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A REVIEW ON: CANCER DISEASE – PRESENT AND CHALLENGE FOR FUTURE

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ABSTRACT

Cancer remains one of the leading causes of death worldwide, a complex and multifaceted disease. Cancer still presents many difficulties, even with improvements in detection and therapy. Currently, the disease is marked by rising global cases (18.1 million in 2018) and deaths (9.6 million), diverse cancer types and subtypes that complicate diagnosis and treatment, emerging drug resistance, and disparities in access to care and outcomes across geographic, socioeconomic, and racial groups.

Looking ahead, future directions for combating cancer include precision medicine, immunotherapy, early detection through advancements in screening and imaging, personalized cancer vaccines, and the integration of artificial intelligence to enhance diagnosis and treatment planning. Research priorities should focus on understanding cancer biology, developing effective therapies, enhancing cancer prevention, addressing disparities, and leveraging technology to improve outcomes.

By addressing these problems and undertaking innovative research, we may improve cancer outcomes, decrease death rates, and increase the quality of life for people with cancer and those who love them. To address the numerous issues surrounding cancer, a multidimensional strategy including policy changes, scientific improvements, and community engagement is needed.

Keywords: Cancer disease, Causes, Treatment, Challenge, Management

INTRODUCTION

Cancer is the unrestrained multiplication of living organisms that leads to tumors that are cancerous, and it happens to be one of the leading causes of death in the world **[1]**.

Tumour cell dissemination of external organs along with surrounding tissues is the primary cause of illness and death for the majority of cancer patients. For many years, a significant amount of study in the biological sciences has focused on the biochemical process by which healthy cells might develop into cancerous cells **[2]**. Despite extensive study and quick advancements over the last decade, malignancy continues to kill individuals around the world. By 2020, when the worldwide population reaches 7.5 million of dollars, roughly 15 million new cancer cases will be diagnosed, and 12 million individuals with cancer will die **[3]**. In the country of India, cancer has evolved into one of the leading causes of mortality, with approximately 2 to 2.5 million cases happening each year, 3 lakhs that include more than 7 lakhs new infections, and roughly 15 lakh people requiring medical care, diagnosis, and follow-up **[4]**. Several strategies that could alter the tumor microenvironment and increase treatment efficacy by improving drug transport to the tumor tissues are being studied in preclinical or clinical settings **[5]**. The first is genotype-directed precision oncology, which focuses on tailoring therapies for subgroups of different tumor forms that have specific genetic abnormalities. Second, concentrate on tumor components. The While the microenvironment, especially the immune response and anti-tumor immunity. In this review, we will quickly discuss the main concepts of these two distinct anticancer treatments. We will also talk about some of the significant obstacles that both sectors of cancer treatment may face in the future **[6]**.

SYMPTOMS: -

The place of development and kind of malignancy determine the symptoms. Chest pain, dyspnea, and coughing are all possible symptoms of carcinoma of the lungs. Diarrhea, constipation, and bleeding are common symptoms of colon cancer. Some cancer types may not display any symptoms at all. Some malignancies, such as cancer of the pancreas, may not cause symptoms until they have progressed to an advanced stage. The majority of tumors may show with the following symptoms.

- Chills
- Fatigue
- Fever
- Loss of appetite
- Malaise
- Night sweats
- Back pain
- Abdominal pain
- Weight loss
- Thickening or lump in the body
- Cough or hoarseness that does not go away
- Obvious change in a wart or mole
- Changes in bowel or bladder habits

- Unexplained bleeding or discharge
- Any sore that does not heal
- Unusual upset stomach or difficulty
- Swallowing **[4, 7]**

TYPES OF CANCER

Cancer forms: There are several forms of cancer, including:

a) Carcinomas: Carcinomas are the most common type of cancer, accounting for 80–90% of all diagnosed cases. The protective layer of skin or tissue is where it starts. This includes the surface of the glands and internal organs. It becomes a solid tumor. prostate cancer, colorectal cancer, lung cancer, and breast cancer.

b) Sarcomas: They only make up around 1% of all cancer cases, making them very uncommon. They begin in the tissues that join and assist the body. It can develop in blood vessels, bone, fat, joints, tendons, nerves, cartilage, muscles, or lymph vessels. Liposarcoma, chondrosarcoma, and osteosarcoma are a few types of sarcomas.

c) Leukemia: Leukemias are malignancies that originate in one of the bone marrow's circulation-forming cells, resulting in abnormal white blood lymphocytes that fail to function properly. Leukemia is the eighth most common neoplasm in adults chronic the most common in children, with subtypes included acute myeloid leukemia, immature lymphocyte leukemia, chronic myeloid, lymphoma leukemia, and leukemia.

d) Lymphomas: Lymphomas are malignancies that originate in the lymphatic circulatory system, a network of vessels and glands which helps in the fight against infection. Hodgkin's disease and non-lymphoma Hodgkin.

e) Cancers of the central nervous system: Tumors of the brain and spinal cord, including primary CNS lymphomas, semicircular pituitary cancerous tumors, gliomas, schwannomas, primitive neuro-ectodermal tumors, vestibular schwannomas, and meningiomas, originate in these tissues.

f) Multiple myeloma: The word "multiple malignancies" refers to a type of cancer that begins in the plasma membrane cells of an immune cell. The bone marrow generates cells known as myeloma, which are cells in the plasma that cause bone cancer. Researchers typically think of it as a blood-forming particle. Kahler disease, as well as lymphoma.

g) **Melanoma:** Originates with cells that grow into Melanocytes. These are specially designed cells that create melanin, the coloring agent that gives the skin its color. Melanomas generally occur on the skin, although they can also appear in the eyes or other pigmented tissues.

h) **Additional Tumor Types:**

1. **Germ Cell Tumors**

   Germ cell cancers are those that arise in the cells responsible for producing sperm or eggs. This can occur in any location of the body and may be benign or malignant.

