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VACCINES FOR LIFE STYLE DISEASES REVIEW

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Abstract

Vaccines are commonly used as a preventive medicine for infectious diseases worldwide, however, clinical trials on an amyloi beta vaccine for Alzheimer's disease represents a new concept in the field of vaccinations. This review highlights about the vaccines which are used for the life threatening life style diseases .Several recent studies indicate the potential of therapeutic vaccines as well as classical vaccines as preventive medicines. A number of therapeutic vaccines for cancer have been developed as novel immunotherapy. Their targets are usually specific antigens in cancer cells, allowing activated cytotoxic T cells (CTLs) to attach and remove the antigen-presenting cancer cells. Although treatment for these has been established for years based on different therapies reducing a series of risk factors, the degree of success has been only limited because of large side effects and non compliance.. In this sense, alternative treatments for lifestyle diseases have come into play where both innate and adaptive immunity have been produced through vaccination it is found to control the disease .Many experimental pre-clinical studies demonstrating proof of concept that vaccination using DNA and protein with an effective use of adjuvants and the optimal route of administration now provide a tangible new therapeutic approach that sets the stage for several of these vaccines to be tested in large, randomized, long-term clinical studies. A vaccine ready for human use will only be accomplished through the close association between academia regulatory government organizations and private industry, allowing the reality of a simple and successful therapy to reduce diseases and its severe clinical complications more over these vaccines posses greater advantages over the various drugs used for the treatment and many of the vaccines are showing promising results.

KEY WORDS: life style vaccines-vaccines for cancer-types-approved vaccines-vaccines under clinical trials- antihypertensive vaccine-cholesterol vaccine – osteoporosis vaccines.

INTRODUCTION

Lifestyle diseases are the diseases associated with the way a person or group of people lives. Lifestyle diseases include Type 2 diabetes, heart disease, Alzheimer's disease, arthritis, atherosclerosis, asthma, cancer, chronic liver disease or cirrhosis, chronic obstructive pulmonary disease, metabolic syndrome, chronic renal failure, osteoporosis, stroke, depression, obesity, diseases associated with smoking ,alcohol and drug abuse [1] . Lifestyle diseases have their onset later in an individual's life and need a longer lifespan and may become the cause of death. If not properly managed, Lifestyle diseases including diabetes and cancer threaten most of the patients and kill millions of people every year. Due to increased side effects and non compliance towards the existing drugs researchers have started to work upon vaccines against lifestyle diseases like hypertension, diabetes, atherosclerosis, Alzheimer's disease etc.

A vaccine is a biological preparation that provides active acquired immunity to a particular disease. If proved safe and cost effective, a vaccine can protect people from diseases and its heavy economic burden. Immunotherapy products are now been developed for every major therapeutic category from anti-infective to autoimmune disorders, oncology, cardiovascular or neurological conditions.

Fig 1: vaccine

Life-style vaccines, defined as vaccines to manage chronic conditions in healthy individuals, are being developed. Vaccines for non-infectious illness could help developing nations tackle the growing burden of chronic disease. Many vaccines are already introduced for the prevention of diseases and several vaccines targeting cancers, cardiovascular disease and hypertension have made it to Phase I and II clinical trials. Several recent studies indicate the potential of therapeutic vaccines as well as classical vaccines as preventive medicines for life style diseases.

VACCINES FOR CANCER

Cancer is the name given for these diseases in which the body cells become abnormal and divide without control. Cancer cells may invade nearby tissues. And they may spread through the bloodstream and lymphatic system to other parts of the body. Its two main characteristics are uncontrolled proliferation of the cells in the human body and ability of these cells to migrate from the original site and spread to distant sites (metastasis). If the spread is not controlled, cancer can result in death.

