CONSTRUCTION OF NOVEL VACCINES ON THE BASIS OF VIRUS-LIKE PARTICLES pdf

1: Virus Like Particles (VLPs) - Creative Biostructure

Construction of Novel Vaccines on the Basis of Virus-Like Particles The human CTL epitope at aa 18 - 27 deserves special notice because it is regarded as a prom ising HBV vaccine candidate.

Polio Vaccine - Immunization Action Coalition Kung ang pagsusumikap na maalis ang sakit mula sa mundo ay matagumpay, balang araw ay hindi na natin kakailanganin ang bakuna sa polio. Ngunit bago natin marating ang araw na iyon, kailangan nating patuloy na ipabakuna ang mga anak natin. Virus-like particles are multimeric, sometimes multiprotein nanostructures assembled from viral structural proteins and are devoid of any genetic material. VLPs present repetitive highdensity displays of viral surface proteins. Importantly, they contain functional viral proteins responsible for cell penetration by the virus, ensuring efficient cell entry and thus tissue-specific targeting, determined by the origin of the virus. The foremost application of VLPs is in vaccinology, where they provide delivery systems that combine good safety profiles with strong immunogenicity and constitute a safe alternative to inactivated infectious viruses. These stable and versatile nanoparticles display excellent adjuvant properties capable of inducing innate and cognate immune responses. They present both, high-density B-cell epitopes, for antibody production and intracellular T- cell epitopes, thus inducing, respectively, potent humoral and cellular immune responses. Uptake of VLPs by antigen-presenting cells leads to efficient immune responses resulting in control of pathogenic microorganisms. These naturally occurring bionanomaterials often emulate the conformation of authentic viruses. VLPs contain repetitive high-density displays of viral surface proteins and as such are a highly adaptable platform for various applications. Importantly, they contain functional viral proteins responsible for cell penetration by the virus, which ensures efficient cell entry. The foremost application of VLPs is in vaccinology, whereby they provide delivery systems that combine good safety profiles with strong immunogenicity. Traditionally, vaccines against viral diseases have been prepared from attenuated or inactivated infectious viral strains. VLPs, devoid of the viral genome but able to penetrate cells and tissues, are a much safer alternative. Moreover, they provide a polyvalent structure that can accommodate multiple copies of antigens and, in addi- tion, are able to stimulate immune cells. Finally, they ensure tissue-specific targeting, determined by the origin of the virus. They present both, highdensity B-cell epitopes for antibody production and intracellular T-cell epitopes, thus inducing respectively, potent humoral and cellular immune responses Beyer et al. Indeed, VLPs show potent adjuvant activity enhancing the immunogenicity of weakly immunogenic peptides and proteins. Mature DCs are the key antigen presenting or antigen-presentig step APC that efficiently mediate antigen transport to lymphoid tissues for the initiation of T cell responses and induction of cell-mediated immunity Zinkernagel, Uptake of the VLPs by APC leads to efficient immune responses and results in the control of pathogenic microorganisms. Like parental viruses, VLPs can be either non-enveloped or enveloped, and spherical or filamentous Fig. Analysis of the published data performed by Zeltins revealed that at least VLPs have been constructed from viruses belonging to 35 different families. They form spontaneously during the viral cycle or in heterologous systems upon expression of one or several viral structural proteins. Depending on the complexity of the VLPs, they can be produced from appropriate recombinant vectors in either prokaryotic or eukaryotic expression systems, or assembled under cell-free conditions. The yield of VLPs production is rather high and even in eukaryotic systems can approach the expression efficiency comparable to that observed for bacterial expression systems. Due to their high molecular weight, VLPs are purified from extracts of expressing cells by sucrose density centrifugation, usually followed by an additional step to remove cellular components loosely attached to them. Chroboczek and others Figure 1. Five L1 monomers form spontaneously one pentameric L1 capsomer, 72 of such capsomers self-assemble into a VLP. From German Cancer Research site http: Electron microscopy EM reproduced from the site of the Vilnius University http: After Nilsson et al. The 3 domains, S, P1, and P2 are colored blue, yellow, and red, respectively. After Guu et al. F Bluetongue virus-like VLPs, requiring the

