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A REVIEW ON CANCER VACCINES

VINODH JAGANTI*[1] , SUKIRTI DAS [2] AND T.SAI SAMPATH [1]

[1] Department of Pharmacology, National Institute of Pharmaceutical Education and Research, Guwahati, India.

[2] Department of Pharmacy, Gauhati Medical College, Guwahati, India.

VINODH JAGANTI

Department of Pharmacology, National Institute of Pharmaceutical Education and Research, Guwahati, India.

*Corresponding author

ABSTRACT

Discovery of a potential anticancer therapy is still a challenge to the scientists. Though many different kinds of therapies are developed none of them has lived up to the task to cure cancer completely. Cancer vaccines are found to be the latest discovery in the field of cancer. Although till date only one cancer vaccine is approved by FDA, there are number of vaccines undergoing preclinical & clinical trials which are promising to be an effective anticancer therapy. This article reviews some of the basic aspects of different types of cancer vaccines along with their drawbacks & future development.

KEYWORDS

Cancer vaccines, Antigen vaccines, Adjuvants, Dendritic cells & DNA vaccines.

INTRODUCTION

Cancer has become one of the most devastating diseases worldwide. Globally there are Currently 10 million new cases of cancer per annum (based on 2000 figures), but the WHO has predicted this figure to be 15 million per year by 2020 [1]. Although there are more than 100 different forms of cancer, more than 80 percent of cases involve just 14 types of cancers like Prostate,Liver,Breast,Lung,Stomach,Colon,Bladder,Skin,Ovary,Kidney,Brain,Leukemia, Pancreas &Testes [2].Despite great efforts to develop better treatments, more than 6 million people worldwide died from cancer in 1997. Currently there are several techniques that are being used to treat cancer like Angiogenesis Blockers, Bone Marrow Transplants, Chemo Therapy, Cryo Surgery, Gene Therapy, Laser Therapy, Photodynamic Therapy, Radio Therapy & Stem Cell Therapy [2].

Vaccines are medicines that boost the immune system's natural ability to protect the body against "foreign invaders," mainly infectious agents, which cause disease. From the time of the first documented vaccine against smallpox by Edward Jenner, developing an effective vaccine to prevent deadly disease caused by existing or newly emerging pathogens has been the goal of many microbiologists and immunologists. Penicillin (1928), measles vaccine (1953), polio vaccine (1954) and insulin (1920s) are just a few of the many medical discoveries made in the last century. Possibly the most exciting achievement of this century will be the discovery of a **Universal Cancer Vaccine**. Scientists are on the verge of developing such a vaccine that will save millions of lives annually when it's discovered. Cancer vaccines are medicines that belong to a class of substances known as Biological response modifiers. They work by stimulating or restoring the immune system's ability to fight infections and disease. The term cancer vaccine refers to a vaccine that prevents infections with cancer-causing viruses, treats existing cancer or prevents the development of cancer in certain high risk individuals. Some cancers, such as cervical cancer and some Liver cancers are caused by viruses, and traditional vaccines against those viruses, such as HPV vaccine and Hepatitis B vaccine, will prevent those cancers. Other cancers are to some extent caused by bacterial infections (e.g. Stomach cancer and Helicobacter pylori [3]) and traditional vaccines against cancer causing bacteria are used to treat them. Scientists have also been trying to develop vaccines against existing cancers. Some researchers believe that our healthy immune system [4] destroys the cancer cells that arise routinely; cancer forms when the immune system was unsuccessful to destroy them [5].

Types of Cancer Vaccines:

Broadly they are of two types

Preventive/Prophylactic vaccines - which prevent cancer from developing in healthy people.

Treatment/Therapeutic vaccines - which treat an existing cancer by strengthening the body's natural defences against the cancer [6].

There are two major categories that cancer vaccines fit into:

Specific Cancer Vaccines – As the name indicates they treat specific type of cancers. Different vaccines are needed to treat different types of cancers.

Universal Cancer Vaccines – They fight cancer cells regardless of cancer type.