Disadvantage or side effect of cancer treatment

Affects normal cells along with the cancer cells which leads to several unpleasant side effects, including

- Alopecia
- dermatitis
- dryness and peeling of skin
- Depression of bone marrow resulting in granulocytopenia, agranulocytosis, thrombocytopenia, aplastic anaemia
- Infections and bleeding
- Oligozoospermia, impotence in male, amenorrhoea in female, mutagenesis.
- Abortions, teratogenesis.
- Hyperuricemia
- Acute renal failure, gout and urate stones.
- Nausea and Vomiting.

CANCER VACCINE

A cancer vaccine is a vaccine that either treats existing cancer or prevents development of a cancer. Vaccines that treat existing cancer are known as therapeutic cancer vaccines. There are currently no vaccines able to prevent all cancers; however vaccines against some oncoviruses have proven extremely effective. Some types of cancer, such as cervical cancer and some liver cancers, are caused by viruses (oncoviruses), and traditional vaccines against those viruses, such as HPV vaccine and hepatitis B vaccine, will prevent those types of cancer.

AIM: stimulating the immune system to be able to recognise cancer cells as abnormal and destroy them. Some vaccines for particular cancers have been developed and are being tested to see whether they can treat cancer, or help to stop it from coming back after cancer treatment.

TYPES OF CANCER VACCINES

Most promising cancer treatment is immunotherapy. There are 2 major categories that cancer vaccines fit into:

1. Specific cancer vaccine
2. Universal cancer vaccines.

five kinds of cancer vaccines being developed are;

Antigen Vaccines: These use tumor-specific antigens -proteins displayed on a tumor cell - to stimulate the immune system.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. Multiple antigens can be used in this type of vaccine to vary the immune system response.

Anti-idiotype Vaccines: In some instances, some cancer treatment antibodies, called idiotype antibodies, act as antigens, triggering an immune response similar to that described above. In this case, the immune system will produce anti-idiotype antibodies to attack the idiotype. Anti idiotype antibodies can be mass-produced to produce a vaccine that can be injected to treat cancer.

Dendritic Cell Vaccines: Dendritic cells break the antigens on the cancer cell surfaces into smaller pieces. The dendritic cells then

displaying those antigen pieces to the killer T cells. in order to make dendritic cell vaccines some of the patients dendritic cells are extracted and immune cell stimulants are used to reproduce large amounts of the cells in the lab. These are then exposed to antigens from the patient's cancer cells. This combination of dendritic cells and antigens is then injected into the patient and the dendritic cells work to program the T cells.

Tumor Cell Vaccines (Autologous /Allogeneic Cells): Autologous and Allogeneic tumor cells were one of the first types of tumor vaccines to be used.

ADVANTAGES;

- They have all the relevant tumor antigens needed by the immune system to mount an effective antitumor response. This is particularly true if Autologous tumor cells are used instead of Allogeneic tumor cells.
- A tumor cell-based immunization allows the development of cancer vaccines without knowing Specific antigens.
- The advantages of tumor cell-based cancer vaccines must be balanced against two major disadvantages: the potential for autoimmunity and the potential for increasing the anergic status of the T cells due to the lack of functional co stimulatory molecules on tumor cells were disappointing and temporarily decreased interest in the field.

Tumor-APC Hybrids: A novel development in cancer Vaccines is the use of tumor-APC fusion technology. The vaccines produced by exposing tumor cells and APCs to PEG or electrical fields, which results in the generation of a tumor-APC hybrid. The rationale behind this approach is that the resulting hybrid will have the appropriate TAA derived from the tumor and the unparalleled co stimulatory capabilities of the APCs.Preclinical studies have provided the rationale for the use of cell hybrids in the cancer vaccine setting. More importantly, the tumor-APC strategy already has been associated with major clinical responses in patients with metastatic renal carcinoma.

DNA Vaccines: With recent DNA research, scientists are finding ways to use the genetic code of proteins produced in cells to aid the immune systems fight against cancer. Bits of DNA from patient's cells are injected into the patient, which instructs the other cells to continuously produce certain antigens. This DNA vaccines increases production of antigens which forces the immune system to respond by producing more T cells.

