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CANCER VACCINE THERAPY": A NOVEL APPROACH FOR CANCER PREVENTION AND TREATMENT

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ABSTRACT

Cancer vaccine therapy is a strategy that utilizes the body's immune system to both prevent and treat cancer. Preventive vaccines work by activating the immune system to identify and destroy cancer-causing infections, such as HPV, which is linked to cervical cancer. Therapeutic vaccines, however, focus on targeting and attacking existing cancer cells, helping the immune system recognize and combat tumors. This promising approach has the potential to complement conventional treatments, lower the risk of cancer recurrence, and improve the overall prognosis for patients. Cancer vaccines are an innovative and evolving field, offering new possibilities for both prevention and treatment, with the potential to work alongside traditional therapies like surgery, chemotherapy, and radiation. this review is based on introduction to some vaccines that are used to eliminate risk of cancer or to treat cancer

KEYWORDS- *tumor cells, foreign invader, cancer, immunotherapy, humanpapilloma virus, hepatitis B vaccine, BCG, Sipuleucel-T*

1. INTRODUCTION

One of the main causes of death in Western nations is cancer. The most common types are lung, breast, prostate, and colorectal cancer. However, as the population changes and new treatments emerge, cases of thyroid, liver, and pancreatic cancer are expected to rise significantly. Since the 1950s, the concept of a cancer vaccine has gone from a wild idea to a real possibility. Over time, it has been receiving the interest of many cancer researchers because of its growing potential. (4) Vaccines can significantly improve patient survival when used to prevent diseases, like traditional vaccines for infections. While preventing cancer before it starts (primary prevention) is still a long-term goal, vaccines for early detection (secondary prevention) and stopping cancer from coming back (tertiary prevention) are already being used in clinics with promising results. Over 100 years ago, Paul Ehrlich first suggested the idea of using the immune system to treat cancer by creating a vaccine with "weakened tumor cells." Although progress was slow for many years, things have changed a lot in the last decade. Following multiple unsuccessful attempts, cancer immunotherapy, particularly cancer vaccines got a big boost in 2010 with the approval of Provenge, a treatment for prostate cancer. (6) Anti-cancer vaccines can be grouped into two main types: therapeutic and preventive. Therapeutic vaccines help treat people who already have cancer, while preventive vaccines (like the HPV vaccine) stop cancer from developing. (5)

- **What Is Vaccine?**

Vaccines train your immune system to defend your body against foreign invaders or abnormal cells that pose a threat. there are to main types of cancer vaccines preventive and therapeutic vaccines (19)