Basic idea on which Cancer Vaccine works: The vaccine, which contains tumour cells or antigens, stimulates the patient's immune system, which produces special cells that kill cancer cells and

prevent relapses of the cancer. Unlike vaccines for other disease that prevent the occurrence of the disease, there isn't a vaccine in development that can prevent the onset of cancer. Cancer vaccines are used only as a treatment after the cancer has been found in a patient. Here is a list of different kinds of cancer vaccines being developed:

1. Antigen vaccines
2. Tumour cell vaccines
3. Anti-Idiotype antibody-based vaccines
4. Dendritic cell vaccines
5. DNA vaccines
6. Viral-vector based vaccines

1. Antigen Vaccines:

Antigen vaccines use tumour-specific antigens to stimulate the immune system. The antigens are usually proteins or pieces of proteins called peptides. By injecting these antigens into the cancerous area of the patient, the immune system will produce an increased amount of antibodies or cytotoxic T lymphocytes, also known as killer T cells, to attack cancer cells that carry that specific antigen. Antigen vaccines boost the immune system by using only one antigen (or a few), rather than whole tumour cells that contain many thousands of antigens. Antigens used in cancer vaccines should preferably be molecules that are different between normal cells and tumour cells ensuring that the vaccination which generates immune response will target for destruction antigen-bearing tumour cells and not normal cells [7]. The vaccines against pathogens satisfies this requirement more easily because their antigens are all foreign to the host and thus immunity generated against them, in most instances, does not cross-react with normal host tissues. In cancer, most antigens are derived from mutated or modified self-proteins against which there is often a certain level of immune tolerance. To elicit anti-tumour immunity without autoimmunity the vaccines have to overcome this tolerance & design of such appropriate vaccine is a great challenge [8]. Scientists have learned how to mass-produce many antigens in the lab. They can also change these antigens to make them more easily recognized by the immune system. This new technology means that large amounts of these very specific antigens can now be given to many patients. Some antigens cause an immune response only in patients with a certain kind of cancer, while others produce immune reactions to more than one kind of cancer. Scientists often combine several antigens in a vaccine to try to get a stronger immune response.

2. Tumour Cell Vaccines:

Tumour cell vaccines are made up of actual cancer cells that have been removed during surgery. The cells are treated in the lab, usually with radiation, so they cannot form more tumours. In most cases, doctors also change the cells in certain ways, often by adding chemicals or new genes, to make them more likely to be seen as foreign by the immune system. The cells are then injected into the patient. The immune system recognizes antigens on these cells, then seeks out and attacks any other cells with these antigens that are still in the body. In some cases, doctors give the vaccine along with substances called adjuvants that increase the immune response. The general boost that adjuvants give to the immune system is meant to make the vaccine work better. Some promising newer versions of these vaccines use tumour cells that are fused to dendritic cells, in the hope of further stimulating the immune system. A possible advantage of tumour cell vaccines over antigen-based vaccine is that not all cancer antigens have been found yet. Using the whole tumour cell may expose the immune system to a large number of important cancer antigens, including some that researchers have not yet recognized. This may make them more effective.

The two basic kinds of tumour cell vaccines are:

Autologous vaccines - Autologous means "coming from the self." These vaccines are made from killed tumour cells taken from the

same person in whom they will later be used. Autologous cancer cells may be re injected shortly after surgery, or they may be grown in the lab or frozen and given later. It can be expensive to create a new, unique vaccine for each patient. Cancer cells tend to mutate over time, so an autologous tumour vaccine might become less effective later if the cancer cells in your body change. Depending on the surgery and the size of your tumour(s), you may not have enough usable cells in the removed tumour to make a vaccine, or there may not be enough to re-treat if the cancer starts growing again. Because of these problems, researchers are also looking at ways to create tumour cell vaccines that could work in any patient with that particular kind of cancer.

Allogeneic vaccines - Allogeneic means "coming from another." These vaccines use cells of a particular cancer type that originally came from someone other than the patient being treated. They are more like off-the-shelf drugs than a vaccine made for just one person. The cells for the vaccine are grown in the lab from a stock of cancer cells kept for that purpose. Some allogeneic tumour vaccines use a mixture of cells which were removed from several patients. The cells are treated and are usually injected along with one or more adjuvant substances to stimulate the immune system.

Tumour cell vaccines have been effective in eliciting an immune response as well as in providing protection in most transplantable tumour mouse-models but less so in spontaneous cancer models that closely simulate human tumours [9].This is apparently because of the immune system's inherent tolerance to many tumour antigens since they are also expressed by normal tissues or presented to T cells in a non-stimulatory environment [10]. Such vaccines can be made more immunogenic by transforming tumour cells to express co-stimulatory molecules, such as granulocyte macrophage-colony Stimulating factor (GM-CSF) [11]. Vaccination with genetically engineered, irradiated melanoma cells modified to secrete GM-CSF was shown to amplify immune responses by improved tumour antigen presentation through increased DC and macrophage recruitment [12]. This facilitated generation of melanoma-specific CD4+ and CD8+ T cells, CD1-restricted NKT-cells and antibodies for successful tumour rejection [13]. Initial testing in phase I clinical trials of this immunization strategy in patients with secondary melanoma demonstrated consistent induction of both cellular and humoral anti-tumour responses, leading to tumour destruction without significant toxicities [13]. Whole tumour cell vaccines are currently being developed to treat threatening cancers such as Acute Myeloid Leukemia (AML) [14].