CANCER VACCINES PREPARATION:

Cancer vaccines are made from the person's own cancer cells that are grown in a laboratory. The cancer cells are treated with heat or radiation, and then they become inactive and can be used for vaccine preparation. Certain proteins may then be taken from the cancer cells and used to make a cancer vaccine.

These include antigens (the proteins on the cello the first types of tumor vaccines to be used. Surface which can stimulate an immune response), in some cases, whole cells may be used to make the vaccine. Often a cancer vaccine will also contain substances that are already known to boost the immune system, such as BCG (the vaccine that protects against tuberculosis). As the cancer vaccine contains similar proteins to the cancer cells, it is hoped that the immune system will be stimulated to start to attack and destroy them.

MODE OF DELIVERY : Cancer vaccines are usually a liquid which is given by an **intradermal injection**. The dosage will depend on the type of cancer being treated and the type of vaccine being used.

APPROVED THERAPEUTIC CANCER VACCINE

- Oncophage (Antigenics Inc approved in Russia in 2008 for kidney cancer).
- Sipuleucel-T (Provenge, manufactured by Dendreon), is approved for use in some men with metastatic prostate cancer. It is designed to stimulate an immune response to PAP, an antigen that is found on most prostate cancer cells. In a clinical trial, sipuleucel-T increased the survival of men with a certain type of metastatic prostate cancer by about 4 months.

The vaccine is created by isolating immune system cells called 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 tumor cells that express PAP.

- **Gardasil** is approved for the prevention of cervical, vaginal, and vulvar cancers in girls and women ages 9 to 26. It is also approved to prevent anal cancer in women and men, and genital warts in men and boys in the same age range. The vaccine prevents infection with the human papillomavirus (HPV), which, if long-lasting, can cause these cancers (as well as other cancers the vaccine is not approved for, such as oral cancer).
- **Cervarix,** which also protects against HPV infection, is approved for the prevention of cervical cancer in girls and women ages 10 to 25.
- The **hepatitis B** vaccine prevents infection with the hepatitis B virus (HBV). Long-lasting infection with HBV can lead to liver cancer.

POSSIBLE SIDE EFFECTS

The possible side effects of cancer vaccines include a

skin reaction at the injection site,

a skin rash or mild flu-like symptoms

Certain cancer vaccine may cause more specific symptoms

CANCER VACCINES WHICH ARE CURRENTLY UNDER CLINICAL TRIALS

Onyvax: (a monoclonal antibody 105AD7 anti-idiotype Vaccine) is used for the treatment of advanced colorectal adenocarcinoma. The vaccine is administered endemic together with the BCG vaccine or intramuscularly together with the alum adjuvant

Cancer VAX: (a polyvalent melanoma vaccine) is being used together with the surgical treatment in the treatment of melanoma III stage.

NY-ESO-1 Peptide Vaccine: is used endermic in the treatment of II-IV stage sarcoma of soft tissues expressing NY-ESO-1, LAGE antigen NY-ESO-1 or LAGE GM-. CSF is to be injected, subcutaneous, in additional to this vaccine.

A Monoclonal Antibody 11D10Anti-idiotype Vaccine and

Monoclonal Antibody 3h1 Anti-idiotype Vaccine: are being used in the treatment of the patients with stage II or IIIA non-small cell lung cancer (T1-3, N1-2, M0) which is administered starting from the 14-45 days after operation

ALVAC-CEA/B7.1,

VG-1000 Vaccine

The name "Tricom" shorthand for a combination of three powerful co-stimulatory molecules - B7-1, ICAM and LFA-3 enhance T-cell response.

HSPPC-96, or Oncophage.

CHALLENGES TO BE ADDRESSED

Cancer vaccines have been researched for a number of years. Some studies in surgical treatment in the treatment of melanoma III stage.