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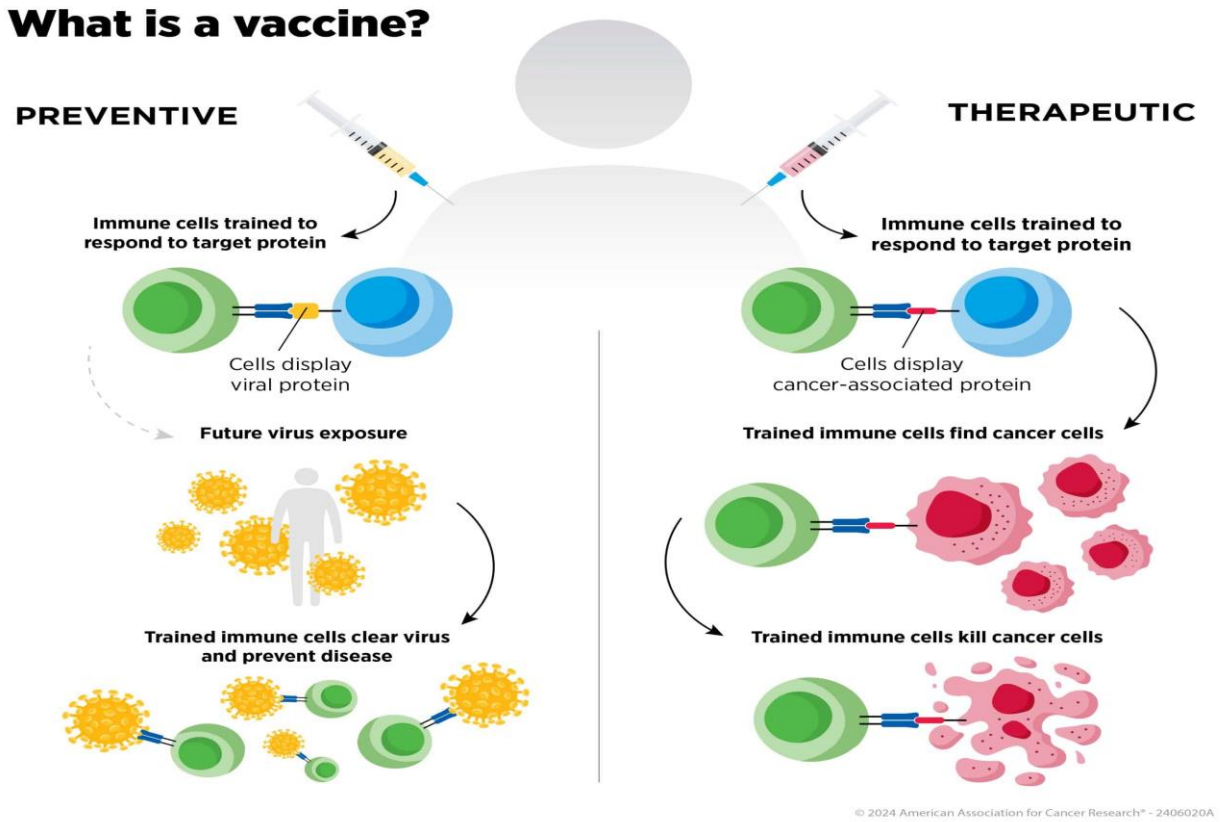

2. PREVENTIVE CANCER VACCINES

Cancer prevention focuses on reducing the number of people who get cancer and die from it. It tries to address cancer at every stage, from healthy cells to when cancer spreads in the body. Prevention is usually divided into three types: primary, secondary, and tertiary prevention (1)

Cancer Prevention	*Aim*	*Target*	*Immunological Example*
Primary	Avoiding Or Getting Rid of Things That Can Increase the Risk of Cancer.	Healthy Individual	Anti-HBV vaccine Anti-HP vaccine
Secondary	Detecting and Treating Disease Early	Peoples who have cancer but show no symptoms yet.	Anti-Her2 and MUC1 vaccine used in preneoplastic lesions
Tertiary	Preventing Relapse And metastatic	Peoples who have survived cancer but still have hidden tumours	Adjuvant monoclonal antibodies. Adjuvant Therapeutic vaccine

3. APPROVED PREVENTIVE CANCER VACCINES

A. Anti - Hepatits B Vaccines

Primary liver cancer, known as hepatocellular carcinoma (HCC), ranks among the most prevalent cancers globally. According to estimates, it comes as the third most common cause of cancer related death in men and the seventh in women. Approximately 70-80% of HCC cases are linked to hepatitis B virus (HBV) as a causative factor. (13)

Early cancer prevention vaccines focused on targeting viruses linked to cancer risk. One of the first successful vaccines in this field was designed to protect against Hepatitis B virus (HBV), a major contributor to chronic liver disease and a known risk factor for the liver cancer known as hepatocellular carcinoma (HCC). (2,3) For many years, the main approach to preventing cancer has focused on changing behaviors to avoid cancer-causing factors in the environment, like smoking, diet, sun exposure, and other