Adjuvants:

Adjuvants are compounds that serve to enhance the magnitude, breadth, quality and longevity of specific immune responses to antigens, but have minimal toxicity or lasting immune effects on their own. Addition of adjuvants to some vaccines may substantially reduce the amount of antigen and/or number of immunizations required to achieve the desired immune responses. With regard to cancer antigens, adjuvants are necessary to boost the desired immune response to weak antigens. For next generation vaccines that require T cell immunity or a broader range of antibody response, adjuvants will be an important solution. For infectious disease vaccines, Aluminium salts (alum) are the most commonly used adjuvants , which are safe and effective for antibody induction [15]. In addition to alum, oil-in-water emulsions & monophosphoryl lipid A (MF59®) + alum, known as AS04 are the two other adjuvants used in approved vaccines [16]. The design of cancer vaccine adjuvants has evolved with the understanding that the synergy of conserved pathogen associated molecular patterns (PAMPs) with specific pattern recognition receptors (PRRs) and downstream signalling leading to activation of NF-kB and IRF-3 and expression of pro-inflammatory cytokines

forms the basis of innate immunity [17]. Many cytokines that are produced in response to activation of innate immunity continue to be used individually as recombinant proteins, fusion partners with selected TAAs (Tumour associated antigens) and co-expressed with TAAs in gene-based cancer vaccines. For example, the immunomodulatory effects of interferon alpha2b (IFN-alpha2b) have been shown to provide therapeutic benefit as an adjuvant therapy for high-risk melanoma [18]. Perhaps the most significant development of cancer vaccine adjuvants has been the addition of various TLR (Toll like receptors) agonists to vaccine formulations, including TLR-3 (poly I:C), TLR-4 (monophosphoryl lipid A; MPL), TLR-5 (flagellin), TLR-7 [Aldara (Immiquimod) is approved for treatment of basal cell carcinoma and genital warts], TLR-7/8 (Resiquimod), and TLR-9 (CpG) [19,20,21,22]. Either individually or in concert, these TLR agonists have been shown to significantly enhance vaccine potency. The TLR-targeted adjuvants are typically formulated as microparticles/ nanoparticles (e.g., oil-in-water emulsions, or saponin-containing formulations including QS-21, ISCOMS and ISCOMATRIX) or liposomes, along with selected antigens [23].

3. Anti-Idiotype antibody-based Vaccines:

Every B cell or plasma cell makes only one kind of antibody. The unique part of each type of antibody is called an Idiotype. Antibodies are made when the immune system responds to antigens. Sometimes the body makes antibodies against other antibodies. Scientists believe these antibodies against antibodies are important in helping to keep the immune system in check. The anti-idiotype antibodies look like the antigen and appear foreign, injecting them into the body causes the immune system to attack the anti-idiotypes, along with the antigens themselves. Scientists have learned how to make these anti-idiotype antibodies in the lab. They can be used as part of a cancer vaccine because they look like the antigens on the cancer cells in the patient's body. Therefore, they can trigger an immune response against that specific cancer. Researchers consider lymphomas to be the most promising targets for anti-idiotype vaccines. This is because all lymphoma cells have unique antigen receptors not present on normal lymphocytes or other normal cells of the body. These unique antigens can be used to make lymphoma vaccines. Early studies of B-cell lymphoma vaccines have been promising.