Laboratory animals (such as mice) have shown promising results, in which vaccines have successfully stimulated the immune system. Research has not always been so successful in humans. However, recent studies have more encouraging results.

The main challenge is in the following areas:

- Many people with cancer have reduced immunity and so their immune systems are not able to react with the vaccines.
- Some tumours produce proteins and chemicals that prevent the immune system from attacking them effectively, even when it has been stimulated by the vaccine.
- Not all tumour cells are the same and some cells may be different to those in the vaccine. These 'different' cells will be resistant to and unaffected by the vaccine.
- Cancer cells suppress the immune system; this is how the cancer is able to grow and develop in the first place. Researchers are using adjuvants in vaccines to try to overcome this problem.
- Because cancer cells develop from a person's own healthy cells, they may not "look" harmful to the immune system. Therefore, instead of being identified as harmful to the body and eliminated, the cancer cells are ignored.

- Larger or more advanced tumors are hard to eliminate using only a vaccine. This is one reason why cancer vaccines are usually given in addition to other treatments.
- The immune systems of people who are sick or older may not be able to produce a strong immune response following vaccination, limiting the vaccine's effectiveness. Also, some cancer treatments may damage a person's immune system, limiting its ability to respond to a vaccine.

VACCINES FOR HYPERTENSION

Hypertension remains an important public health challenge. High BP is associated with an increased risk of mortality and morbidity from stroke, coronary heart disease, congestive heart failure, and end-stage renal disease; it also has a negative impact on the quality of life. Hypertension cannot be eliminated because there are no vaccines to prevent the development of hypertension, but, its incidence can be decreased by reducing the risk factors for its development, which include obesity, high dietary intake of fat and sodium and low intake of potassium, physical inactivity, smoking, and excessive alcohol intake. More recently, immunization against

- Angiotensin-I with PMD-3117 vaccine
- Angiotensin-II with CYT006-AngQb vaccine
- Targeting angiotensin-II type 1A receptor with ATR12181 vaccine has provided optimism in the development of a hypertension vaccine. AngQb vaccine has proved to become the first vaccine ever to lower (− 9/− 4 mm Hg) blood pressure inhuman beings. Vaccine could induce long lasting effects with a dosing interval of months, increasing patient acceptability and compliance and thus a better control of high blood pressure. Our objective will be to focus on the importance of the RAS and to explore the extent of safety; efficacy and the future implications of vaccine against the RAS.Researchers began experimenting with vaccines against the renin-angiotensin system to control hypertension around six decades ago. Other vaccine candidates against hypertension have shown promising results they are namely;
- pHAV-4Ang IIs
- AngI-R,
- ATRQβ-001

Concept of Peptide Vaccine for Hypertension

Our immune system can distinguish self from non-self because the immune system has evolved central and peripheral self-tolerance checkpoints to remove or silence auto reactive lymphocytes. B cells that react to self-antigens become anergic and functionally silent. In order for dormant B cells to proliferate, B cells need to interact with activated T-helper cells recognizing antigen-derived peptides on MHC (major histocompatibility complex) class II molecules presented by B cells. T cells that react with self-antigen, having escaped thymic deletion and existing in peripheral lymphoid organs, may be activated by antigen stimulation in the presence of strong adjuvants. Although our therapeutic vaccine would essentially need to break down peripheral tolerance to induce a reaction against endogenous molecules, the preferred strategy in the development of vaccines against self-antigens is to circumvent T-cell tolerance rather than to break it. The outcome of amyloid beta vaccination provides support for the theory that the adverse effects of the vaccine were due to a T-cell-mediated autoimmune response this theory also gains support from the presence of a T-cell epitope in the amyloid beta used for immunization, which was considered to be responsible for eliciting autoimmunity. Consequently, the vaccine was modified to exclude T-cell epitopes, therefore avoiding T-cell activation without disrupting the B-cell epitopes responsible for antibody production. While considering this strategy, we speculate that because angiotensin II is only eight amino acids long, which is shorter than amyloid beta (40–42 amino acids long), it might not provide a T-cell epitope. It is known that angiotensin II can provide a B-cell epitope because the existence of anti-angiotensin II antibodies has been confirmed in several experiments. Thus, we will examine whether or not angiotensin II can activate T-cells in our therapeutic vaccine system.