2. **Neuroendocrine Tumors:**

   The term "neuroendocrine tumor" refers to originate from hormone-releasing cells that blood in reaction to a neurological signal system. It develops from cells that emit blood hormones in reaction to a signal from the neurological system. These cancers have the potential to produce hormone levels that are greater than usual, will cause a wide range of symptoms. It could be either innocuous or cancerous **[8, 9]**.

CAUSES OF CANCER-

Cells maintain themselves in a survival quiescent and glycolytic adaption state in response to any form of cell aggression, whether it be chemical, physical, viral, or bacterial **[10]**. Cancer arises when normal cells differentiate into tumor cells in an extensive procedure that frequently progresses from an earlier stage of cancer to a malignant tumor. These changes are the result of the interaction involving an individual's genetic composition and three types of external factors, such as:

1. **Chemical carcinogens-**The drug alcohol, asbestos-containing materials, smoke from cigarettes, aspergillus (a contaminants in food), and the arsenic (a water-borne pollutant), as well as physical carcinogens such as ultraviolet and ionizing radiation.
2. **Biological carcinogens-** including parasitic, bacterial, or viral infections. WHO maintains a classification of chemicals that cause cancer through the International Agency for Research on Cancer (IARC), its cancer research agency.

The probability of cancer rises considerably as people age, most likely due to a development of risks for specific malignancies, which worsen with age. The propensity for cellular repair processes to become less effective throughout age is accompanied by an accumulation of overall risk **[11]**.

THE DEVELOPMENT OF CANCER –

Tumor clonal diversity, or the creation of tumors from individual cells that begin to

reproduce abnormally, is a fundamental feature of tumor. However, the recognition that the growth is polyclonal does not suggest that the tumor's precursor cell whose gave rise to it has already evolved all of the characteristics of a malignant cell. Leukemia, on the other hand, is the consequence of a lengthy procedure in which cells go through a series of alterations before becoming malignant. The simple fact that most cancerous tumors arise later in life demonstrates the multistep process involved in cancer development. Cancer is assumed to grow at anatomical levels throughout a series of phases consisting of screening for individuals with progressively increased propensity for invasion and metastasis.

Tumor initiation- The earliest stage of this procedure is thought to be attributed to a mutation in the genome that results in abnormal single-cell proliferation. Cell proliferation causes a population of malignant cells derived from clones to multiply.

Tumor progression- Transplantation is the procedure by which a new clone of cancerous cells forms due to an increased rate development or other traits that provide it with an advantage in selection, such as the continuation of life, invasion, or metastasis. The tumor community continues to increase as new mutations occur throughout the cells themselves **[12]**.