4. Dendritic Cell Vaccines:

Dendritic cells are special antigen-presenting cells that help the immune system recognize cancer cells. They break down cancer cells into smaller pieces (including antigens), then hold out, or "present," these antigens to T cells. This makes it easier for the immune system cells to recognize and attack them. Dendritic cells are the most effective antigen-presenting cells known. Dendritic cell vaccines are autologous vaccines, and must be made individually for each patient. The process used to create them is complex and expensive. Doctors remove some of the cells that grow into dendritic cells (from the blood) and treat them in the lab to make them multiply and turn into dendritic cells. This creates many more dendritic cells than if they just used cells taken from the patient. These dendritic cells are then exposed to cancer cells or cancer antigens. Other methods are to change their genes so that they make their own antigens or to fuse the dendritic cells with tumour cells. These procedures lead to dendritic cells with cancer antigens on their surface. The dendritic cells are then injected back into the body. The dendritic cells that have cancer antigens on their surface are better able to help the immune system recognize and destroy cancer cells that have those antigens on them. Several DC-based cancer vaccines have been developed to date including DC loaded with tumour peptides or whole proteins [24], DC loaded with tumour-derived mRNA or DNA [25],DC transduced with viral vectors such as retroviruses [26], lentiviruses [27] , adenoviruses [28], fowl pox [29] and alphaviruses [30] containing the tumour antigen or gene of interest, whole

necrotic or apoptotic tumour cells [31], tumour cell lysates [32] and DC-fused with tumour cells [33].Although the potential of DC-based vaccines to induce an antigen-specific response have been shown in many clinical trials and preclinical animal models [34], choosing the best DC population from several DC cell subsets with distinct properties and functions has been a challenge. Each subset of DC has a unique capability of activating either Th1, Th2 or Th17 cells [35]. Once a particular DC subset has been isolated or generated, it must undergo a maturation process to enhance its ability to activate T cells. Recent studies have proved that the use of immature DC may down-regulate immune responses [36]. Comparison of immature versus mature DC have shown the superiority of mature DC in the induction of immune responses in cancer patients [37] & more importantly, the use of mature DC has been shown to correlate with a better clinical outcome [38]. Although DC-based cancer vaccines appear promising in terms of efficacy, many outstanding issues have been emphasized by recent trials, such as the need to define a standardized protocol and to minimize time and cost required for such treatments [36].

5. DNA Vaccines:

When tumour cells or antigens are injected into the body as a vaccine, they may cause the desired immune response at first, but they may become less effective over time. This is because the immune system recognizes them as foreign and quickly destroys them. Without any further stimulation, the immune system often returns to its normal (pre-vaccine) state of activity. To get around this, scientists have looked for a way to provide a steady supply of antigens to keep the immune response going. DNA vaccines are based on bacterial plasmids that have been engineered to express the disease-specific antigen using promoter elements that are active in mammalian cells. They also contain a transcriptional terminator to terminate transcription in mammalian cells & a selectable marker to facilitate production of the plasmids in transformed bacterial cells [39].The mode of action of plasmid DNA vaccines is two-fold. Firstly, the antigen encoded by the plasmid is produced in host cells, either in professional antigen presenting cells (APCs) leading to direct priming of immune responses or in non-professional cells from where they can be transferred to APCs leading to cross-priming. Secondly, because DNA plasmids are derived from bacteria they stimulate the innate immune system by interacting with Toll-like receptor 9 [40].
Major advantages are:
1. Ease of production.
2. Cheaply & conveniently produced & purified.
3. Do not require special handling or storage conditions.
4. They elicit immune responses only to the encoded antigens, compared to other types of nucleic acid-based vaccines that depend on tumour antigen expression by various viral vectors.
5. They elicit bothCD8+ andCD4+ T cell responses, as well as humoral immune responses, because the encoded antigen is processed through both endogenous and exogenous pathways thus enabling presentation of peptide via both MHC I and MHC II [41].
6. Plasmid DNA-based products are safe [42] and there are now several products in late-stage clinical testing.

The only drawback of DNA vaccines, especially if using oncogenic DNA, is the potential of the DNA to integrate into the genome of the cell that takes it up, thus potentially promoting malignancy. Using RNA instead, a more recent approach, can avoid the integration problem [43]. The efficacy of RNA-based vaccines, on the other hand, can be compromised by degradation of the RNA by RNAses in body fluids and skin.

7. viral-vector based vaccines:

These vaccines use special delivery systems (called vectors) to make them more effective. They aren't really a separate category of vaccine; for example, there are vector-based antigen vaccines and vector-based DNA

vaccines. Vectors are special viruses, bacteria, yeast cells, or other structures that can be used to get antigens or DNA into the body. The vectors are often germs that have been altered to make sure they can no longer cause disease.

Advantages of using vectors:

1. They can deliver more than one cancer antigen at a time, which make the body's immune system more likely to mount a response.
2. They mimic a natural infection, and thus provide the necessary "danger signals" required for optimal activation of antigen presenting cells.
3. They are easier and less expensive to make than some other vaccines.

