

Reconstruction and Prevention: Nanotechnology and Tissue Engineering Approaches for Cancer Patients

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ABSTRACT

Cancer is a complex disease responsible for one-in-sixth deaths. Various environmental contaminants: heavy metals, synthetic organic dyes, asbestos, polychlorinated biphenyls (PCBs), and polycyclic aromatic hydrocarbons are carcinogenic in nature. This paper investigates the potential of nanotechnology in tissue repair and cancer prevention by environmental remediation of carcinogenic pollutants. Solid lipid nanoparticles, including liposomes, are promising candidates for targeted drug delivery and tissue engineering applications. These nanocarriers can be engineered to selectively bind to diseased cells, delivering therapeutic drugs and potentially facilitating tissue repair processes. The development of those nanoparticles can benefit from combining it with Artificial Intelligence, i.e. AI can help to determine the shape and the size of the solid lipid nanoparticles targeting damaged tissues, and more importantly their biocompatibility to prevent further harm to the already damaged tissues. Molecular imaging techniques used for early detection and monitoring of carcinogenic cells can identify areas of damaged tissue with high sensitivity. This information can then be used to guide the targeted delivery of nanocarriers to the tumor site. Beyond drug delivery and tissue engineering applications, nanotechnology holds potential for cancer prevention strategies by environmental remediation of known carcinogenic pollutants. For example, ferric oxide nanoparticles have been shown to eliminate cadmium and arsenic from toxic substances.

Introduction

It is well known that cancer is one the most problematic diseases throughout the world. Every year about ten million people die from it, which makes cancer responsible for about one-in-sixth deaths (Roser et al., 2024). To make matters worse, the environment contains many carcinogenic pollutants that contaminate soil and drinking water (Roy et al., 2021).

Substances such as petroleum, radionuclides, nuclear, and missile fuel pose a serious threat to people exposed to them daily. For example, an electrician can be exposed to arsenic, which causes skin cancer. In addition, in the world, up to 93% of cancer cases are non-hereditary and caused by interactions with the environment, and 7% of the cases are hereditary. People in underdeveloped places are especially threatened since they usually work labor-intensive jobs, in which the respective environment is unsanitary and has cancer-causing compounds. Materials such as cigarettes and cigars are also harmful as people who smoke them significantly increase their chances of getting lung cancer.

The distribution of carcinogenic materials in the United States varies significantly across geographic regions, influenced by factors like industrial activity, agricultural practices, and natural geological formations. In the Eastern parts, especially New York and Pennsylvania, there is a lot of pollution, which also means carcinogenic material is very prevalent in these parts. However, in the central plains of America, there is little trace of pollution due to low populations, vast farmlands, and a low number of cars. The western parts also have little pollution with one exception: California. In California, the air pollution is so dangerous that many schools limit recess time and utilize air purifiers to combat toxic chemicals from the pollution. This means that carcinogenic material is a constant threat to California residents. The current prevention measures of pollution in America include federal funding programs, a Zero-Carbon

Fuel Standard, and more support for the federal Diesel Emission Reduction Act program; nanotechnology methods could be developed too (Kent and Lewis, 2022).

In Pennsylvania, especially in the southeastern part, pollution levels are extremely high, so prevention is definitely needed. Currently, in southeastern Pennsylvania, the company PECO operates in order to warn nearby residents of threatening weather conditions and strives to make energy production more efficient, which then lowers pollutants.

For people who already have cancer and have, as a result, lost a lot of muscle and tissues, tissue engineering, which involves the use of nanostructures, could be much better than the standard method of organ transplant; reconstructed tissue in these people would help them to recover faster and higher their chances of survival (Perán et al., 2013).