simultaneous expression of four distinct proteins in varying amounts. After Thuenemann et al. After Smith et al. After Perrone et al. When large protein domains are needed as an antigen, they might be more difficult to display on VLPs, as such insertions may be incompatible with the VLP assembly. In that case, a chemical conjugation can be a solution. Some VLP vaccines have been licensed and commercialized, others have entered clinical development, while many are in the proof-of-hypothesis stage. Hepatitis B virus infection is one of the most common human diseases. Each year over one million people die from HBV-related chronic liver diseases. Hepatitis B vaccine became the first recombinant protein-based vaccine for humans, approved by the Vol. It is based on a recombinant HBV surface antigen HBsAg , which upon production in yeast or mammalian cells forms 22nm spherical VLPs that are adsorbed on an aluminum hydroxide gel Greiner et al. Contrary to mammalian-derived HBsAg particles, yeast-derived particles contain unglycosylated S protein. Highly hydrophobic S protein in HBsAg VLPs is in tight association with lipids that have been shown to be responsible for the antigenic properties of HBsAg particles, stabilizing their structure and protein conformation. Thus, these VLPs exhibit a lipoprotein-like structure with an ordered and rather rigid lipid interface and a more hydrophobic and fluid inner core. Protein molecules included in each particle display a protruding part and another one deeply inserted into the lipid core Greiner et al. A course of 2â€”3 vaccine injections is given intramuscularly, the second injection at least one month after the first one and the third injection being administered up to six months after the first one. The induced anti-HBV antibodies and immune system memory provide immunity to hepatitis B infection. Engerix-B contains purified surface antigen HBsAg of HBV expressed in yeast, and although it is not glycosylated, it is immunogenically and physically similar to the antigen isolated from the plasma of chronic carriers Drug master file at http: Protection lasts for at least 25 years in cases of adequate initial response to vaccination, but some guidelines now recommend a single booster after 5 years. The hepatitis B vaccine was found to be generally safe although the Engerix B vaccine appeared to triple the risk of CNS inflammatory demyelination in infant boys Mikaeloff et al. A possible culprit is thiomersal, a mercury-containing vaccine preservative that is currently being phased out in many countries. About 30 to 40 types of HPV can be transmitted through sexual contact, via the anogenital region. Persistent infection with high-risk HPV types â€” different from the ones that cause skin warts â€” may progress to precancerous lesions and invasive cancer. Cervical cancer is an important public health problem worldwide, especially in developing countries. Two kinds of prophylactic HPV vaccines exist: These vaccines contain in addition adjuvants such as alumina aluminum hydroxide and AS04 with monophosphoryl lipid A MPL in Cervarix, and amorphous aluminum hydroxyphosphate sulfate in Gardasil. Such vaccines are highly efficacious if given before exposure to HPV, i. The current duration of protection is 8. Research is also directed towards the development of a prophylactic L2 vaccine and therapeutic vaccines active after infection. However, this vaccine, although it elicited antibodies against p24 and Ty was not able to slow the progression of HIV-1 disease Lindenburg et al. This vaccine decreased the blood pressure of Ang II-induced hypertensive mice Chen et al. Some clinical trials concern investigation of anticancer VLP vaccines. Upon administration, this vaccine may activate the immune system to exert a specific cytotoxic T lymphocyte CTL response against cancer cells expressing Melan A antigen that is upregulated in most melanomas. Indeed, Melan A vaccination resulted in an increase of T-cells at the injection site Goldinger et al. Split vaccines are produced in the same way as whole virus vaccines, but virus particles are disrupted using detergents. Subunit vaccines consist of purified HA and NA proteins, with the other viral components removed. Growing and preparation of such vaccines is rather long and expensive. Development of recombinant HA-based vaccines might help to overcome these limitations, but some doubts persist concerning the effectiveness of vaccines based only on HA. Presumably they are not able to elicit cell-mediated immunity and thus to immunize against different influenza strains. Influenza VLPs composed of more than one influenza protein could conceivably provide a solution to these shortcomings. For this purpose, corresponding influenza genes are usually cloned into the baculovirus vectors in order to produce multipro- J. Chroboczek and others tein influenza VLPs in insect cells. Assembled VLPs are then secreted as enveloped,

