANOPARTICLES AS LUNG CANCER TREATMENT

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AT FIRST GLANCE: CANCER RESEARCH

Within the world of engineering and healthcare, cancer research has taken huge prevalence in the media. Millions of people, including myself, join together every year for fundraisers for organizations such as the American Cancer Society and Stand Up to Cancer. However, less noticeable in the spotlight is the role of gene therapy in cancer treatment. Drugs such as Paclitaxel exemplify the use of nanoparticles to transport drugs directly to malignant lung cancer cells even after metastasis, or the spread of cancer cells throughout the body. Targeted drug delivery systems using genetically engineered drugs packaged in nanoparticles provide a relatively safe form of treatment in comparison with chemotherapies.

As a hopeful bioengineer, and as a family member of more than one cancer victim, I am extremely interested in researching effective cancer cures. I know first-hand that hope for a better tomorrow is one of the best things a cancer patient can receive. Researchers worldwide agree that the aforementioned type of technology is the most promising form of cancer treatment. Because of the disease’s widespread lethality, focusing engineering and societal resources on lung cancer research is important for the public’s well-being, and the development of nanoparticle-based drug delivery systems proves to be an effective cancer drug.

WHY DOES CANCER TREATMENT MATTER?

The war on cancer has not gone unnoticed by me. My great-grandfather passed away due to lung cancer a few years ago, and it was incredibly hard on my family to watch him fade away after months of treatment. Lung cancer is the most lethal and the most prominent form of cancer. According to the American Cancer Society, “more patients die from lung cancer alone than prostate, breast, and colon cancers combined in the USA” [1]. Cancer is a worldwide pandemic, and the devastation it causes cannot be prevented without the help of engineering. Specifically, bioengineers and chemical engineers would play the biggest role in using applications of nanotechnology and genetic engineering to find cancer solutions.

A CLOSER LOOK AT “PERSONALIZED MEDICINE”

The field of health care can be characterized by one world: broad. However, human beings themselves cannot be so generalized, especially when they look for medical treatment. The human genome, or DNA sequence, varies ever so slightly within each person. These variances are enough to cause everyone to look different, and for everyone’s body to behave differently throughout their lifetime. They are also the reason why every cancer case is different, as the cause of cancer is defective gene coding in cells. The National Academy of Engineering notates this phenomenon and recognizes the need for “personalized medicine.” They define personalized medicine as an approach to preventing, diagnosing, treating, and monitoring disease in ways that achieve optimal individual health-care decisions [2]. Genetic studies, modifications, and treatments can be personalized to each specific case in order to successfully target malignant cancer cells.

A CLOSER LOOK AT CANCER AND ITS TREATMENT

Cancer: The Disease

In the body, cancer cells are always present. Generally, cancer cells are any cell that has a genetic deficiency resulting from the incorrect replication of DNA. The checkpoints in their cell life cycles malfunction and they fail to express important characteristics such as their growth limit factor or their cell death program. They can then begin to rapidly divide, forming masses called tumors that repress bodily organs by applying pressure. Sometimes, the cancers metastasize, or spread throughout the body via the bloodstream [3]. Since these cells are always present to some degree, the pursuit of a cancer cure is really the pursuit of a cancer treatment.

Cancer: The Treatment

Traditionally, cancers are treated by means of chemotherapy and/or surgery. Chemotherapy involves populating the patient’s system with a drug aimed at killing
cancer cells. This method is viewed as effective because it can hypothetically target a relatively broad range of cells. [4] However, it poses many problems. Because the drugs are circulating throughout the body, they worsen the health of the individual as a whole by killing healthy cells. This is why cancer patients undergoing chemotherapy often lose all their hair [4]. These problems could be solved if a treatment that zeroed in further on the specific tumor cells can be utilized.