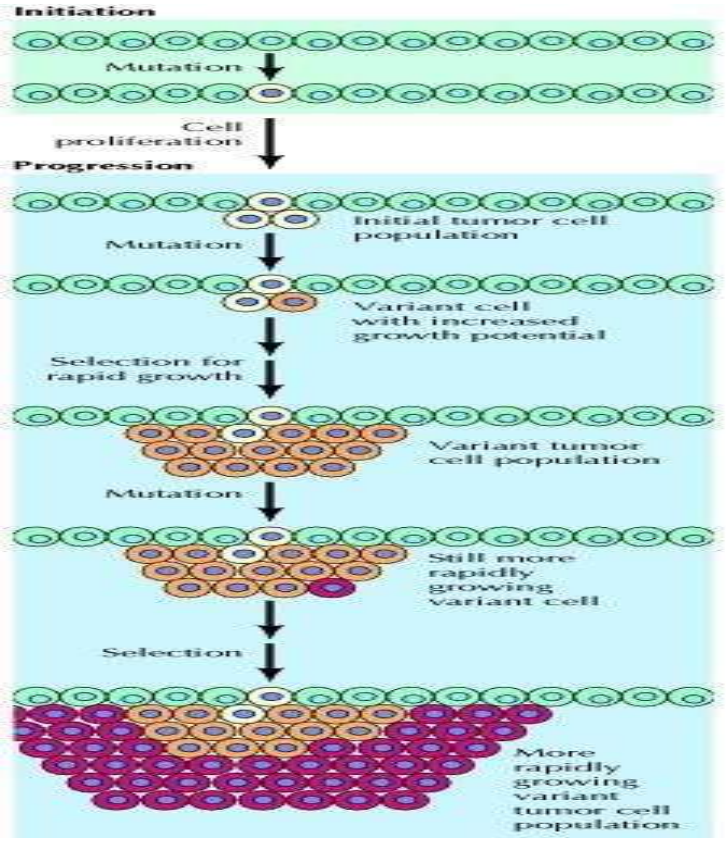

Figure 1: Development of cancer

TREATMENT OF CANCER –

1. **Stem cell therapy -** The bone marrow (BM) includes undifferentiated cells termed stem cells, which can grow into any type of body cell. Stem cell therapy is another cancer treatment option that is regarded to be safe and effective. Stem cell applications are still under exploratory clinical trials; for instance, its potential for repairing other damaged tissue is being investigated. Currently, mesenchymal stem cells (MSCs) derived from the BM, adipose tissues, and connective tissues are being employed in clinical trials **[13]**.
2. **Chemoradiation Therapy-** Radiation therapy uses radiation with tremendous energy to kill malignant cells and shrink malignancies. It can be used individually or in conjunction with chemotherapy or surgery.[9] In response to sunlight exposure, the body's outer layer produces a form of vitamin D (Vit D), a hormone similar to estrogen. Cholecalciferol (Vit D3) used superficially has previously been used to treat the condition and, more recently, as one component of an initiative to treat AK manifestations with 5-FU irradiation **[14]**. Radiation therapy, or preoperative chemotherapy and radiation combined, is recommended to minimize the histopathological complexity of local illnesses and enhance survival. seen in more gastrointestinal malignancies **[15]**.
3. **Surgery**- Surgery may be used to identify, treat, or prevent cancer. The overwhelming majority of patients with cancer will require surgery of some type. It usually gives the best chance of recovery, especially if the cancer has not spread to other body parts **[16]**.
4. **Targeted therapy**- TDCs provide precise as well as efficient cancer cell elimination through the combination of selective targeting with a strong killing impact. Targeted combined drugs (TDCs) are a promising cancer therapeutic technique because they can precisely destroy cancer cells **[17]**.
5. **Immunotherapy**- TDCs deliver accurate and effective cancer cell eradication by combining targeted destruction with a powerful killing impact. TDCs are a potentially cancer treatment option as they can specifically attack cancer cells **[17]**.
6. **Gene therapy-** The treatment of genes is the use of specific genetic

information to alter the encoding of a gene product or the biological properties of structures in order to combat a range of diseases. The CRISPR-Cas9 gene modification method, which has shown great promise in treating a range of cancer types, allows researchers to purposely alter or destroy genes that help with cancer development **[19]**.

7. **Harmone therapy** treatment with estrogen minimizes or prevents the spread of malignancies that use hormones for proliferation. Hormonal therapy is also known as hormone treatment or endocrine therapy **[20]**.

CANCER DISEASE: PRESENT AND CHALLENGE FOR FUTURE.

1. Targeted drug conjugates in cancer therapy:

TDCs are a type of precision medicine that targets cancer cells directly while preserving healthy cells in an effort to treat diseases like cancer more successfully. TDCs require three key components: the targeted ligand are the linking agent, and the payload. In terms of ligand discovery, work is still being done to determine and develop new compounds with higher effectiveness and performance that can bind precisely to tumor cell markers. These consist of new types such as peptides from which can be produced for high discrimination; single-domain antibodies, also known as the nanobodies, that remain stable while having the ability to effectively penetrate tissues, and and bispecific immunoglobulins, which can target two distinct antigens. Conventional TDCs often contain cytotoxic chemicals that destroy cancer cells. Nonetheless, there is a desire to develop non-cytotoxic compounds with novel modes of action. These include a sequence that alters gene function and radioelements utilized by focused treatment with radiation. To keep the combined substance stable in the circulatory system while only releasing the payload at the tumor site, the linker that joins the intending ligand and the payload must be carefully engineered. To ensure coordinated and effective carrier release, linker breakthrough technology comprises developing linkers that can be hydrolyzed under certain enzymatic characteristics seen in tumour cells or the tumour microenvironment. The transition from random to particular to the location conjugation marks a substantial progress in conjugation techniques. Site-specific conjugation improves pharmacological accuracy, peace of mind, and safety profiles by guaranteeing that every TDC molecule has a consistent number of payloads. This disciplined strategy also contributes to consistent treatment outcomes.

The dearth of viable medicines in the development pipeline presents major

obstacles to SMDC research as a component of targeted therapy. With an emphasis on folate receptors, only a small number of targeted ligands have been thoroughly evaluated. Some SMDCs show some degree of renal uptake, which may persist after renal clearance. Furthermore, SMDCs' flexibility and ease of administration are limited by their low oral bioavailability. Their weak solubility is the reason for this, and more research is required to get over this restriction. In targeted medication therapy, there is no one delivery method or development model that works for the majority of indications. Improvements in conjugation processes and ongoing innovation in targeting systems, linkers, and payloads have the potential to raise the therapeutic index of TDCs and give cancer patients better therapy alternatives **[21]**. Compared to ADCs, PDCs are smaller and may have more tissue penetration, making them more promising therapeutic agents **[22]**. Their small size, however, poses difficulties, notably in terms of quick clearance through the kidneys, which limits their ability to aggregate efficiently at pharmacological sites **[23]**.