The concept of therapeutic vaccine is shown in Figure 2. Stable and sufficient antibody production requires helper T-cell activation to assist in the polyclonal expansion of B-cells; therefore, antigens must contain both B-cell and T-cell epitopes. To avoid T-cell epitopes from our target molecule, immunogenic molecules (i.e., KLH) are conjugated with the antigen. Consequently,

T-cells would be activated by KLH, instead of the epitopes of our target molecule. It is important to confirm that antibodies against the target molecule (i.e., Angiotensin II) are successfully induced after immunization with the target molecule, thereby confirming the existence of a B-cell epitope on target molecule. As for T-cell epitopes, performing T-cell proliferation assays and ELISPOT assays, which may indicate to the responsiveness of T-cells to target molecule. Ang II-KLH has been used as an Ang II peptide vaccine in mice. The results indicated that Ang II-KLH and KLH induced T-cell activation but Ang II did not, which means that KLH contains a T-cell epitope, but Ang II does not. Importantly, the sources of T-cell epitopes and B-cell epitopes can be different.This situation is reflected in the relationship between a hapten and its carrier, in which the hapten has the only B-cell epitope and the carrier possesses the T-cell epitope. Based on this mechanism for our therapeutic vaccine system, autoimmune diseases caused by cytotoxic T-cells can be avoided.

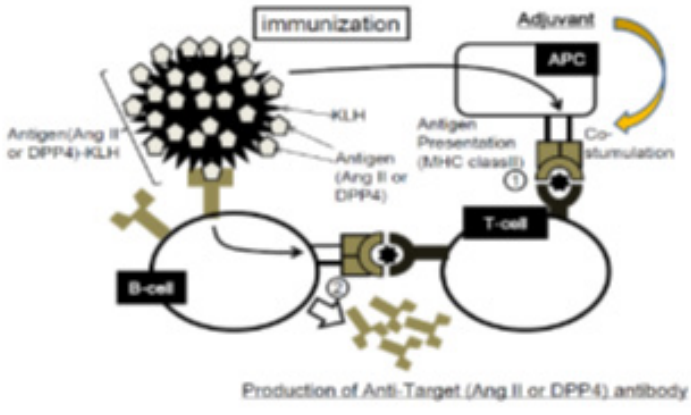

Figure 2: Conceptual schematic of therapeutic vaccine.
(Step1) APCs (the antigen, i.e., Ang II or DPP4, in this case is known as a hapten) phagocytise the antigen-KLH conjugate and present a T-cell epitope of KLH to T-cells through.

CYT-006-AngQb Hypertensive vaccine

CYT-006-AngQb, under development by Cytos Biotechnology AG, is a vaccine in which a peptide derived from the angiotensin II molecule is conjugated to the surface of the highly repetitive structure of virus-like particles. CYT-006-AngQb was designed to treat hypertension with the benefit of relatively long-lasting effects that do not require daily dosing. In spontaneously hypertensive rat models, CYT-006-AngQb induced strong angiotensin-II-specific antibodies and reduced systolic blood pressure. In a phase I clinical trial, single doses of CYT- 006-AngQb were well tolerated in healthy males. In a phase II trial, multiple doses of CYT-006-AngQb administered to patients with mild-to-moderate hypertension reduced blood pressure; the average half-life was longer than all currently available oral hypertension medications. There were no significant side effects except for local skin reactions at the injection site. Given the novel mechanism of CYT-006-AngQb, and the potential to complement other hypertension treatments, success in ongoing phase II trials in patients with hypertension would potentially make this therapy a valuable addition to the therapeutic armamentarium for hypertension. Immunization against angiotensin II may offer a valuable alternative to conventional drugs for the treatment of hypertension, because vaccines induce relatively long-lasting effects and do not require daily dosing. Here we describe the preclinical development and the phase I clinical trial testing of a virus-like particle (VLP)-based antihypertensive vaccine.