While there is no definitive cure for most types of cancer, one logical idea would be to help cancer patients to suppress cancer. Chemotherapy and radiation therapy are two current options used to treat cancer patients, but these treatments can often be costly and can result in severe side effects (*Chemotherapy side effect*): nausea, and vomiting, fatigue, constipation, and hair loss. Instead of using these treatments, tissue engineering and better remediation of carcinogenic pollutants in the environment could be the answer. Nanotechnology can be used to deliver drugs, build lost tissue in cancer patients, which will decrease the cost of the cancer treatment, and to clean environmental carcinogenic pollutants. Penn Medicine found that using nanoparticles to transport mRNA into T cells to attack tumors is very effective in treating cancer patients. As a result, creating reconstructed tissue in cancer patients will then be less likely to become ruined by tumors (Ng, 2020). Developing better “reconstruction strategies” of lost tissue in cancer patients would have a significant effect on humanity (Parsa, 2012). The tissue engineering, which involves the use of nanostructures can be more efficient and cost effective than the standard method of organ transplant with faster recovery time and higher chances of survival (Perán et al., 2013).

The nanocarriers systems can benefit from implementing artificial neural networks (ANN), which can process large amounts of data about possible locations of tumor sites and thus facilitate targeted drug delivery. In terms of environmental remediation, oxides of nano metal oxides have been utilized to treat sites containing two of the major carcinogenic pollutants - cadmium and arsenic. Eliminating environmental threats using nanotechnology treatments can not only save many lives but can also create safer working places.

This paper explores how nanotechnology can benefit cancer treatment using nanocarriers for drug delivery, tissue engineering to reconstruct lost cells and to improve the current cancer treatment without the side effects of chemotherapy. In addition, environmental pollutants and industrial exposure to toxic chemicals can increase the risk of cancer, thus making environmental remediation an important part of cancer prevention. Using nanoparticles to remove toxic material such as arsenic and cadmium from soil will ultimately lessen cancer cases.

Methods

The information in this article was gathered through other literature reviews correlated to the topic of this article. At first, about 50 articles were gathered to maximize the amount of studies and information in this article. The articles were gathered using keywords such as “nanotechnology,” “AI,” and “environment” on the *National Library of Medicine* website and using the Google Search Engine. However, a lot of the gathered articles did not include information related to tissue engineering or the prevention of carcinogenic materials in the environment, so they were discarded. For example, about 20 articles happened to be from the United States, and after reviewing them, more than twelve of them were discarded because they consisted of information dealing with cancer treatments such as chemotherapy instead of treatments related to tissue engineering. As a result, after discarding the unrelated articles, which came from different parts of the world including the United States, the Middle East, and China, 12 articles remained, and all of them are used in this article. The images in the article were created using an application called “BioRenderer” and using images from the 12 articles in this paper.

Nanotechnology

Nanomaterials possess unique physicochemical properties due to large surface to volume ratio and excess surface energy, which results in higher reactivity in comparison with the macroscopic analogues. Different inorganic and organic molecules, including large biomolecules such as RNA, DNA, and proteins, can be attached to the surface, and transported by the nanoparticles. Their modifiable size and surface results in higher stability and the potential to attach various hydrophilic and hydrophobic drugs depending on the preferred routes of administration. On the other hand, the potential toxicity of some synthetic nanoparticles, brings up concerns about the health risks, especially when they are implemented in different processes. However, natural lipids, phospholipids, chitosan, dextran, and carbon nanomaterials, including carbon nanotubes, are biocompatible and can be safely used for tissue engineering (Mosleh-Shirazi et al., 2022).

The Nobel laureate Alexis Carrel is considered the father of regenerative medicine and organ transplant surgery. This type of medicine makes regenerating human tissue possible through replacing or repairing injured tissues or organs, which restores the functionalities of malfunctioning cells. Modern enhancements in the implementation of nanotechnology in tissue regeneration have revolved around utilizing functionalized inorganic nanomaterials to transport cells, which tracks the progression of tissue regeneration in real-time and enhances the effectiveness of the treatment. Inorganic nanoparticles, nanomaterials, Quantum Dots (QDs), artificial macromolecules, carbon nanotubes, lipid-by-layer nanoparticles, which are all commonly used in other applications, can also play a role in regenerative medicine. In the future, nano-based regenerative medicine can result in a new method in healthcare by creating operative targeting systems for stem cell-based treatments (Javadhesari et al., 2022).