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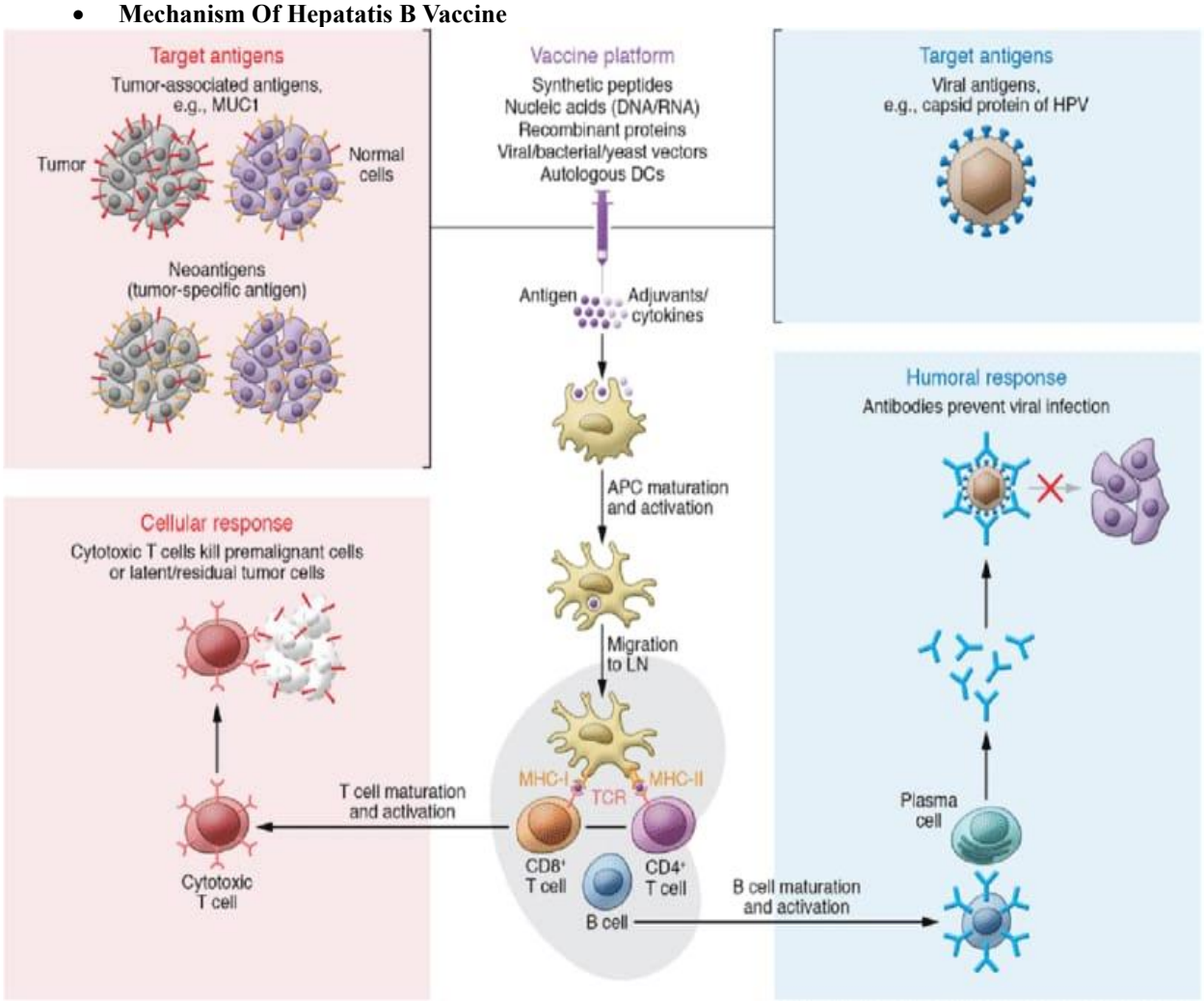
lifestyle choices. Public health efforts have helped lower people's exposure to these known cancer risks, but behavior-based prevention has its limitations, and treatments are still needed once cancer develops. Vaccines' remarkable effectiveness in preventing infectious diseases has inspired fresh ideas about using preventive vaccines to protect against certain types of cancer as well. The vaccination against Hepatitis B (HBV) has been available since the early 1980s, and the World Health Organization (WHO) recommends giving it to infants soon after birth. (9) Receiving three doses provides strong, long-lasting protection against long-term HBV infection. This vaccine was the first proven to lower the risk of liver cancer (hepatocellular carcinoma, or HCC) in people who received it (9) Taiwan was among the first countries to launch a national HBV vaccination program. They started by vaccinating infants born to mothers with HBV, and in 1984 expanded it to include all infants. Studies later showed that Taiwanese children who received the vaccine had much lower rates of liver cancer for up to 20 years after the program began (7,8)