An angiotensin II-derived peptide was conjugated to the VLP Qβ (AngQb).

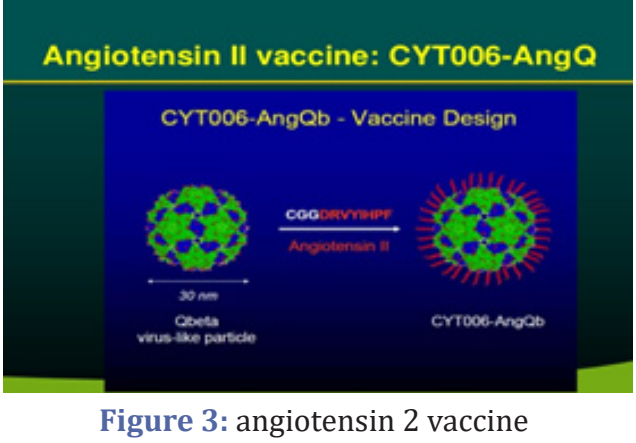

Figure 3: angiotensin 2 vaccine

AngQb reduces blood pressure in SHR to levels obtained with an ACE inhibitor, and is immunogenic and well tolerated in humans.

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Therefore, vaccination against angiotensin II has the potential to become a useful antihypertensive treatment providing long-lasting effects and improving patient compliance. Worldwide, the prevalence of noncommunicable chronic diseases is increasing. The use of vaccines to induce autoantibodies that neutralize disease-related proteins offers a means to effectively and affordably treat such diseases. Twenty vaccines designed to induce therapeutic autoantibodies were clinically tested in the past 12 years. Immunodrugs are therapeutic vaccines comprising VLPs covalently conjugated with self-antigens that induce neutralizing autoantibody responses. Four such VLP-based vaccines have been clinically tested and one has achieved proof of principle: a reduction of blood pressure in hypertensive patients. To facilitate preliminary clinical testing, novel nonclinical study programs have been developed. Safety study designs have considered the underlying B and T cell immunology and have examined potential toxicities of vaccine components and primary and secondary pharmacodynamic action of the vaccines.

Year	Vaccines	Phase/Sample size	Results
2003	Ang 1 analog with KLH(PMD3117)	Phase 1:50 healthy men	Increase in anti-Ang 1 antibody titer.No changes in the bloodpressure.No problems in safety evaluation
2004	Ang 1 analog with KLH(PMD3117)	Phase 2:27 hypertensive patient(double blind)	Increase in anti-Ang 1 antibody titer.No changes in the bloodpressure.No problems in safety evaluation
2006	Ang 2 (Ang Qb) with Alum	Phase 1:16 healthy men(12 vaccine;4 placebo)	Increase in anti-Ang 2 antibody titer.No changes in the bloodpressure.No problems in safety evaluation
2008	Ang 2 (Ang Qb) with Alum	Phase 2:72 hypertensive patients(24 high-dose vaccine,24 low-dose vaccine,24 placebo)	Increase in anti-Ang 2 antibody titer.Significant decrease in blood pressure only for the high-dose vaccine group.No problems in safety evaluation.
2010	Angiotensin therapeutic vaccine by novel adjuvant,Co-Vaccine HT	Phase 2b;Randomized,double blind,placebo-controlled	Terminated because of dose-limitting adverse effects.
2018	Ang 2 DNA vaccine(AG-MG0201)	Phase 1/2a:24 patients(9 high dose,9 low dose,6 placebo)	Ongoing
Ang indicates Angiotensin;and KLH,Keyhole limpet hemocyanin			