Nanoparticles are used in the regeneration of bone tissue by influencing bone cells to begin developing and regenerating bones that are severely damaged. Nanoparticles could potentially be used in scaffold-based and scaffold-free methods of tissue engineering to further osteogenesis and recreate bone tissues. Therefore, these particles could contribute an osteogenic function by controlling the reactions in the body that cause inflammation and osteo/angio/osteoclast signaling pathways including the FAK/RhoA/YAP1 pathway that controls the communication between stress fibers and the development of bones, MAPK pathway that attaches the surface of a cell to its nucleus to acquire signals taking outside of the cell, particularly osteoblast signals, BMP/Smad pathway that advances osteogenesis and amplifies the transcription process of osteogenic marker genes which include Runx2, and Wnt/ β -catenin pathway, which adjusts cells related to osteoblasts and affects many stages of bone development (Javaadhesari et al., 2022).

The nanoparticles, which are used to regenerate damaged tissues, could also be enhanced with antimicrobial properties to kill or stop the growth of microorganisms. Another possibility is to add biological properties as tissue-specific growth factors and then create new tissues that are similar to the original tissues of the human body and in line with a person's preferred properties and characteristics. Even though nanoparticles and their applications in the regeneration of bone, tooth, skin, heart, neurons, and bladder tissues may yield promising results, these applications still need to be further researched (Javadhesari et al., 2022).

Solid lipid nanoparticles, also known as SLNs, were discovered in the 1990s and functioned as a superseded transporter for liposomes, emulsions, and nanostructures that were polymer-based. Because of their strong hydrophobic lipid core surrounded by monolayer phospholipids, they are more stable than liposomes when undergoing biological processes. A solid lipid nanoparticles assembly is shown in Figure 1. In these transportation systems, the features of colloidal lipid emulsions are frequently used in solid particulates. They are less toxic compared to mesoporous silica or polymeric nanomaterials used in the same applications since they are more biocompatible. In addition, SLNs that are composed of 0.1-30% lipid matrix expand throughout the watery solution and stabilize at 0.5 - 5 percent of the surfactant when needed (Mosleh-Shirazi et al., 2022). In the context of cancer, solid lipid nanoparticles can be utilized in transporting biological material needed for reconstructing tissues in cancer patients. In addition, they will pose less of a threat to cancer patients due to their better biocompatibility.

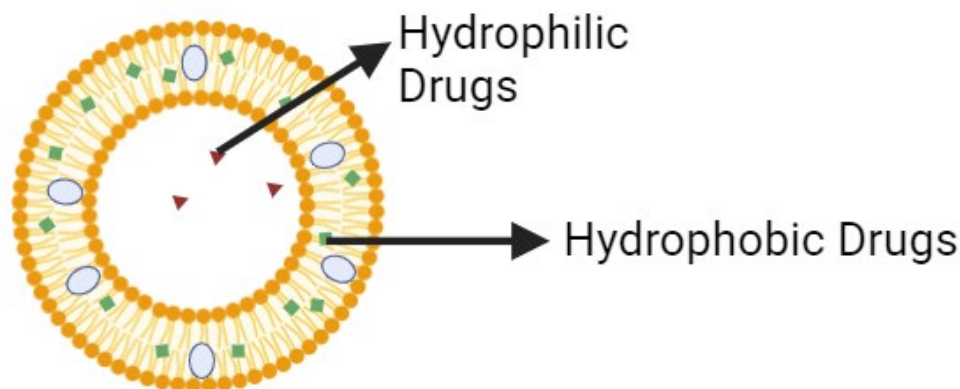


Figure 1. Assembly method for nanoscale delivery of small molecules. The hydrophobic tails of the lipid molecules form the inner layer and the hydrophilic heads the outer layers. As a result, the different types of drugs can be attached to the tails or the heads layer depending on their properties. Overall, the image shows a variation of a solid lipid nanoparticle.