pleomorphic particles Fig. These vaccines were shown to display conformation-dependent antigenic epitopes associated with HA oligomers and induced robust anti-HA and anti-NA antibody responses in clinical studies. In the latter case the vaccine consists of recombinant H5 and N1 proteins produced in a plant-based expression system and assembled into virus-like particles together with the adjuvant glucopyranosyl Lipid A GLA-AF or with the alum adjuvant. None of the influenza VLP vaccines has been approved so far. It appears that in these trials, apart from investigating the immune response, emphasis is placed on the use of appropriate adjuvants in order to obtain a more pronounced response of the immune system. This is surprising since it has been demonstrated that VLPs display excellent adjuvant properties, capable of inducing innate and cognate immune responses. However, it is plausible that since polymorphous, asymmetric influenza VLPs do not contain repetitive high-density viral surface proteins like the homogenous symmetrical VLPs, they are not capable of presenting epitopes in a way required for eliciting a strong immune response. Indeed, it has been shown that when the cytotoxic T lymphocyte epitope, a peptide derived from influenza A virus, was presented on a symmetrical platform formed of SV40 VLP, influenza-specific CTLs were induced, and heterosubtypic protection against influenza A viruses was achieved without the need of adjuvants Kawano et al. When constructing a novel influenza vaccine, we used the VLP platform built from a protein derived from the adenovirus Ad for carrying the epitopes of influenza virus, with the goal of establishing immunity against influenza and not against Ad infection Szurgot et al. Adenoviral dodecahedra are non-enveloped symmetrical VLPs built from 12 pentons, which are non-covalent complexes composed of pentameric penton bases and trimeric fiber proteins, both proteins being responsible for intracellular penetration of the virus Fig. These VLPs, smaller than the virus of origin, are generated during the life cycle of certain adenovirus serotypes, including human adenovirus serotype 3 Ad3 , where they participate in spread of progeny virus through loosening of tight junctions Fender et al. These so called dodecahedra-fibre DFs of 4. Formation of these particles is solely due to penton base interactions, as attested, upon expression of the penton base protein alone, by the formation of dodecahedra devoid of fibers, with molecular weight of 3. Stability of the dodecameric structure does not depend on disulfide bridges or cations as in other VLPs Simon et al. Instead, the major mechanism of stability lies in interlocking of the 60 N-terminal domains derived from 12 pentameric penton bases, which results in formation of a strong net stabilizing the VLP Szolajska et al. Dds retain integrity under different physicochemical conditions, which enables their convenient storage as well as attachment of therapeutic agents Zochowska et al. Dds efficiently penetrate cellular plasma membrane and access the cytoplasm, whereupon up to particles can be observed in one cell in vitro Garcel et al. This extraordinary internalization capacity makes Dd a very attractive delivery tool. Ad3 Dd inventors first proposed the use of adenoviral dodecahedron for human gene therapy as an alternative to whole adenovirus Fender et al. Later, both DF and Dd have been used as vectors for direct intracellular delivery of anti-cancer agents covalently attached to the vector surface or as facilitators of drug delivery to tumors Fender et al. Intracellular delivery, important in both therapeutic and fundamental applications, faces two major challenges: It appears that adenoviral Dd displays properties of the virus of its origin that ensures a remarkably efficient penetration without endosomal sequestration. Another possible application of dodecahedron, typical for VLPs, is in vaccine construction as a delivery platform for foreign antigens.

CONSTRUCTION OF NOVEL VACCINES ON THE BASIS OF VIRUS-LIKE PARTICLES pdf

2: PEI Press Releases Paul-Ehrlich-Institut - Modular virus-like particles as vaccine platform?

Construction of novel vaccines on the basis of the virus-like particles: Hepatitis B virus proteins as vaccine carriers. In Y. E. Khudyakov (Ed.), Medicinal protein engineering (pp.). Boca Raton: CRC Press.