2. Towards an optimal model for gastric cancer peritoneal metastasis: current challenges:

Other disadvantages of spontaneously gastric cancer models developed with chemical carcinogens, the presence of Helicobacter or transgenic technologies including a longer tumor growth period (approximately 10-12 months) and the absence of peritoneal spread. infected 144 C57BL/6 mice with the bacterium H. pylori and MNU. MNU with H. pylori infection significantly enhanced the risk of stomach neoplasia and adenocarcinoma. However, none of the patients showed signs of distant metastases. As a result, investigators frequently employ implantation to generate prototypes of abdominal metastatic of stomach cancer. This review will focus on the present level of technologies and the challenges associated with developing simulations of cancer of the stomach and peritoneal metastasis. These problems include the selection of model animals and their provenance. These difficulties include the choice of model animals the origin of xenograft tumors, transplantation techniques and strategies, and dynamic tumor progression monitoring **[24]**.

3. Phytosomes in treating cancer: advancement, challenges, and future outlook

The phytosomal medication distribution strategy and its impact on diverse disease circumstances should be thoroughly characterized, optimized, and statistically and subjectively evaluated. Despite the fact that the subject has been thoroughly explored, the study's focus should be broadened to include the challenges,

stability, and pharmacological superiority of such pharmacological administration systems. Solvent evaporation is a traditional technique for producing phyto-phospholipid complexes. However, the process requires a large number of unit operations, each of which takes time. The drying procedure, which has not been modified in the research, has a significant impact on product quality, including particle size, appearance, and hygroscopicity. Supercritical fluid technique enables fine control of particle size and distribution at degrees below freezing, surpassing the constraints of traditional approaches. There is little proof that phospholipid complexes of pharmaceutical drugs improve pharmacokinetic properties, either in vivo or in vitro. The focus has been on assessing the pharmacokinetic properties of phyto-phospholipid complexes, rather than the therapeutic aspects of the formulations themselves. More research is needed to link increased bioavailability to improved clinical effectiveness **[25]**.

The second challenge is the synthesis of phytosomes on a large scale. Nonetheless, the product's attributes should be maintained after scaling up. This has to do with how practical laboratory techniques are in an industrial setting. Commercial manufacturing of pH-sensitive phytosomes has been hard due to their low physicochemical stability, despite their simple formulation procedure. A lot of time passes between product creation and effective commercialization. Despite all of the benefits, there aren't many phytosomal products available on the market. Verifying safety following the creation of an effective formulation is a significant barrier to the commercialization of phytosomes. However, a number of factors, including metabolism, excretion, bioaccumulation, and biocompatibility, should be assessed before to marketing. Additionally, pharmacokinetic and pharmacodynamic properties in humans and animals should be assessed following the development of a phyto-some to show their superiority over pure phyto-constituents **[26]**.

4. Clinical challenges in prostate cancer management:

Another factor contributing to the uncertainty is the absence of a causal understanding of the relationship between the activity of tumor cells at the metastatic niche and the attributes of the metastatic niche as seen. Filling up these information gaps may help us understand organotropism and the course of metastatic illness. CTCs provide challenges due to their short lifespan and significant variability, but they may also provide valuable insights for therapeutic interventions. In PCa-BM, CTCs present potential and challenges for both basic investigators and physicians.

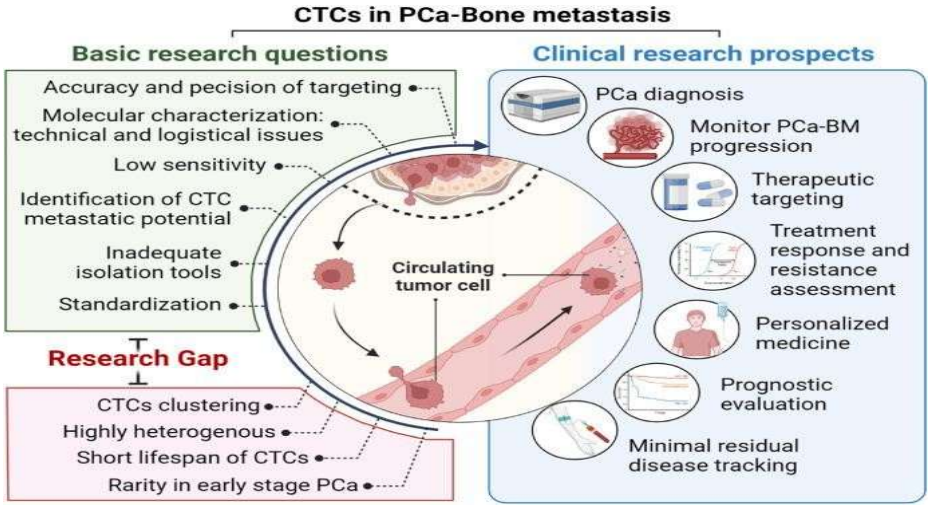

Figure: 2 The challenges and prospects of CTCs in PCa-BM.

CTCs have inherent issues such as diversity, rarity, and short duration in the system of circulation, which can be solved through a mixture of medical and clinical research. Fundamental research is needed to improve the methodologies and equipment used for identifying and assessing CTCs, while durable clinical consultations and experimentation are needed for evaluating the efficacy of CTC-based approaches in multiple aspects of Pica and cartilage eventually PCa-BM administration, from initial detection too little to no residual disease monitoring. The study of the primary tumor's surrounds (such as extravasation) and the movement of CTCs in the blood and systemic circulatory systems forms the basis of our present knowledge of how cancerous cells, specifically CTCs, respond to different biochemical and biomechanical stimuli. Future research that includes not only the mechanical motion While the microenvironment but also the chemical composition of the transformed into minerals and marrow tissues will aid in clarifying the role of both Molecular Signaling and biomechanical motions are factors in the progression of metastatic PCa to bone tissues, especially when patients' aging and the corresponding bone-cellular and microenvironmental changes are taken into consideration. Furthermore, understanding the specific features of CTCs in individuals, as well as conducting microscopic studies of PCa organotropism, may lead to the development of personalized treatments **[27]**.