Source: Murthy, 2024

Nanomaterials can be transported towards tumors passively or actively after the process of introducing them to the circulatory system. Nanocarriers can be assisted from the particular result of EPR (Enhanced permeability and retention effect) in tumors through the use of passive transmission, allowing them to break free from the bloodstream and enter the extravascular area in which they gather near solid tumors. Nanoparticles should be smaller than 100 nanometers in order to augment their efficiency. Because of the fluctuation in the bloodstream of the tumor, the biophysiological constraints, and in some cases the tension of the intercellular structure, the position of nanostructures inside the tumor would be inconsistent. Using different ligands as small molecules, peptides, oligosaccharides for surface functionalization can allow the nanoparticles to bypass this barrier and accurately target tumors. An antigen or receptor could be utilized as the target substance; however, it has to reside over the malignant cells and indicate close to zero or borderline thresholds for healthy cells (Mosleh-Shirazi et al., 2022).

Liposomes are natural nanoparticles consisting mostly of amphipathic phospholipids, which enclose an inner aqueous region created by a circular, spontaneous formation of a lipid bilayer. Liposomes have the ability to store hydrophilic drugs and sustain an internal aqueous structure and as a result, have the capability to be joined to cell membranes during the cellular phase of endocytosis and to emit medications frequently. Those nanocarriers products exhibit enhanced pharmacokinetics and pharmacodynamics. The liposomes surfaces are usually functionalized with polyethylene glycol (PEG) and glycolipids to prevent their rapid removal from methodical circulation using reticulo-endothelial system phagocytic activity. The implementation of PEG or other conjugates soluble in water on the outer surface of all variations of nanosized vectors, including liposomes, improves their biological fluid stability while simultaneously creates an active system of hydrophilic and neutral surface chains that lower protein opsonization and activates nanomaterials to possibility isolate from RES macrophages. This enhances the half-life of nanoparticles, which affects their longevity in the bloodstream and, coupled with their capability to graft targets, facilitates them reaching the tumor site (Mosleh-Shirazi et al., 2022). A liposome delivering material is shown on Figure 2.

Liposome Delivering Material to Defeat the Cancer Cell and Reconstructing Lost Tissue

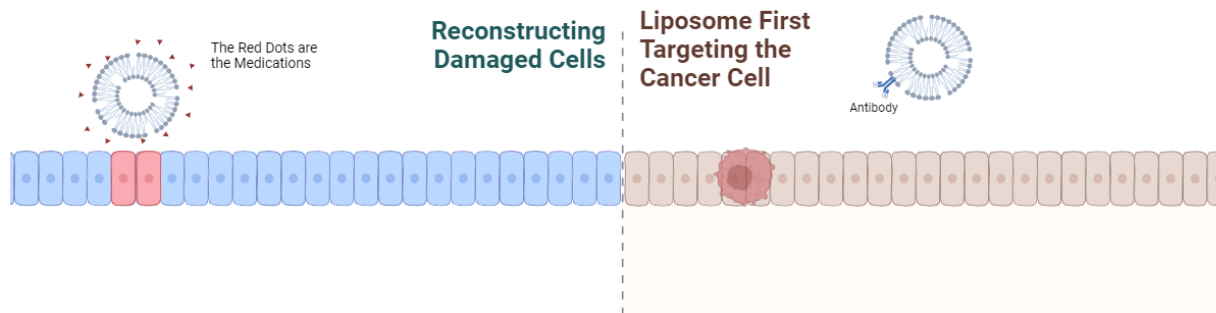


Figure 2. Method for eliminating carcinogenic material and then repairing damaged tissue using tissue engineering approaches.