Vaccination is the most effective way to reduce rates of morbidity and mortality caused by influenza viruses. Frequent genetic shift and drift among influenza-virus strains with the resultant disparity between circulating and vaccine virus strains limits the effectiveness of the available conventional influenza vaccines. One approach to overcome this limitation is to develop a universal influenza vaccine that could provide protection against all subtypes of influenza viruses. Moreover, the development of a novel or improved universal influenza vaccines may be greatly facilitated by new technologies including virus-like particles, T-cell-inducing peptides and recombinant proteins, synthetic viruses, broadly neutralizing antibodies, and nucleic acid-based vaccines. This review discusses recent scientific advances in the development of next-generation universal influenza vaccines. Introduction Seasonal influenza viruses circulate worldwide, spread easily from person to person, and result in the hospitalization of three to five million individuals worldwide each year 1 , 2. These infections are responsible for ,â€", deaths, mainly among those with immature or compromised immunity, e. However, all age groups can be affected, and the impact can increase significantly with an emergent human influenza-virus strain during a pandemic 3. Influenza viruses are constantly evolving through genome mutation and reassortment. Pandemic influenza has claimed millions of lives globally; the â€" H1N1 pandemic alone claimed 50â€" million lives 4 , 9. The genome of the influenza virus consists of 8 single-stranded RNA segments encoding 11 proteins, including the surface glycoproteins hemagglutinin HA and neuraminidase NA. The human influenza virus is classified into three distinct types A, B, and C, on the basis of major antigenic differences. Influenza A and B viruses are responsible for annual human epidemics, whereas the influenza C virus is known to infect both humans and pigs and causes very mild upper respiratory tract disease in humans 10 , Vaccination is an effective approach for the control and prevention of influenza. Currently, trivalent inactivated-virus TIV vaccines against seasonal influenza viruses are the most frequently used influenza vaccines with a steady migration to tetravalent or quadrivalent vaccines QIV. TIV vaccines are composed of three influenza-virus strains 2 A subtypes, H3N2, H1N1, and 1 B type selected primarily on the basis of forecasted prevalence during the targeted influenza season. QIV vaccines include the second B lineage TIV vaccines come in three different formulations; the whole virus, split virus, and subunit. Whole-virus vaccines are prepared from embryonated chicken eggs, inoculated with virus, followed by chemical inactivation and purification steps. Split-virus vaccines are prepared by treatment of influenza-virus particles by diethyl ether or detergent e. Subunit vaccines contain HA and NA proteins and are prepared by applying further purification steps with detergents or diethyl ether 19 , A recombinant HA rHA -based subunit vaccine has been approved recently; and this vaccine showed higher seroconversion rates in healthy adults including elderly adults, compared with a non-recombinant TIV vaccine Inactivated vaccines primarily induce protective antibodies against epitopes on HA. Split and subunit formulations are used more frequently than the other formulations and both induce comparable immunity. Whole-virus formulation has been less preferred because of a potential association with increased reactogenicity In the USA, inactivated vaccines are approved from 6 months of age, and rHA formulations are approved for those 18 years of age and older. Live-attenuated influenza vaccines LAIV mimic aspects of natural influenza-virus infection, but without virus pathogenicity, and induce both humoral and cell-mediated immunity Potential causes of reduced effectiveness of A H1N1 pdm09 in LAIV are evidenced by lower replication in alveolar cell lines and reduced binding to sialic acid receptors receptors for influenza-virus binding Nevertheless, both TIV and QIV vaccines require reformulation with new influenza strains each influenza season, and their effectiveness is not guaranteed because it is primarily dependent on the match between the forecasted strains in the vaccines and the actual prevalent strains in circulation. Is there a need for a Universal Influenza Vaccine? Influenza-virus