Table 1: List of drugs under clinical trials

VACCINES FOR CHOLESTEROL

The body produces cholesterol to make vitamin D, hormones and molecules that digest food. But if there is too much it can block arteries leading to heart diseases and stroke. Millions of people regularly take cholesterol-lowering statins to prevent heart-related illness. Statins are a type of medication that work by blocking a substance your body needs to make cholesterol and can also help the liver reabsorb cholesterol that's built up as plaque on artery walls.Statins have long been the reliable go-to for patients with high cholesterol, but come with potentially serious side effects like muscle pain, an increased risk of diabetes, and cognitive loss. Thus vaccines against cholesterol are being developed and are under clinical trials.

PROPOSED MECHANISM OF ACTION

The vaccine targets a protein called PCSK9 that's involved the management of cholesterol levels in the blood. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is an enzyme encoded by the PCSK9 gene in humans. PCSK9 binds to the receptor for low-density lipoprotein (LDL) cholesterol.

In the liver, the LDL receptor removes LDL cholesterol from the blood. When PCSK9 binds to the LDL receptor, the receptor is broken down and can no longer remove LDL cholesterol from the blood. If PCSK9 is blocked, more LDL receptors will be present on the surface of the liver and will remove more LDL cholesterol from the blood. Therefore, blocking PCSK9 can lower blood cholesterol levels. Similar genes (orthologs) are found across many species. PCSK9 is inactive when first synthesized, because a section of peptide chains blocks their activity; proprotein convertases remove that section to activate the enzyme.

PCSK9 has medical significance because it acts in cholesterol homeostasis. Drugs that can block PCSK9, thus lowering low-density lipoprotein cholesterol (LDL-C). The first two PCSK9 inhibitors, alirocumab and evolocumab, were approved by the U.S. Food and Drug Administration in 2015 for lowering cholesterol where statins and other drugs were insufficient. The manufacturers did not submit data to show that the drugs actually improved outcomes of cardiovascular disease, but they assumed that lowering cholesterol would improve cardiovascular disease. By interfering with PCSK9, the researchers are able to lower cholesterol in the blood, and have shown that just one vaccination has significantly cut down on LDL cholesterol (considered the bad type of cholesterol) levels in lab animals. The vaccine works by using virus-like particles to train the immune system to produce antibodies which attack parts of the body that it would not normally notice. Virus-like particles look like viruses but don't contain genetic material and are not infectious. However they closely resemble the PCSK9 protein so that the body begins to think the protein is a foreign body. It is the same method that was used to create the HPV vaccine. One of the most exciting things about this new vaccine is it seems to be much more effective than statins alone. The protein PCSK9 is a common target for drug makers to lower cholesterol. Recently, a new class of drugs called PCSK9-inhibitors were approved in the United States. They're thought to be possible game-changers for cholesterol treatment. Statins can have side effects, which is why researchers have looked for other options, including the vaccine.Several drug companies have been developing high cholesterol treatments that target PCSK9 -- for example, Alirocumab and Evolocumab, which the FDA recently approved. Results have been positive, but their treatments, which use monoclonal antibodies, are prohibitively expensive; treatment costs upwards of $10,000 per year.The new vaccine appears to be even more effective than these monoclonal antibody-based treatments, at a fraction of the cost. The researchers now plan to expand their studies in macaques and find commercial partners to move the technology forward.

VACCINES FOR OSTEOPOROSIS

Healthcare providers involved in the fight against osteoporosis now have one more weapon in their arsenal, as the FDA recently approved the sale of Prolia (denosumab), a twice-yearly injection indicated for postmenopausal women.