5. Current Situation and Challenges of Polyhydroxyalkanoates-Derive Nanocarriers for Cancer Therapy:

Nowadays, the main and side chains of commercialized PHA have exceptionally stable ester bonds. Although this stability helps to maintain the polymer's integrity, it makes it difficult to chemically graft or modify the surface of PHA nanoparticles in

order to achieve targeted drug delivery or improve therapeutic efficacy. Surface modification is often necessary to improve targeting, circulation time, and interaction with cancer cells. This suggests that more diverse and efficient targeted therapies may be challenging to deploy using current PHA nanoparticles. The aforementioned difficulties may be addressed by developing new PHAs with more reactive side chains, such as hydroxyl or amino groups. As an alternative, PHA can break down into oligomers, and reactive functional groups can be added to PHA chains through introducing functional monomers or copolymers during chemical polymerization ensuing chemical changes. Furthermore, surface alterations brought about by PhaP or PhaC have been shown to be successful and provide workable methods for improving PHA-NC functionality. There are few data on PHA-NC delivery routes because the majority of PHA-NC research in the treatment of cancer concentrates on in vitro studies and chemotherapeutic pill formulation optimization. The only delivery method known is intravenously administration; exhalation, subcutaneous, orally, and intramuscular injection have yet to be used or verified. Nonetheless, oral administration represents one of among the most patient-friendly pharmaceutical delivery methods, with a reputation for ease of application and high compliance among patients. Anticancer PHA-NCs have to be customized for oral administration, implementing into consideration the power source drugs' and tiny carriers' equilibrium in the small intestine, intestinal absorption capacity, targeting specificity, and effects on organs such as the liver, kidneys, the gastrointestinal tract, and the gastrointestinal tract. Furthermore, taking advantage of hydrogels' excellent injectability and biocompatibility, mixing PHA nanoparticles **[28]**.

6. Cancer detection problem:

It is discovered that the use of CNN architectures for medical image analysis has advanced significantly. Modern CNN models do not perform as well on medical images as they do on natural ones. This is due to the extremely complicated structure of medical images and the considerably smaller grayscale differences between the many tissue classes of the human body. Additionally, it has been shown that early cancer detection has significantly improved **[29]**.

7. Bacteriotherapy: challenges and limitations

Chemotherapy and radiation therapy are well acknowledged as the pillars of treatment for cancer, however their efficacy differs across cancer patients, as illustrated in **Figure 3**. The low cytotoxicity of bacteria at therapeutic doses is a major hurdle to their use as anticancer medicines. Systemic

infections caused by bacteria can pose a significant threat to living organisms. Furthermore, 15–45% of test mice may die even if the genes generating the toxin and virulence factors are deleted. One major problem with bacterial-based cancer treatment is incomplete tumor lysis, in which bacteria are unable to eliminate malignant tissue. To get the desired results, combination treatments like chemotherapy and bacteriotherapy are frequently needed. The primary challenge is accurately delivering and reaching live bacteria in tumors, which frequently calls for intra-tumor injections in bacterial therapy **[30]**. One of the main concerns with bacterial therapy is the possibility of DNA changes. Consider a scenario in which a mutation or nucleic acid alteration occurs in the host body's bacterial genetic composition. The bacteria can lose its original anticancer action as a result of the conversion in that case. A number of problems could be indicated by this, such as untreated malignancies **[31]**.