evolution is typically considered in terms of antigenic driftâ€”the occurrence of minor changes in the virus genotype within the same virus typeâ€”and antigenic shiftâ€—emergence of new and potentially pandemic strains by the reassortment of viral genomes 13 , 30 , Seasonal antigenic drifts usually consist of minor amino acid mutations in the HA globular head domain that may result in some changes to the pattern of glycosylation in this domain 32 , These changes in the HA-glycosylation pattern affect the infectivity of the virus and its ability to escape from antibodies elicited by previous strains or vaccines As a result, current influenza vaccines, which provide antibody-dominated subtype-specific protection against influenza viruses, need to be updated and produced every year before each influenza season fall to winter period in the northern hemisphere because of mismatches between the vaccine strains and the prevalent circulating virus subtypes. The adult human population has some levels of cross-protective antibodies against circulating seasonal influenza strains due to previous virus exposures or vaccinations, therefore, developing only mild disease symptoms upon infection 34 , By contrast, the absence of preexisting immunity to an emerging pandemic strain can lead to severe pulmonary infections and death. Adjuvants are formulated with the antigenic component of the vaccine to increase immunogenicity. Seasonal and pandemic influenza vaccines adjuvanted with oil-in-water emulsions AS03 or MF59, in comparison with non-adjuvanted vaccines, elicit higher titers of neutralizing antibodies with higher affinities and broader cross-reactive specificities to other influenza types and promote the persistence of long-lasting memory B cells in subjects from varied age groups 36 â€” Compared with existing cell-derived and recombinant influenza vaccines, conventional egg-based influenza vaccines are usually effective and have some limitations: Studies have shown that cultivation of influenza virus in fertilized chicken eggs often results in adapting mutations in HA and that can alter virus antigenicity and may sometimes decrease efficacy of influenza vaccines 44 â€— Mammalian cell-derived influenza vaccine provide several advantages over egg-based vaccines including influenza virus propagated in mammalian cell culture system remain unchanged, provide better or comparable protection, fast production and does not require extensive advance planning, availability of controlled production system involving bio-reactors, higher yield, faster production cycle and production can be easily scaled up by adding bioreactors 43 , 47 , A recent study has shown comparable yield of virus from 1,l bioreactor, 12, roller bottles or 30, chicken eggs These collective advantages increase cost-effectiveness of cell-based influenza vaccines. Despite several benefits, cell culture system also have some limitations including, scaling-up different cell lines is biggest challenge, obligation of expensive new facilities and extensive adventitious virus testing required 43 , These collective constraints call for new design and development of unique universal influenza vaccines that could provide long-lasting immunity against all subtypes of influenza viruses, and significantly reduce the disease burden associated with influenza-virus infections. Properties of Target Antigens for Vaccine Development Antibodies that neutralize influenza-virus entry into host epithelial cells typically target HA, the main surface glycoprotein of the virion. HA is composed of globular and stalk domains and is expressed as a trimer at the surface of the virion. At the initial stage of infection, when influenza virus enters the respiratory tract, HA binds to sialic acid residues present on the surface of epithelial cells and allows the virus to be engulfed by the cells The globular domain is highly variable across subtypes, whereas the stalk domain is much more conserved. Hence, the stalk domain is a potential target for the development of a universal influenza vaccine 51 , However, HA-head-specific antibodies have a greater neutralizing capacity than cross-reactive HA-stalk-specific antibodies, which are found at very low frequency 53 , Neuraminidase is a tetrameric glycoprotein present on the surface of influenza viruses 55 , NA is important at the pre-infection, post-infection, and re-infections stages. NA is involved in the release of newly produced viruses from host cells and prevents the aggregation of virus particles by cleavage of sialic acids from respiratory tract mucins 57 â€— NA may also participate in the fusion of viral and cell membranes 60 and facilitates budding of new virions by restricting their aggregation NA is generally less immunogenic and lacking monodominant properties and therefore a less attractive target than HA Despite this, NA has been used as a vaccine candidate in various vaccine formulations and as a target of various antiviral drugs, because of a lower rate of antigenic