The different types of cancer imaging processes can help scientists to improve the targeted reconstruction of tissues by sending the nanoparticles to wherever the process detects cancer cells.

During the past few decades, the implementation of nanoparticles in diagnosing and regulating cancer has directed attention to many types of nanoparticles that are currently being used for molecular imaging. Because of their advantages such as small size and biocompatibility, they have become notable in modern cancer research and diagnosis. The nanosized semiconductors, quantum dots, and iron oxide nanocrystals, have specific optical and magnetic properties, which makes them potential candidates for imaging and diagnostics. Distinct anti-tumor drugs and biomolecules such as peptides, antibodies or other chemical substances, could be utilized alongside nanoparticles to recognize particular tumors, which are helpful for the early identification and screening of cancer cells (Jin et al., 2020).

For cancer diagnostics, imaging of tumor tissue with nanoparticles has made it possible to detect cancer in its early stages. In lung cancer, the detection of metastases can be determined by developing immune superparamagnetic iron oxide nanoparticles (SPIONs) that can be used in MRI imaging with the cancer cell lines as the target for the SPIONs. Recent studies have shown a high specificity of SPIONs with no known side effects, making them suitable building blocks for aerosols in lung cancer MRI imaging (Jin et al., 2020).

Magnetic powder imaging has also been used in tomographic imaging technology where it has shown a high resolution and sensitivity to cancer tissues. In animal experiments, nebulization of the lungs has been achieved using magnetic nanoparticles (MNPs) with Epidermal growth factor receptor (EGFR), a commonly expressed protein in non-small cell lung cancer (NSCLC) cases as a target. Further, in vitro studies using nanosystem for positron emission tomography (PET) have also been developed based on self-assembled amphiphilic dendritic molecules. These dendritic molecules spontaneously assemble into uniform supramolecular nanoparticles with abundant PET reporting units on the surface (Jin et al., 2020).

Artificial Intelligence

The development of AI is extremely important as it can detect which cells benefit or get hindered due to exposure to nanoparticles. Information from ANN, artificial neural networks, can be used to develop nanomaterials that can attack tumor cells and rebuild any lost or deformed tissue the tumor cells may have caused.

Artificial Intelligence is an innovation in technology that helps machines and computer applications to mimic human intelligence, acquiring knowledge from experience through iterative processing and algorithmic training. The AI gathers large sets of information using intelligent, iterative processing algorithms in order to learn from patterns and features in the information that they examine (CSU Global, 2021). Machine Learning is one of the reasons that AI can identify patterns in data, reveal insights, and enhance the results of the particular task the system has been directed to achieve. In addition, Deep Learning utilizes artificial neural networks that act as biological neural networks in the brain of a human in order to handle information, identify connections between data sets, and derive inferences, which are based on positive and negative reinforcement (CSU Global, 2021).

In addition, diagnosis of cancer and its treatment can be assisted greatly by the use of ANN even though this field is still in early development. ANN algorithms can be utilized to enhance nanopharmaceuticals formulations for better transport and drug delivery targeting by analyzing and predicting the interactions between MHNs, Magnetic Hybrid Nanoparticles, in nanocarriers, drugs, biological mediators, or cell membranes and by evaluating drug encapsulation efficiency. Moreover, ANN can improve clinical results while, at the same time, assist in reducing toxicity by enhancing the efficiency of drug delivery and outline of the MHNs (Govindan et al., 2023).

In one study that showcased ANN's value, G-Fe₃O₄ were deliberately introduced to an alternating current magnetic field at a frequency value of 633 kHz and a strength value of 9.1mT. Later, an ANN model was utilized in order to analyze localized antitumor outcomes. According to the neural net time-series model, the most superior nanohybrid composition was almost 100% accurate. The NARX models implemented in this study incorporated external inputs for every component of the model. A mean square error (MSE) validated the predicted results in the study. F45G55 is a model that contains 45% magnetite and 55% graphene and showed the best results after 71 epochs in the training stage. As a result, the results showed that F45G55 nanohybrids possessed the highest mean squared error for applications of hyperthermia with small doses and an extreme specific absorption rate.