- **Mechanism Of Hepatatis B Vaccine**



B. Human papilloma Virus Vaccine

Human papillomavirus (HPV) is a sexually transmitted virus linked to several types of cancer, including cervical, throat, anal, penile, and vulvar or vaginal cancers. (10) HPV infection causes several different cancers. Cervical cancer is the third most frequent cancer among women worldwide, primarily caused by HPV infection. Cervical cancer accounts for about 500,000 new cases and 250,000 deaths annually. (11) HPV vaccines have been available since 2006 and are recommended as preventive vaccines for both males and females starting at age 11, ideally before they become sexually active. This is due to the fact that vaccination is most effective prior to viral exposure. Three varieties of HPV vaccinations are available.

1. Cervarix - protects against HPV types 16 and 18.
2. Gardasil-4 - protects against HPV 6, 11, 16, and 18.
3. Gardasil-9 - is effective against HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58. (12).

These vaccines are safe and very effective, especially in young people, where they create a strong, long-lasting immune response that provides protection well into adulthood. Clinical trials have shown that HPV vaccines offer high protection against HPV-related diseases. (12)

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4. THERAPEUTIC CANCER VACCINES

Immunotherapy is an effective treatment for cancer and can be used alongside surgery, chemotherapy, and radiation therapy. Therapeutic cancer vaccines, especially personalised ones, are a well-advanced field of immunotherapy. Unlike preventive vaccines, which are given to healthy people to prevent diseases like hepatitis B and human papillomavirus, therapeutic cancer vaccines work by using specific tumor antigens to boost the immune system of cancer patients, helping them to fight their cancer. (14)

- **General mechanism of Therapeutic Cancer Vaccines**

Therapeutic cancer vaccines aim to stimulate the immune system to kill tumour cells, target specific antigens, minimise adverse effects, and prevent autoimmune responses. (21) These vaccines must also establish a robust immune memory to counter future cancer cells, which is crucial for long-term treatment success (22) Cancer relapses, rather than primary tumors, are largely responsible for the high mortality rate in cancer (23)

Cancer vaccines enhance the body's immune system, both cellular and humoral, to combat cancer. These vaccinations usually increase the generation of CD8+ T-cells that are specific to cancer and are able to identify and eliminate cancer cells. (24) Cytotoxic T lymphocytes (CTLs) detect cancer antigens by binding to their T-cell receptor (TCR). Through TCR signaling pathways, such as the release of perforin or serine protease, or by upregulating molecules like CD95L or TRAIL, CTLs initiate cancer cell death. For effective action, CTLs are activated by tumor dendritic cells (DCs), specifically CD103+ migrating DCs, which are antigen-presenting cells (APCs) (29). These DCs prepare CTLs using three mechanisms: presenting cancer antigens on MHC-I, using co-stimulatory molecules (CD80/86 and CD28/152), and releasing cytokines like IL-12 and TNF-α. Both CTLs and CD4+ Th cells gain specific characteristics upon activation that enhance CTL effectiveness (30). Additionally, CD4+ Th cells are activated similarly to CD8+ T-cells, but the tumor antigen is presented on MHC-II instead of MHC-I. (25) CTLs use cytotoxic methods to release cytokines and induce cell death. Studies have shown that CTL production of IFN-γ and TNF-α is linked to reduced tumor growth and increased patient survival. Adopting a Th1 phenotype, characterised by the secretion of IFN-γ, TNF-α, and IL-2, leads to improved patient survival. Some studies suggest that combining the Th1 response with Th17 (characterized by IL-17 production) may be even more beneficial [70]. Since each T-cell has a unique TCR for a single antigen, responses that generate a broad range of antitumor T-cells are more effective. (25) The optimal immune response to vaccination may differ by cancer type. Cancer vaccines can also use antibody-mediated cytotoxicity to control cancer. Cancer cells with antibodies attached can be targeted for destruction through antibody-mediated cytotoxicity or phagocytosis. (26) In humoral immunotherapy, patients develop anticancer antibodies, which are recognised by innate immune cells such as natural killer cells, macrophages, and neutrophils, leading to cell death or phagocytosis. (27) Additionally, the activation of other innate immunity systems, such as T-cells, can enhance the adaptive immune response targeted by cancer vaccines. For example, innate lymphoid cells (ILCs) like NK cells or invariant NK T-cells (iNKT) support CTLs in controlling cancer cells. Cancer cells that inhibit T-cell identification by downregulating MHC-I or overstimulating NK cell receptors (e.g., NKG2D, 4-1BB) can nevertheless be destroyed by NK cells. (28) When iNKT cells activate, they release Th1 or Th2 cytokines and increase CD40L expression. iNKT cells also enhance adaptive immune responses by boosting DC activity, which contributes to improved outcomes in cancer treatment.