drift than HA 57 , 59 , 62 â€” Apart from HA and NA surface glycoproteins, the matrix proteins 1 and 2 M1 and M2, respectively , are encoded by influenza-virus genes with partially overlapping reading frames 66 , M1 is a major constituent of the viral capsids and M2 functions as a proton channel in viral envelope. Studies suggest that the amino acid sequence of M2 extracellular domain M2e is conserved in influenza A viruses IAV and is, therefore, a target for the development of a universal influenza vaccine 68 , M2e-containing vaccines have shown encouraging results in animal models 68 â€” Nucleoprotein NP is an influenza-virus protein that is associates with viral RNA and essential for viral assembly 3. NP is highly conserved across influenza subtypes and is a potential antigen for a universal influenza vaccine VLPs mimic certain aspects of the conformational, structural and antigenic properties of native influenza viruses, making VLPs a useful platform for vaccine development 74 , The development of certain universal influenza vaccines have utilized the VLP platform because VLPs have self-assembly properties, VLPs can comprise more than one protein or protein chimeras cVLPs and produced in a heterologous expression system, and VLPs can be formulated with adjuvants 74 , VLPs activate innate immunity by stimulating antigen presenting cells and this can lead to the induction of effective B- and T-cell immunity specific to those antigens present in the VLP 75 , 77 â€” It is reported that highly organized and repetitive protein epitopes can directly activate B-cells by cross-linking B-cell receptors Approaches for universal influenza vaccine development. VLPs produced by cloning of HA, NA, and M1 gene sequences of influenza virus into the expression vector followed by transfection in to insect cells. MDCK cells are transfected with plasmid DNA encoding influenza-virus backbone genes and error-free HA and NA gene segments, synthesized by an enzymatic and cell-free assembly technique. After transfection, vaccine viruses are rescued from MDCK cells. Influenza genes encoding HA protein are placed in to the carrier virus vector to express HA protein on the virus surface. Virus-like particles have been used in strategies for presenting epitopes from numerous different virus subtypes and engineered epitopes derived from conserved regions of viral proteins 82 â€” In a recent mouse study, Schwartzman et al. After intranasal vaccination, mice were protected against lethal influenza-virus challenge from homologous same strains as in the vaccine; H1N1 and H7N1 , intrasubtypic antigenically different strains of the same subtypes; H5N1 and H7N9 , and heterosubtypic subtypes not included in the vaccine; H2N1, H6N1, H10N1, and H11N1 Hence these results suggested that this approach was suitable for developing an effective clinical vaccine against currently circulating influenza strains and potential pandemic influenza strains. In other studies, the highly conserved HA-stalk domain was used in VLPs to induce broadly cross-reactive protective immunity 84 , 88 , Although viral-surface-protein-based VLPs have appeared promising tool for developing universal vaccine, some of the strategies have also included M2e protein. M2e is a very promising target for universal vaccine development because of the conserved nature of the protein. M2e has been included in VLPs as a genetically engineered fusion protein e. Although the abovementioned VLP strategies have shown promise in animal models, some of the vaccine formulations have required adjuvants to enhance VLP immunogenicity. Some of these adjuvants have been based on toll-like receptor TLR ligands. TLRs are structurally conserved molecules that recognize ligands of microbial origins. Engagement of TLRs on innate cells results in the production of pro-inflammatory cytokines and chemokines, and an enhanced ability to eliminate the pathogens The advantages of VLP-based vaccines are that the immune system of the host recognizes VLPs in a similar way to the original virus particles, and chimeric VLPs induce highly effective cross-reactive heterosubtypic immune responses The existence of several licensed prophylactic VLP-based vaccines e. Broadly Reactive Antibody- and T-Cell-Inducing Strategies Antibody- and T-cell-mediated immune responses are the keys components of adaptive immune system. B cells are the source of antibodies and antibody-based immunotherapy is a very efficient approach in the treatment of various diseases caused by microbial infections Most current seasonal and pandemic influenza vaccines induce high-titers of functional and neutralizing antibodies against HA and NA proteins. Because the HA-head domain tends to contain epitopes that are immunodominant over those in the stalk, Krammer et al. Repeated vaccinations with chimeric HA constructs containing the same stalk domain but different heads, induced stalk-directed antibodies that mediated

heterotypic immunity In addition, an inactivated split-virion vaccine adjuvanted with AS03 derived from a recombinant virus expressing an IAV group 1 chimeric HA has been evaluated in mice and shown to induce protective H1 stalk-reactive antibodies Ferrets are excellent experimental animal models for the investigation of influenza-virus pathogenicity and immunobiology because of their susceptibility to influenza-virus infection and ability to develop disease symptoms similar to humans â€” Sequential immunization studies with chimeric HA generated by exchanging head domains and retaining same HA-stalk domain , successfully induced broadly reactive antibody responses in ferrets â€” An alternative strategy based on broadly reactive monoclonal antibodies could confer cross-protective and long-lasting immunity against influenza-virus infections. Studies on monoclonal antibodies have shown that conserved regions exist within the HA head domain. This antibody fragment neutralized H1N1 and H3N2 strains. However, the parental antibody neutralized many more strains from H1, H2, H13, and H16 subtypes suggesting that the avidity associated with bivalent interactions of the antibody and HA molecules contributed to enhancing cross-reactivity As discussed earlier, the stalk region of HA is highly conserved and stalk-specific neutralizing antibodies cross-react with different virus subtypes.

CONSTRUCTION OF NOVEL VACCINES ON THE BASIS OF VIRUS-LIKE PARTICLES pdf

3: Virus-like particles as vaccine - Acta Biochimica Polonica - PDF Free Download

Construction of novel vaccines on the basis of the virus-like particles: hepatitis B virus proteins as vaccine carriers, p. In Y. E. Khudyakov (ed.), Medicinal protein engineering. CRC Press Taylor & Francis Group, Boca Raton, FL.