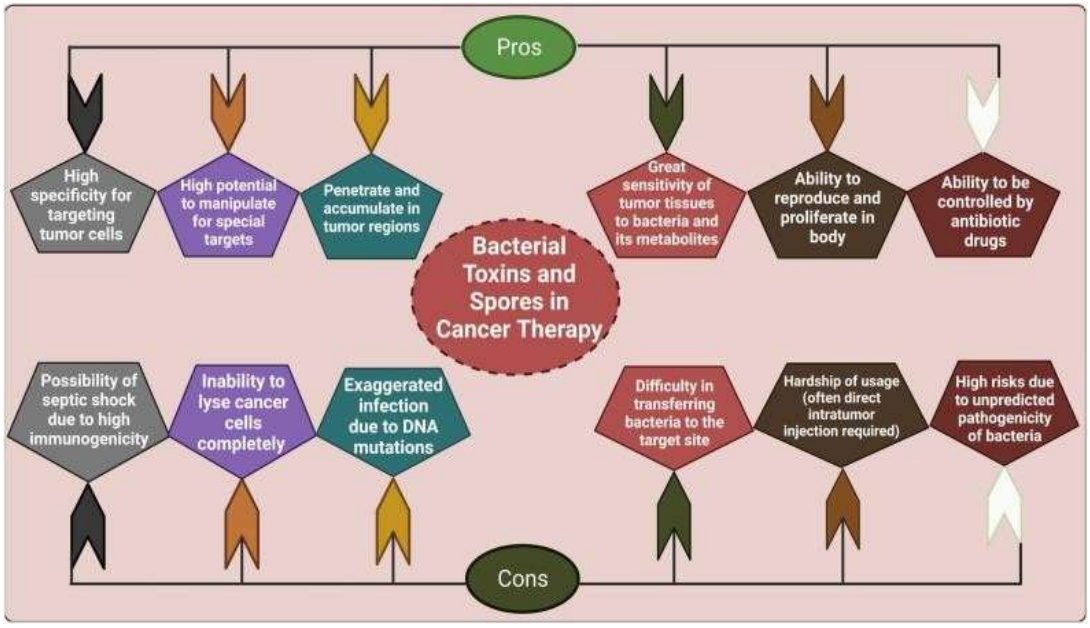

Figure: 3 Pros and Cons of Bacteriotherapy

8. Morbidity and mortality among long-term survivors of pediatric cancer-

The most common late effects of juvenile cancer include early mortality, development and advancement, organ and system operation, secondary malignancies, and psychosocial difficulties. This affects the patient's physical, mental, and emotional well- being as well as their ability to fulfill their responsibilities at home, at work, school, and in the community, which in turn affects their health-related quality of life. According to estimates, 20% to 80% of CCSs suffer from serious or life-threatening consequences, and 60% to 90% of them acquire one or more chronic health issues.

Traditionally, the late effects reported in CCSs are divided into:

a) **Early mortality:** Children who have survived cancer are more likely to die than the overall population, primarily due to the fact that they are more likely to get second cancers, experience late-effect problems, and age too soon.
b) **Physical issues:** Excellent literature reviews have examined a variety of issues, including neurologic and neurocognitive issues, endocrine-metabolic issues, cardiovascular issues, gastrointestinal issues, respiratory issues, musculoskeletal issues, renal issues, reproductive issues, sensory issues, and second tumors. Because of the article's restricted length, we will not go into great detail on these burdens; instead, we give the reader the relevant references.
c) **Psychosocial issues:** These issues are more common in survivors who have a higher burden of organic disease and are commonly coupled. As a result, even if 80% to 90% of CCSs say they are happy, they are more likely than their siblings and the overall population to experience mental health and psychiatric issues. Emotional anguish, anxiety, sadness, suicidal thoughts, somatization, and post-traumatic stress disorder are among the issues mentioned. Others demonstrate resilience and positive psychological attributes associated with post-traumatic growth. In social situations, individuals may face difficulties in their interactions with their peers, poor performance in school, and less frequent admission to higher learning, which can lead to professional problems and unemployment. This may have been caused by neurocognitive deficiencies, other severe long-term effects, or the malignancy itself reduced financial resources, less independence from the family, problems with their spouses or partners, fewer marriages, and fewer children. Researchers and physicians face significant challenges in estimating the exact degree of morbidity and death in CCSs due to a multitude of linked health concerns. Considerable approaches. the diversity in the population that is under study (age, number of participants, representation, type of cancer, hospital-based vs. population-centered, duration of follow-up), study design (qualitative, case-control, cohorts (a total clinical

trial, systematic review), data source (those with populations registers, patient self-reported information clinical assessments), study outcomes (mortality, adverse event), and study design has resulted in several decades of evidence **[32]**.

9. Cardio-oncology:

The therapy of cardiovascular damage linked to cancer treatments is the focus of the quickly expanding discipline of cardio-oncology **[33]**. Cardiovascular disorders in cancer patients are largely caused by the negative cardiovascular effects of cancer treatments. Several studies have demonstrated that anthracyclines, ErbB2/HER2 inhibitors, androgen deprivation therapy, immune checkpoint inhibitors, epidermal growth factor receptor inhibitors, vascular endothelial growth factor (VEGF) signalling pathway inhibitors, and radiation can all cause cardiotoxicity. Research has shown that arrhythmias, such as atrial fibrillation and ventricular tachyarrhythmias, can be significant side effects and even predictors of cancer therapy-related cardiotoxicity, despite the fact that heart failure and ischemic heart disease are well-known cardiotoxic effects of cancer treatments. Furthermore, because of its nonspecific clinical presentation, pulmonary hypertension could be another unrecognized cardiotoxic side effect of cancer therapy **[34]**. On the other hand, compared to the general population, persons with CVD are more likely to get cancer. Healthcare professionals and the healthcare system face both tremendous potential and challenges as a result of these two illnesses coexisting and interacting **[35]**.

10. Ultrasound-targeted nanobubbles combined with cancer immunotherapy:

1. Immunological and tumor complexity –

One of the most significant biological challenges is the complexity of the tumor's tumor microenvironment and the immune system's response. The presence of cells that suppress immunity and hormones in the tumor environment is just one of several factors that can influence the immune system's complicated response to cancer. These elements may reduce UTN's efficacy when paired with cancer immunotherapy. Furthermore, tumors can vary from one patient to another and even within a single tumor. Resistance and differing reactions to treatment may result from this variability. Therefore, tailoring UTN-based therapy is extremely difficult due to tumor heterogeneity and patient responses **[36]**.