These studies established that ANN models can be effectively used in the outline and development of magnetic nanoparticles for applications of MHT (Govindan et al., 2023).

Meanwhile, ANN models have been used to evaluate the cytotoxicity of nanoparticles as a function of their size. Particle size, concentration, incubation time, and surface charge of nanoparticles were selected as inputs for the ANN model, and percentage cell viability (%CV) as output. Magnetic nanoparticles with greater hydrodynamic sizes have a lower chance of penetrating cells; thus, they have a higher %CV. In this model, the zeta potential of nanoparticles was examined under different laboratory conditions. It was concluded that HEK293-T cells adhered better to NPs with higher PZP. However, a robust algorithm requires as much information as possible to work effectively (Govindan et al., 2023).

Using ANN models can help scientists to determine the shape and size of solid lipid nanoparticles targeting damaged tissues. In addition, these models can also determine the toxicity of the nanoparticles in order to prevent further harm to the already damaged tissues.

Other Treatments that Eliminate and Detect Carcinogenic Cells

The therapies PTT/PDT, Photothermal and photodynamic therapy, which use nanotechnology to terminate cancer cells, will make it easier for solid lipid nanoparticles such as liposomes to reconstruct tissues in areas where carcinogenic material has been eliminated. This means that the liposome in the proposed image above would not have to carry its antibodies to eliminate tumors found on lost tissue in cancer patients and go straight into delivering medications to the damaged tissue.

PTT/PDT harnesses energy from light sources to treat carcinogenic cells. PTT/PDT uses this light energy to create heat or light-activated drugs to terminate carcinogenic cells. PTT/PDT utilizes a photosensitizer, a light-activated drug which is absorbed by carcinogenic cells and then initiated by light energy to create heat and kill off carcinogenic cells. In the process of PTT, a laser is utilized to create heat that kills carcinogenic cells. PTT/PDT is helpful when treating particular types of cancer, which include head and neck cancer, bladder cancer, and a few forms of skin

cancer. Magnetic nanoparticles, also known as MNPs, have also been utilized in therapies such as photothermal and photodynamic. In photothermal therapy, photosensitizing agents including magnetic nanoparticles are put into the body and absorbed by carcinogenic cells. The agent is, as a result, activated by a certain wavelength of light, which then creates heat to get rid of the carcinogenic tissues. (Govindan et al., 2023).

Environmental remediation of carcinogenic pollutants

Beyond treating cancer and the tissue engineering and regeneration, the number of the cancer cases worldwide could be significantly decreased by reducing the amount of carcinogenic pollutants in the environment. Soil contamination and degradation continue to be a significant environmental problem, with remediation becoming a global challenge. Degrading soil reservoirs throughout the world has a great influence on agricultural production and food safety; therefore, this needs to be addressed right away. Heavy metals, herbicides, and POPs-persistent organic pollutants contaminate soil, adding to the issue (Roy et al., 2021). These pollutants are extremely significant as they are also carcinogenic materials.

Carbon-based nanomaterials, carbon nanotubes, metal oxides (ferric oxide and titanium oxide), and various nanocomposites are some of the engineered nanomaterials that have been utilized to immobilize soil contaminants. For example, ferric oxide nanoparticles have an extraordinary potential to absorb and immobilize heavy metals such as cadmium and arsenic, two carcinogenic materials, from various media samples. Oily sewage is an adverse problem affecting aquatic local life. Iron nanoparticles are successful in removal of Total Petroleum Hydrocarbons (TPHs), some of which are carcinogenic (benzene) from water with enhanced results of 88.34%. Thus, nanotechnology-based treatments are able to provide high-performance treated water, which has less impurities and toxic substances (Roy et al., 2021). In terms of cancer prevention, removing heavy metals and hydrocarbons from the soil would significantly reduce the amount of carcinogenic materials and thus the risk for cancer.