5. APPROVED THERAPEUTIC CANCER VACCINES

A. Bacillus Calmette- Guerin (BCG) vaccine

Bovis Mycobacterium Following 230 trials on the original disease-causing germ, M. bovis, scientists developed a type of bacteria known as Bacillus Calmette-Guérin (BCG). Over thirteen years, Albert Calmette and Camille Guérin worked on changing this germ until it became safe. In 1921, they showed that this new bacterium did not make animals sick and could protect them from tuberculosis. This discovery led to the large-scale production of the BCG vaccine, which is still the only vaccine available to prevent tuberculosis in people today. BCG may be a novel treatment option for certain cancer patients, according to studies being done at the same time on the use of other bacteria, such as Streptococcus pyogenes and Serratia marcescens, to treat cancer. (15) In order to stop the disease from progressing and recurring, BCG has been the standard treatment for individuals with high-risk non-muscle-invasive bladder cancer (NMIBCIn order to stimulate the immune system to fight cancer cells, the vaccine must be injected straight into the bladder. (16) BCG has been shown to be more effective than chemotherapy, especially for aggressive cancers and when used with reinduction and maintenance therapy. (17) In addition to avoiding infections, BCG has a 70–75% success rate for carcinoma-in-situ and a 50–60% success rate against tiny tumours. Generally, the positive effects of BCG last a long time, with about 70% of patients remaining in remission after five years. However, it's less clear how well BCG can help with advanced-stage cancers, as there haven't been enough strong studies to determine this. (18)

B. Sipuleucel -T(provengeu)

The core concept of immunotherapy is to stimulate the body's immune system to combat tumors. Sipuleucel-T provides this by the use of dendritic cells, Dendritic cells are the most effective antigen-presenting cells in the human body and play a crucial role in activating B- and T-lymphocytes, which help regulate the immune response. It was the first immunotherapy product to be approved by the US FDA. It is specifically approved for men with asymptomatic or mildly symptomatic metastatic castration-resistant prostate cancer, as it has been shown to improve survival rates.