VLPs are used in studies to identify viral protein components. Therapeutic and Imaging Agents[edit] VLPs are a candidate delivery system for genes or other therapeutics. VLPs contain repetitive, high density displays of viral surface proteins that present conformational viral epitopes that can elicit strong T cell and B cell immune responses. In early clinical trials, VLP vaccines for influenza appeared to provide complete protection against both the Influenza A virus subtype H5N1 and the flu pandemic. These are important in phytopathology , as they can cause hypovirulence in some species of phytopathogenic fungi. However, because of their hydrophobic domains, membrane proteins are difficult to manipulate outside of living cells. Lipoparticles can incorporate a wide variety of structurally intact membrane proteins, including G protein-coupled receptors GPCR s, ion channels and viral Envelopes. Lipoparticles provide a platform for numerous applications including antibody screening, production of immunogens and ligand binding assays. This is rational as long as the VLP assembly takes place inside the host cell in vivo , though the self-assembly event was found in vitro from the very beginning of the study about viral assembly. In some cases a protein of interest can be genetically fused to the viral coat protein. This method has shown to be very effective at directing the immune response against the attached molecule, thereby inducing high levels of neutralizing antibody titers and breaking immune self-tolerance. Current Opinion in Molecular Therapeutics. A robust, semisynthetic targeted drug delivery platform. Dual-surface-modified bacteriophage MS2 as an ideal scaffold for a viral capsid-based drug delivery system. Delineating key epitopes by dissecting the capsid proteins". American Society for Microbiology. Retrieved June 8, Archived from the original PDF on Journal of Biomolecular Screening. Philosophical Transactions of the Royal Society B.

CONSTRUCTION OF NOVEL VACCINES ON THE BASIS OF VIRUS-LIKE PARTICLES pdf

4: Virus-like particle - Wikipedia

Construction of novel vaccines on the basis of virus-like particles: hepatitis B virus proteins as vaccine carriers By Paul Pumpens, Rainer Ulrich, KÄ™stutis Sasnauskas, Andris Kazaks, Velta Ose and Elmar Grens.

Notably, several VLP-derived vaccine candidates have been successfully obtained by our cutting-edge VLPs technique platform. Our seasoned scientists are pleased to offer the best service and the most qualified products to serve every specific demand from our customers all over the world. Virus-like particles VLPs are artificial protein structures with the similar overall structure to their corresponding native viruses. They resemble viruses with self-assembly property but losing original infectious ability due to the genome modifications. VLPs are symmetrically built from hundreds of coat proteins, which can be genetically engineered to present a regular arrangement of epitope chains on the desired positions of the outer surface. Compared with monomeric or oligomeric protein carriers, VLPs are able to provide not only a higher density of foreign proteins per particle but also support a distinctive three-dimensional conformation, which is especially important for the presentation of conformational epitopes. Currently, VLPs has been recognized as one of the most promising and extensively studied molecular carriers or nanoparticles, for a variety of applications. Since the s, over VLPs originated from microbial, insect, plant and mammalian viruses have been constructed and characterized. One crucial step for successful VLPs production lies in the proper choice of appropriate expression host system. In general, selection of an ideal system depends on many factors, e. Creative Biolabs has established a broad range of well-established expression platforms, which can meet diverse research and industrial objectives: VLP Production in E. Furthermore, this system can offer proper membrane protein folding and assembly, which has manifested superior reliability and high success rate. In fact, some vaccines derived from VLPs have been used as medical products commercially, and other VLP-based products are already at different stages of the clinical study. Several remarkable advantages have been achieved in the development of VLPs as gene therapy tools and new delivery nanomaterials. Generally speaking, VLPs have great potential for a number of applications including: Our team has vast experience in designing and developing VLP products to deliver integral antigens with both arms of the adaptive immunity. Our VLPs-based vaccine formulation is able to enhance the antigen immunogenicity remarkably by using adjuvant aluminum salts. Moreover, special methods will be employed to reduce preservative and VLPs aggregation. VLPs can serve as a perfect immunogen which can elicit highly potent immune responses in vivo. We have successfully raised many antibody binders using VLP immunization strategy, particularly against viral antigens or membrane antigens. Our team now provides highly purified and stable VLPs containing a great variety of membrane proteins in the form of lipoparticles to satisfying different demands such as ligand binding assays, antibody screening, and immunogen production. We can develop sophisticated VLPs to enable highly specific cell targeting. Alternative approaches are available including vitamins, peptides, nucleic acids aptamers , and carbohydrates proteins mainly antibodies. Creative Biolabs now offers state-of-the-art virus-like particles VLPs service based on our unparalleled technology platform. Please feel free to inquire us for further discussions. Vaccination and delivery systems. Biopolymers, 3 , Protein delivery using engineered virus-like particles. Proceedings of the National Academy of Sciences, 41 , Josefsberg J O, Buckland B. Biotechnology and bioengineering, 6 , Biotechnology and bioengineering, 3 , Chen Q, Lai H. Plant-derived virus-like particles as vaccines Plant-derived virus-like particles as vaccines. Construction of a baculovirus-silkworm multigene expression system and its application on producing virus-like particles. PloS one, 7 3 , e Construction and characterization of virus-like particles: Molecular biotechnology, 53 1 , Virus-like particles as a highly efficient vaccine platform: Vaccine, 31 1 ,