The first viral vector used was vaccinia, a poxvirus, over 20 years ago [44]. Since then several other vectors have been developed based on the poxviruses, such as the modified vaccinia virus Ankara (MVA) [45], which is a non-replicating vaccinia virus, and avian poxviruses, such as fowlpox [46] and canarypox [47]. Naked DNA and RNA can be made more immunogenic by incorporating them into viral vectors. Live recombinant viral vaccines have been tested in cancer for the past 10 years [48]. An optimal viral vector vaccine should be effective in inducing long-term antibody and T cell responses, and importantly, it must be clinically safe, i.e. the viral vector must not be able to replicate in patient's cells. Like plasmid DNA vaccines, recombinant viral vectors deliver the transgene to the MHC class I antigen processing and presentation pathway. In addition, the viral vector activates strong innate immune responses promoting the recruitment of antigen-specific T cells through TLR-dependent and TLR-independent pathways [49]. These virus-induced innate inflammatory signals influence the type I IFN dependence of CD8+ T cells for clonal expansion and memory formation [50]. Although the use of viral vector vaccines as immunotherapy along with chemotherapy is gaining popularity, there is still much to be learned about the vectors to optimize the efficacy of the vaccine.

Combining vaccines with conventional therapies for cancer:

In many of the clinical trials of cancer treatment vaccines that are now under way, vaccines are being given with other forms of cancer therapy. Therapies that have been combined with cancer treatment vaccines include surgery, chemotherapy, radiation therapy, and some forms of targeted therapy, including therapies that are intended to boost immune system responses against cancer. Several studies have suggested that cancer treatment vaccines may be most effective when given in combination with other forms of cancer therapy [51]. In addition, in some clinical trials, cancer treatment vaccines have appeared to increase the effectiveness of other cancer therapies [52]. Additional evidence suggests that surgical removal of large tumour masses may enhance the effectiveness of cancer treatment vaccines [52]. In patients with extensive disease, the immune system may be overwhelmed by the cancer. Surgical removal of the tumour may make it easier for the body to develop an immune response. Researchers are also designing clinical trials to answer questions such as whether a specific cancer treatment vaccine works best when it is administered before chemotherapy, after chemotherapy, or at the same time as chemotherapy. Answers to such questions may not only provide information about how best to use a specific cancer treatment vaccine but also reveal additional basic principles to guide the future development of combination therapies involving vaccines.

Side effects of cancer vaccines:

Vaccines intended to prevent or treat cancer appear to have safety profiles comparable to those of traditional vaccines [53]. However, the side effects of cancer vaccines can vary among vaccine formulations and from one person to another. The most commonly reported side effect of cancer vaccines is inflammation at

the site of injection, including redness, pain, swelling, warming of the skin, and occasionally a rash. People sometimes experience flulike symptoms after receiving a cancer vaccine, including fever, chills, dizziness, nausea or vomiting, muscle ache, fatigue, headache, and occasional breathing difficulties. Other, more serious health problems like asthma, appendicitis, pelvic inflammatory disease, and certain autoimmune diseases, including arthritis and systemic lupus erythematosus have been reported in smaller numbers of people after receiving a cancer vaccine. Vaccines, like any other medication affecting the immune system, can cause adverse effects that may prove life threatening. For example, severe hypersensitivity (allergic) reactions to specific vaccine ingredients have occurred following vaccination. However, such severe reactions are quite rare.

FDA approved cancer vaccine:

In April 2010, the FDA approved the first cancer treatment vaccine. This vaccine, Sipuleucel-T (Provenge®, manufactured by Dendreon), is approved for use in some men with metastatic prostate cancer. In a clinical trial, Sipuleucel-T increased the survival of men with a certain type of metastatic prostate cancer by about 4 months [54]. It is designed to stimulate an immune response to prostatic acid phosphatase(PAP), an antigen present on most prostate cancers. The vaccine is created by isolating immune system cells called antigen-presenting cells (APCs) from a patient's blood through a procedure called Leukapheresis. The APCs are sent to Dendreon, where they are cultured with a protein called PAP-GM-CSF. This protein consists of PAP linked to another protein called granulocyte-macrophage colony-stimulating factor (GM-CSF). The latter protein stimulates the immune system and enhances antigen presentation.APC cells cultured with PAP-GM-CSF constitute the active component of Sipuleucel-T. Each patient's cells are returned to the patient's treating physician and infused into the patient. Patients receive three treatments, usually 2 weeks apart, with each round of treatment requiring the same manufacturing process. Although the precise mechanism of action of Sipuleucel-T is not known, it appears that the APCs that have taken up PAP-GM-CSF stimulate T cells of the immune system to kill tumour cells that express PAP.