MECHANISM

Prolia (denosumab) is a human IgG2 monoclonal antibody with affinity and specificity for human RANKL. Denosumab has an approximate molecular weight of 147 kudu and is produced in genetically engineered mammalian (Chinese hamster ovary) cells. In postmenopausal women, the absence of estrogens sets up a deregulation of RANK ligand, which is a protein that participates in the production and activity of osteoclasts, In the postmenopausal state, there is an excessive abundance of RANK ligand floating around because the estrogens is no longer regulating it, leading to an aggressive resorbing of bone. Bisphosphonate drugs such as Fosamax (alendronate), Actonel, and Reclast work by layering on the surface of bone and are consumed by the osteoclasts, reducing their activity and remaining in bone for a relatively long time. However, Prolia works by ratcheting down the message that leads to excessive osteoclast-driven bone removal and is active in the body for only six months. The way that denosumab (Prolia) works is that it's a fully human monoclonal antibody to RANK ligand. So when you give somebody a shot in the arm of this drug every six months, they get a six-month period during which the antibody is active, after which it stops working. For the six months that it's circulating in your system, you have a reduction in RANK ligand levels which leads to a reduction in the signal to the osteoclasts that makes them overly aggressive. This drug works by preventing the osteoclasts from maturing or resorbing bone Prolia is a sterile, preservative-free, clear, and colourless to pale yellow solution.

COMPOSITION

- Each 1 mL single-use prefilled syringe of Prolia contains 60 mg denosumab (60 mg/mL solution), 4.7%sorbitol, 17 mM acetate, 0.01% polysorbate 20, Water for Injection (USP), and sodium hydroxide to a pH of 5.2.
- Each 1 mL single-use vial of Prolia contains 60 mg denosumab (60 mg/mill solution), 4.7% sorbitol, 17 am acetate, Water for Injection (USP), and sodium hydroxide to a pH of 5.2.

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SIDE EFFECTS: difficulty breathing; swelling of your face, lips, tongue, or throat.

ADVANTAGES: medication adherence and twice a year s.c injection.

DISADVANTAGES: expensive.

CONCLUSION

Wide varieties of drugs are available for the treatment of all the life style diseases but long term treatment is still costly, tedious, and at the population level sometimes unsuccessful more over those drugs may cause variety of side effects in patients. So it is important to overcome this situation in future. Vaccines have classically been developed to prevent infectious diseases but the same is now developed to treat the non infectious disease and found successful. More trials involving human subjects are needed to establish the safety and efficacy of certain life style vaccines, under development. The vaccines prove to be safe and cost-effective in the long run; would step-up the control of the diseases. Vaccines for non-infectious illness could help developing nations tackle the growing burden of chronic disease. A Favourable trend for Vaccinology has been fuelled by recent major breakthroughs in the sciences of immunology, molecular biology, genomics, proteomics, Physico-chemistry and computers that promise a bright future for prevention of lifestyle diseases.Vaccines are being made more user-friendly by the development of combined vaccines and less painful and invasive inoculation techniques than the traditional syringe and needle. Chronic diseases also require a different approach, focussing on continuity of care, monitoring and long-term follow-up. The health systems of emerging economies don't have the experience or capacity to manage this. But a vaccine will need to be administered once or twice a year there by increasing patient compliance and cost effective treatment and thus overcome all the difficulties associated with all the disadvantages relating to current medications and thus the lifestyle vaccines will probably find the topmost position among the modern medication treatment.

ABBREVIATIONS

APC-antigen presenting cells

PAP- prostatic acid phosphatase

GM-CSF-Granulocyte-macrophage colony stimulating factor

apo = apolipoprotein;

DAMP = danger-associated molecular pattern

DC = dendritic cell

Ig = immunoglobulin;

LDL= low-density lipoprotein;

NK = natural killer;

NKT = natural killer T cell;

oxLDL = oxidatively-modified LDL

PAMP = pathogen-associated molecular pattern;

PC = phosphorylcholine

TLR = Toll-like receptor

Treg = regulatory T cell

VEGFR = vascular endothelial growth factor

RANKL= receptor activator of nuclear factor kappa-B ligand

CTB= cholera toxin B subunit

VLP=virus like particles

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