2. Precision delivery and stability of

nanobubbles-

The key technological issues with UTN are delivery and stability. For nanobubbles in to be effective, they must be administered to the tumor site continuously and accurately. The number of particles, stability, and surface properties of the nanobubbles, as well as a high-frequency parameters used to activate them, must all be properly controlled for this targeted **[37]**. Another important factor is stability, because in order to ensure efficient delivery and registration at the location of interest, the internal strength of nanobubbles must be kept during circulation **[38]**. Additionally, two crucial factors for clinical translation are the consistency of the therapeutic benefits of nanobubbles and the scalability of their production. These issues are being addressed by developments in ultrasonic engineering and nanotechnology **[36]**.

11. The challenges and potential directions of liquid biopsy in the future-

To support therapeutic decision-making, investigate the clinical use of tumor cells and ctDNA as predictor and diagnostic diagnostics for HCC. In modern clinical practice, however, liquid biopsy biomarkers face additional challenges.

1. Given the scarcity of liquid biopsy biomarkers in blood, a major issue is the lack of uniformity in techniques for sample preservation, enrichment, and detection. Normalization processes are crucial for developing trustworthy, widely recognized biomarkers. Furthermore, little is known about the molecular mechanisms by which liquid biopsy biomarkers are secreted and enter the bloodstream. This ignorance could make it more difficult to interpret changes during dynamic monitoring and to use them in therapeutic settings later on.
2. Another challenge in CTC research is replicating a favorable environment that supports CTC survival and growth. Fortunately, developing models that closely mirror the in vivo environment, such as patient-derived xenografts (PDX) and patient-derived organoids (PDO), offer new avenues for studying CTCs. There are various therapeutic applications since CTC-derived PDX and PDO models allow unique CTCs to grow in vitro and facilitate drug sensitivity testing without the need for a biopsy. Although these models have been extensively investigated in other cancer types, they are now

rarely used in liver cancer research. Using CTC-derived PDX and PDO models presents a significant opportunity to increase the clinical usage of liquid biopsy in liver cancer **[39]**.

12. Cancer-associated fibroblasts in pancreatic ductal adenocarcinoma therapy –

The inability to limit CAFs' tumor-promoting actions while maintaining their tumor- suppressive capabilities makes targeting them in PDAC a significant clinical problem. The creation of intelligent agents filled with nanoprobes is made possible by nanotechnology, which presents a hopeful remedy. These substances may be able to minimize adverse effects by selectively controlling the activation of tumor-restraining CAFs and the suppression of tumor-promoting CAFs within the particular tumor microenvironment. Furthermore, a particular marker is the primary focus of the existing CAFs-based target treatment approaches, which severely restricts their clinical applicability. Due to their capacity to change states, focusing on a single CAF phenotype may ignore other important subtypes. Therefore, single-marker therapy may not be effective enough. The wide range of functional functions that CAFs play in PDAC poses a major challenge, even though methods based on CAF function have greater potential. Nevertheless, PDAC organoid culture systems obtained from patients have demonstrated significant potential in forecasting individual treatment responses, possibly providing a way around these restrictions. The development of more individualized and successful treatments for PDAC patients is anticipated to be enhanced by this strategy **[40]**.

13. Challenges according resoures in breast cancer

Breast cancer can demand expensive medical resources. As a result, the patients' available treatment plan may differ depending on the nation, usually according to socioeconomic development **[41]**. High-, moderate-, and low-resource countries are the three categories into which the Asian nations can be divided.

1. Low-resource nations (such as Nepal, Pakistan, and Iraq) have been shown to have poor prognostic value and very limited resources for cancer diagnosis and treatment **[42, 43]**. Generally speaking, the primary issues in low-resource nations are the lack of necessary diagnostic and treatment facilities, the community's low awareness of breast cancer, and an insufficient or subpar healthcare system. Low-resource nations like Nepal have a disjointed health care infrastructure and very few radiation devices (like mammograms). at Nepal, almost

80.0% of cancer patients were discovered to be at the metastatic stage, at which point palliative care was the sole course of action **[42]**.

2. Moderately resourced nations like Malaysia, Turkey, and Iran have disjointed healthcare systems, usually in terms of breast cancer priority, data registry quality, interdisciplinary coordination, and health care management standardization **[44]**. In countries with moderate resources, other issues include expensive medical procedures and medications that are not covered by insurance. Metastatic patients may have limited options and can only choose cost-effective treatments (for example, 40.0 and 15.0% of patients with breast cancer, respectively, choose second-line and third-line treatments) **[41]**.
3. High-resource nations like Singapore and Japan are known to have low mortality rates and a high number of incidences (e.g., Singapore: incidence ASR of 77.9/100,000 and mortality ASR of 17.8/100,000; Japan: incidence ASR of 76.3/100,000 and death ASR of 9.9/100,000). A well-established healthcare system and breast cancer protocol are strongly linked to low mortality ASR, but major urbanization and rising socioeconomic status are strongly linked to high incidence ASR in these nations. In contrast, 80.0% of Japanese patients with breast cancer received second-line treatment, significantly increasing their chances of survival compared to those in moderate-resource nations **[45]**.