Future of Cancer Vaccines:

The discovery of cancer vaccines is going on fast pace. There are number of cancer vaccines undergoing clinical trials. Here is the list of companies and their vaccines in development.

1. Dendreon Corp (DNDN) -Neuvenge, for HER2/neu expressing cancers such as Breast, Bladder, colon, Ovarian.
2. Celldex Therapeutics- CDX110, CDX1307 and CDX1401.
3. Heat Biologics- ImPACT Therapy against NSCLC and other cancers.
4. Geron Corporation- GRNVAC1.
5. BN ImmunoTherapeutics - PROSTVAC.
6. Globe Immune –Tarmogens, GI-4000.
7. Advaxis - ADXS11-001, ADXS31-001, ADXS31-164.
8. Accentia Biopharmaceuticals majority owned subsidiary Biovest International-BiovaxID.
9. GeneMax Corp- GMXX.
10. Apthera, Inc. –NeuVax.
11. Avax Technologies -AC Vaccine.
12. Generex Biotechnology through its wholly-owned immunotherapeutic subsidiary Antigen Express (Ae-37).
13. Immatics biotechnologies - IMA901 for renal cancer .
14. Scancell Holdings-SCIB1.
15. Merck - in 2009, starting phase III trials of Stimuvax for breast cancer [55]. It had promising results from a phase IIB trial for inoperable lung cancer.
16. Oncotherapy Science - The first world peptide vaccines are produced. Some of vaccines are now in phase 2&3 .

Failure of cancer vaccines at clinical trials:

Most clinical trials investigating a cancer vaccine have failed or had very modest

responses by standardized oncologic assessment criteria described as the RECIST criteria . The precise reasons are unknown, but possible explanations include:

1. Disease stage being treated was too advanced: it is difficult to get the immune system to fight bulky tumour deposits, because tumours actively suppress the immune system using a variety of mechanisms (e.g. secretion of cytokines that inhibit immune activity). The most suitable stage for a cancer vaccine is likely to be early disease, when the tumour volume is low, but the problem there is that clinical trials take upwards of five years and require high numbers of patients to reach measurable end points.
2. Escape loss variants - cancer vaccines that target just one tumour antigen are likely to be less effective. The most effective cancer vaccine is likely to raise an immune response against a broad range of tumour antigens to minimise the chance of the tumour being able to mutate and become resistant to the therapy.
3. Prior treatments - numerous clinical trials in the past have treated patients who have received numerous cycles of chemotherapy. Chemotherapy is often myelosuppressive and destroys the immune system. There is little point giving a cancer vaccine to a patient who is immune suppressed.
4. Some tumours progress very rapidly and/or unpredictably, and they can literally outpace the immune system. It may take two to three months for an immune response to a vaccine to mature, but some cancers (e.g. advanced pancreatic) can produce marked clinical deterioration, or even death, within this timeframe.

CONCLUSION

Cancer has become one of the most devastating diseases worldwide. Different types of cancer treatment therapies have been discovered with the strenuous efforts of scientists but none of them stood out as potential anticancer therapy. Cancer vaccines represent an emerging type of biological therapy that is still mostly experimental. Many clinical trials are underway to test vaccines as potential treatments for a wide variety of cancer types. Possibly the most exciting achievement of this century will be the discovery of a Universal Cancer Vaccine. The ultimate goal of vaccine-based cancer immunotherapy is to elicit a potent immune response that will cause the eradication of the tumour as well as generate a long-term memory response that will guarantee complete remission and keep the cancer in check. The obvious advantages of cancer vaccines are the ability to target both surface and intracellular antigens through the induction of a potent cellular and humoral response, as well as the potential for a response of greater duration, thus obviating the need for long-term multiple administration of the therapeutic or preventive agents. As of yet success with cancer vaccines is limited. The one and only cancer vaccine approved by FDA for treatment of prostate cancer was Sipuleucel-T (Provenge®, manufactured by Dendreon). Advances in basic and translational immunology, and the ever increasing numbers of cancer vaccines under development in academic research laboratories as well as in the pharmaceutical and biotechnology companies, makes the goal of developing efficacious vaccines against cancer achievable in the not too distant future.

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