In terms of traditional methods, coagulation and flocculation have been used to treat polluted water. These methods enhance the biodegradability of waste material and remove micropollutants (Amuda et al., 2007). In addition, compounds such as ferric chloride and polymers are included into these methods to destabilize the colloidal materials and small particles, which then accumulate into large groups that are settleable. Treating metal pollutants in wastewater and then removing soluble compounds by forming flocs is a physicochemical approach (Iwuozor, 2019). This approach helps to eliminate suspended solids (SS) and organic material. Coagulation combined with the process of ozonation has been utilized for waste sanitary landfill leachates (Poznyak et al., 2008). The coagulation-flocculation process assists in the removal of nutrient pollutants such as P and nitrogen (Aguilar et al., 2002). After the process of coagulation and flocculation is over, the resulting large clumps of colloidal materials and small particles can easily be removed, which substantially reduces carcinogenic threats in polluted water.

In terms of the prevention of carcinogenic pollutants in water, both carbon-based and non-carbon-based nanomaterials can enhance the cleansing of aquatic bodies. Segregating contaminants depends on their chemical and physical reaction with the surface of the nanomaterial (Bansal et al., 2015). In addition, nanomaterials such as carbon nanotubes, silica nanoparticles, and Zinc and titanium oxides can function as nanocomposite filtration membranes to capture carcinogenic material in polluted water. These nanomaterials can also be used in the remediations of lysis, adsorption, and oxidation (Singh et al., 2012).

Dye pollutants are harmful for humans because most of them are carcinogenic. Dyes were used in many products such as textiles, paintings, pigments for thousands of years. Currently, about 0.1 million different types of synthetic dyes are manufactured in various industries. In terms of usage, about 1.6 million tons of dyes are used yearly (Tan et al., 2015). In order to remove these dye pollutants, especially methylene blue dye, from water, scientists could utilize electrospun polyether sulfone nanofibers containing vanadium nanoparticles. Due to the nanofibers' low isoelectric point, they develop a highly hydroxylated surface area when introduced to an alkaline medium, promoting the adsorption of cationic methylene blue molecules (Homaeigohar et al., 2016). However, the method of adsorption will not mitigate all of the dye contaminants.

Conclusion

Nanotechnology has various implications in tissue engineering and the remediation of carcinogenic materials in the environment, which can decrease the cancer risk. AI and magnetic powder imaging are two ways scientists can actually locate tumors in cancer patients. There are also other methods, such as using liposomes that carry antibodies and other medications to eliminate carcinogenic cells and reconstruct tissue, that can be used to treat the carcinogenic material after AI or other types of imaging have found it. The use of PTT/PDT is recommended as these treatments will make the functions of liposomes that are made for tissue engineering a lot easier since they will only have to reconstruct tissue and can leave treating tumors to PTT/PDT. Finally, the prevention of pollutants containing carcinogenic material is very significant as 90% of cancer cases are due to exposure to the environment. Carbon nanotubes and nano ferric oxides are two types of nanomaterials, which can be used to remove carcinogenic cadmium and arsenic. Electrospun polyether sulfone nanofibers containing vanadium nanoparticles are used for remediation of dye pollutants, especially methylene blue dye. Iron nanoparticles are successfully used to remove Total Petroleum Hydrocarbons (TPHs), some of which are carcinogenic (benzene).

Acknowledgements

The production of this paper would not have been possible without the accommodation from the Gifted Gabber team, Professor Virgel, Professor Lilova, and Coach Jo. Their help enhanced the information in this paper and made it more understandable for those who are not familiar with the topic. In addition, the images in this paper were developed with the help from Professor Virgel and Professor Lilova as they referred to many reputable websites for creating the images and showcased the process of making the images.

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