In reference to surgical treatment methods, they are effective at removing easily accessible tumor clumps, but they offer no true severance from the cellular threat within the body. Cancer cells can be left behind at the site, and once the cancer metastasizes, it cannot be surgically removed [4]. Personally, I identify with these victims because my great-grandfather’s cancer had metastasized, and it was long enough ago that there was no better treatment for him. Furthermore, reliance on surgical methods or chemotherapy alone does not provide fair treatment to late-stage-cancer victims, and more advanced research is necessary to treat a large portion of cancer cases.

**Lung Cancer**

As each cancer differs depending on where it originates in the body, I would like to take a moment to talk about lung cancer specifically. Personally I have the most experience with lung cancer because many members of my family used to smoke and therefore developed some form of the disease. Lung cancer results from growing populations of abnormal cells that do not assimilate into the healthy tissue of the rest of the lung. One specific type of lung cancer, called small cell lung cancer (SCLC) consists of small, rapidly dividing cells that travel throughout the body. Smoking is normally the cause of SCLC [1]. Most of the nanoparticle-based studies I have found focus on treating SCLC because it clearly represents the metastasis of a cancer that must be targeted by special drug delivery throughout the body.

**GENE THERAPY**

**The Therapeutic Method**

In order to develop a magical drug that targets specific somatic cells, researchers are looking towards gene therapy. Generally, gene therapy is the use of manipulated genetic codes to treat a disease. Kent I. Nastiuk of Roswell Park Cancer Institute’s Center for Personalized Medicine and John J. Krolewski of the Department of Cancer Genetics have done a very recent study on “Opportunities and Challenges in Combination Gene Cancer Therapy.” Their research report states that gene therapy is the most recently applied form of cancer treatment [4]. Stem cells have been the focus of much research. It was recently discovered that small amounts of cancer stem cells reside within lung tumors, and that those stem cells display most of the same characteristics as healthy lung stem cells [5]. Therefore, stem cells can be incorporated into gene therapy studies concerning those cancer cells.

Multiple methods of gene therapy in lung cancer treatment have been proposed, including the use of stem cell markers [5], and also the use of nanoparticles capable of targeting cancer cells [6], and the restoration of gene expression such as the tumor suppressor p53 [4]. This knowledge is helpful to bioengineers because they can develop different combinations of cancer therapy in order to better treat the general public.

For a better explanation of the connection between these three technologies, stem cell markers and nanoparticles are both methods for the drug delivery, while the tumor suppressor p53 is an example of an actual drug component. The International Journal of Nanomedicine website states that chemical and biological engineers study different nanoparticles that can be constructed as the vessel with which to carry either chemotherapeutic, immunologic, etc. types of drugs [7]. The gene therapy method further discussed will be a broadening of drug delivery using nanoparticles.

**Treatment with Nanoparticles**

As a general description, gene therapy involves using manipulated nucleotides and proteins to target and regulate abnormal genetic expressions. Those abnormal genes studied by Hung-Yen Lee, Kamal A Mohammed, and Majmunissa Nasreen of the College of Medicine in North Florida are those related to cancer development [6]. In an article on nanoparticle-based targeted gene therapy dealing with lung cancer specifically by Lee, Mohammed, and Nasreen, the connection between targeted cancer treatment and the increase in safety for the body is acknowledged. Explicitly, “the major goal of targeted gene therapy is to bring forward a safe and efficient treatment to cancer patients via specifically targeting and deterring cancer cells in the body” [6]. It is also currently explained as the most rapidly developing form of cancer treatment [6]. As a result, targeted gene therapy is a popular course of study.

When manufacturing the drug molecules, engineers use multiple different types of nanoparticles as vessels such as polymers, liposomes, lipids, and metal-based systems. They package the desired gene inside its carrier and form a complex drug system. This is necessary because DNA and RNA molecules, the genetic material of a cell, cannot enter a cell through cell membranes on their own. Additionally, the carriers can be built to be more compatible for uptake by cancer cells and less compatible for uptake by healthy cells, which is where they get the term “targeting” nanoparticles [6]. There are numerous combinations of molecules that can be manufactured into these systems.