14. Biobanks in chronic disease management:

1. **Data security and privacy protection:**

Maintaining privacy and data security is essential to biobank management. Data in biobanks must be protected using cutting-edge encryption technology. To avoid illegal access and data breaches, this involves encrypting data that is transmitted and stored. Strict access control procedures are also essential for ensuring data security. This implies that access to pertinent data should be rigorously restricted based on the demands of authorized researchers and medical practitioners. Data in biobanks frequently undergoes anonymization or de-identification to further safeguard patient privacy. This entails eliminating any data that can directly identify a person, including names, residences, and social security numbers, preserving their

privacy while enabling the data to be utilized for significant medical research. Additionally, biobank operations must adhere to pertinent legal and ethical standards. This entails following the law's requirements for the protection of personal data and making sure that data collection and use are lawful. Furthermore, it is critical from an ethical standpoint to ensure that patients provided complete detailed permission for the use of their data. Despite various steps taken to protect data in biobanks that are the evolution of cyberattack strategies and technical breakthroughs continue to offer substantial challenges to data safety and confidentiality. Future research should focus on better and more reliable data protection **[46-48]**.

2. Ethical issues and sample collection:

Numerous intricate ethical concerns are raised by the creation and management of biobanks, especially during the sample collection phase. These concerns include ethical guidelines for sample management and usage in addition to participant rights and welfare. Obtaining participants' informed consent is a fundamental ethical principle in the process of collecting samples. This implies that after thoroughly understanding the goals, procedures, possible dangers, and advantages of the research, participants must actively choose whether or not to participate. For vulnerable groups like children, those with cognitive disabilities, or economically challenged groups, obtaining informed permission is especially crucial and complicated. In these situations, researchers must take further precautions to guarantee that participants comprehend and willingly participate. Rights of ownership and use of There are important ethical concerns with samples as well. Researchers must respect participants' privacy and wishes when using their biological samples because they usually have some sort of rights over them. The informed consent approach must also address concerns regarding sample data handling and if samples can be used in unnamed future research endeavors. The equitable distribution of the potential financial rewards of biobank-based research is a critical ethical concern. This includes ensuring that participants or their communities benefit appropriately from the use of their samples, such as through improved healthcare or financial remuneration. As biobanks develop in size and reach, the complexity of ethical considerations will increase. Future research must focus on finding a balance between protecting individual rights and furthering scientific research. Given the

increase in international collaborative research, more cross-cultural and transnational ethical norms must be developed and harmonized **[49]**.

3. Technical standards and data interoperability-

For biomedical research to progress, samples and data under biobank oversight must be preserved. Initiatives like the Minimum Information About Biobank Data exchange (MIABIS) seek to standardize biobank nomenclature and promote data exchange standards. MIABIS supports data exchange and sample sharing among research groups by offering an orderly mechanism for describing biobanks, sample collections, and related research. By establishing a uniform language for biobank data sharing, MIABIS and its core terminology have played a crucial role in enabling research organizations to share biobank samples and data more effectively.

MIABIS has expanded its architecture to include specific features for characterizing samples and donors at the person level in response to the demand for comprehensive biobank searches. This addition includes a "event" component that describes qualities that are only loosely related to samples or donors, which is necessary for contextualizing biospecimen collections. These developments in biobanking data formats illustrate the transition to increasingly sophisticated, interoperable datasets by allowing for accurate and complete inquiries into biobank holdings **[50]**.

Human biospecimens are treated with respect and in accordance with the law since biobanks strictly follow ethical and legal criteria. Donor informed permission, privacy protection, and data secrecy are all essential for ethical compliance. Legal duties, on the other hand, include complying with national and international regulations governing biobanking activities, such as data protection and human research protocols. To maintain the trust of sample donors and promote research that may result in the creation of novel medications, it is critical to ensure the right quality of samples and data, as well as ethical and legal compliance.

The development of clear and efficient access protocols considerably increases the effectiveness of biobanks. To encourage collaboration and maximize the impact of biospecimens on medical discoveries, researchers must be given clear instructions on how to access biobank samples and data. The stated biobanking requirements emphasize the importance of clear and effective access mechanisms while striving to give

researchers with high-quality samples appropriate for their intended use.

Finally, biobank operations require strict adherence to legal and ethical frameworks as well as the execution of technical standards such as MIABIS. These processes promote scientific openness and collaboration while also safeguarding the integrity and quality of biobank materials. As biobanking techniques evolve, stakeholders' continuing involvement and the adoption of flexible, interoperable data formats will be critical to overcoming current challenges and capitalizing on the opportunities available in this ever-changing area **[51]**.

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CONCLUSION: -

Cancer remains a significant worldwide health challenge that requires continuous investigation, diagnosis, and treatment. Despite progress, cancer's complexity, heterogeneity, and adaptive nature continue to pose significant obstacles. To overcome these challenges, future directions should prioritize interdisciplinary research collaborations, precision medicine, immunotherapy, early detection, and artificial intelligence-driven innovations. Effective cancer management requires improved access to care, reduced disparities, enhanced patient education, integrated healthcare systems, and policy reforms. Conquering cancer demands a multifaceted approach, combining scientific advancements, policy changes, and community engagement. By fostering global cooperation, leveraging technology, and addressing socioeconomic determinants, we can enhance patient outcomes, reduce mortality rates, develop personalized treatments, and improve prevention and early detection. Ultimately, collective action, unwavering commitment, and innovative thinking will transform the fight against cancer into a triumph of human resilience and scientific progress, creating a brighter future for cancer patients, families, and communities worldwide.

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