CONSTRUCTION OF NOVEL VACCINES ON THE BASIS OF VIRUS-LIKE PARTICLES pdf

5: Frontiers | Novel Platforms for the Development of a Universal Influenza Vaccine | Immunology

Pumpens P. et al. Construction of novel vaccines on the basis of the virus-like particles: Hepatitis B virus proteins as vaccine carriers in Medicinal Protein Engineering (ed. Khudyakov Y.), (CRC Press, Taylor & Francis Group,).

VLPs capture conformationally-intact membrane proteins directly from the cell surface, enabling these complex proteins to be manipulated as soluble proteins. Sample kits are also available for purchase for preliminary application testing. Virus-like particles VLPs have evolved to become a widely accepted technology, especially in the field of vaccinology. In fact, some VLP-based vaccines are currently used as commercial medical products, and other VLP-based products are at different stages of clinical study. Several remarkable advantages have been achieved in the development of VLPs as gene therapy tools and new nanomaterials. In recent years, the technologies develop very fast that are used to characterize the structural integrity, stability, and components, including the encapsidated nucleic acids, of newly synthesized VLPs. Moreover, some of the modifications that are required to construct VLP-based carriers of viral origin with defined properties can be provided. VLPs have been produced from components of a wide variety of virus families including Parvoviridae e. HIV , Flaviviridae e. Hepatitis C virus and bacteriophages e. VLPs can be produced in multiple cell culture systems including bacteria, mammalian cell lines, insect cell lines, yeast and plant cells. The understanding of self-assembly of VLPs was once based on viral assembly. This is rational as long as the VLP assembly takes place inside the host cell in vivo , though the self-assembly event was found in vitro from the very beginning of the study about viral assembly. Study also reveals that in vitro assembly of VLPs competes with aggregation and certain mechanisms exist inside the cell to prevent the formation of aggregates while assembly is ongoing. Attaching proteins, nucleic acids, or small molecules to the VLP surface, such as for targeting a specific cell type or for raising an immune response is useful. In some cases, a protein of interest can be genetically fused to the viral coat protein. However, this approach sometimes leads to impaired VLP assembly and has limited utility if the targeting agent is not protein-based. This method has shown to be very effective at directing the immune response against the attached molecule, thereby inducing high levels of neutralizing antibody titers and breaking immune self-tolerance. VLPs provide an alternative to living cells, membrane preparations, and detergent-solubilized proteins by offering concentrated membrane proteins in their native conformation. VLPs are used throughout drug and antibody discovery and characterization, and have been integrated into a wide variety of existing platforms.

6: Medicinal Protein Engineering - CRC Press Book

A multivalent vaccine candidate against hepatitis B virus (HBV) and hepatitis C virus (HCV) infections was constructed on the basis of HBV core (HBc) virus-like particles (VLPs) as carriers.

7: Virus-Like Particles (VLPs) - Creative Biolabs

Human vaccines against three viruses employ recombinant virus-like particles (VLPs). VLPs are excellent vaccine antigens because they faithfully mimic the native virions. Post-purification reassembly of VLPs can improve antigenicity and vaccine efficacy.

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