In example, liposomes, or spherical sets of phospholipid molecules, are used to trap small amounts of a therapeutic drug because they can travel through small veins
without adding the danger of clotting. The particles can carry specific molecules on their surfaces that target the cancer cells. Once they reach the cells, liposomes are able to combine with the membrane, as cell membranes are also made of phospholipids. Lastly, unwanted remnants can exit the cell bodies because of the particle’s lysosomal properties, meaning they can break down unwanted matter [7]. This is another desired characteristic of nanoparticle-based systems.

Afterwards, the delivered genes are then incorporated into the cell’s system to induce a desired effect such as cell apoptosis, or programmed cell death. They may trigger response pathways within the cell when recognized by cell receptors to inspire the creation of new proteins that hinder cell division as well. [4]. Finally, a patient testing these therapies will have experienced a relatively comfortable treatment that suppresses their tumors’ growth without suppressing their immune system or other bodily functions.

DEEPER EXPLANATION AS A DRUG STUDY: PACLITAXEL

While nanoparticle-based drug delivery systems are still relatively new, there are a few approved drugs that have become desired chemotherapy replacements. One such drug used in the treatment of breast, ovarian, and lung cancer is called Paclitaxel. This specific drug enters the body intravenously, and is generally given to the patient every three weeks. The website for Cancer Treatment Centers of America explains that Paclitaxel uses antimicrotubule agents to inhibit cell replication of tumors [8]. In this way, drugs such as Paclitaxel can interact with cancer cells to pause tumor growth.

In terms of creating the drug, the International Journal of Nanomedicine gives a detailed explanation of the technology. Paclitaxel is bound to the nanoparticles called albumin, a protein, which recognizes the tumor cells via albumin receptors and has been genetically restructured to carry drugs through the body [9]. It causes the cytosol in tumor cells to become increasingly toxic while simultaneously sustaining the therapeutic effect of the drug [7]. The drug Paclitaxel itself then interacts with tubulin in the cells. It contains genetic information that blocks the disassembly of microtubules in the cytosol. By inhibiting microtubule breakdown, it refuses to allow one cell to undergo its division cycle and break into two [9]. Therefore, this drug is efficient in slowing tumor growth because it concentrates its effect in malignant cells instead of harming random cells throughout the body, as a non-targeting drug would.

The Efficiency of Paclitaxel

While it is true that Paclitaxel is a relatively safe form of treatment because it uses the tumors as a target, patients still often experience some side effects. Some of them include nausea and vomiting, stomach pain, hair loss, numbness, and fainting [8]. These results occur because Paclitaxel is in fact a system made from the packaging of a chemotherapy drug. Hypothetically, these side effects could be minimized by other drug methods that have yet to be approved by the FDA. However, the Cancer Treatment Center of America promotes Paclitaxel for its safety and effectiveness for treating metastasized cancers [8]. It is a valuable stepping stone in the advancement of gene therapy using nanoparticles in the treatment of cancers.

THE IMPACT OF PERSONALIZED CANCER TREATMENT

All over the world, cancer attacks the bodies of millions of people. A statement often repeated during Relay for Life fundraisers for the American Cancer Society is “everyone knows someone.” Everyone knows someone who has had cancer, who has cancer, or is affected by cancer because someone in their life was diagnosed. Each of their experiences are so different that researchers and engineers have to take a personalized approach to treatment versus shooting an all-purpose medicine into the body. Cancer research is important to society because it is a silent killer, and it is one of the most common diseases. In the perspective of an engineer, this research would be an important application of nanotechnology and genetic engineering.

The Holistic View

Ultimately, the point of engineering is to solve problems and protect the general public from potential threats. For this reason, the treatment of cancer and other lethal diseases should remain a major focus in engineering research. I see much hope in terms of lowering the mortality rates for lung cancer because of the research being done using tumor-targeting drugs. Paclitaxel and other nanoparticle-based drugs are forging a new path in the world of cancer treatment. Hopefully one day, no one will have to go through the pain I went through of losing a loved one due to cancer because the drugs will be so advanced. I believe that nanoparticle delivery systems for gene therapies will be the reason that day comes.

REFERENCES

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