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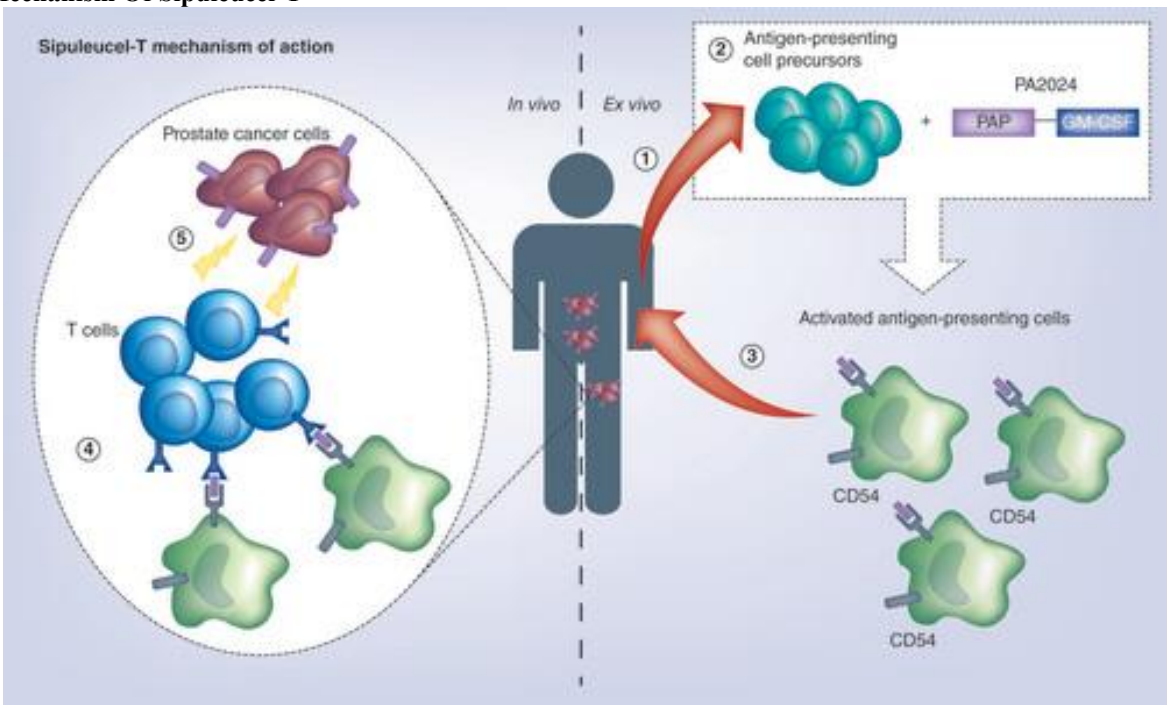
- **Mechanism Of Sipuleucel-T**



6. CURRENT THERAPIES AS CANCER VACCINES (20)

Name Of Vaccine\ Antigen	Type of Vaccine	Targeted Site	Combination\ Route of Administration
Sipuleucel-T	Dendritic cell vaccine	Metastases Castrate resistant cancer that is slient or barely symptomatic	Intramuscularly
Gardasil	Human Papilloma virus	Women's Vulvar,vaginal and cervical cancer	Given Intramuscularly in the grater posterolateral portion of thigh
Cervarix	Human Papilloma virus	Types 16 &18 of carcinogenic human papilloma virus	3 Injection of 0.5ml each into the muscle
BCG	-	Bladder cancer in its superficial stages,colon cancer, lungs cancer & melonoma	Intravenous, subcutaneous, directly into tumours, intranasally,pharyngeally
Onyvax	Antiidio type Vaccine	Colorectal adenocarcinoma	Either intramuscularlly with the alum adjuvant or endemic with BCG Vaccine
Cancer Vax	Autologous vaccine	Surgery for the management patient with stage 3 melanoma	Along with BCG Vaccine, another vaccine is administered.
Lenalidomide	-	Multiple myeloma	Oral

7. CONCLUSION

Cancer vaccine therapy shows promising potential for both prevention and treatment of cancer. As a preventive measure, vaccines such as the HPV and hepatitis B vaccines have been effective in reducing risks of cancers related to these viruses, like cervical and liver cancers. Cancer vaccines work therapeutically by enhancing the immune system's capacity to identify and fight cancer cells.

Although some cancer vaccines, like sipuleucel-T for prostate cancer, have shown success, therapeutic vaccines face challenges. Cancer cells can evade immune detection, and immune responses may vary among individuals. However, advancements in personalized medicine, mRNA technology, and combination therapies with immune checkpoint inhibitors are paving the way for more effective cancer vaccines. In conclusion, while cancer vaccine therapy is not yet a universal solution, it represents a powerful tool in cancer prevention and a promising field for future cancer treatment options. Continued research is essential to optimize its efficacy and broaden its applicability across different types of cancer.

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