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Phage display—A powerful technique for immunotherapy

2. Vaccine delivery

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Phage display is a powerful technique in medical and health biotechnology. This technology has led to formation of antibody libraries and has provided techniques for fast and efficient search of these libraries.

The phage display technique has been used in studying the protein-protein or protein-ligand interactions, constructing of the antibody and antibody fragments and improving the affinity of proteins to receptors.

Recently phage display has been widely used to study immunization process, develop novel vaccines and investigate allergen-antibody interactions. This technology can provide new tools for protection against viral, fungal and bacterial infections. It may become a valuable tool in cancer therapies, abuse and allergies treatment. This review presents the recent advancements in diagnostic and therapeutic applications of phage display. In particular the applicability of this technology to study the immunization process, construction of new vaccines and development of safer and more efficient delivery strategies has been described.

Introduction

Phage display is a tool for molecular evolution, enzymology and study of antibodies. Moreover, it has been used in analyzing the protein-protein or protein-ligand interactions. This technique allows to identify and develop modulators of receptors and enzymes,[1-3] (to) determine the substrate specificity[4,5] and (to) obtain stable proteins and enzymes for biotechnological and analytical applications.[6-8] Antibodies and antibody fragments originating from phage display are widely used in therapeutic development and diagnostics.[9-11] They are commonly used in methods such as ELISA,[12] immunoblotting,[13] immunofluorescence microscopy,[14] affinity chromatography,[15] flow cytometry,[16] microarrays assays,[17] hemagglutination assays,[18] bead based assays,[19] proximity ligation assays,[20,21] molecular imaging,[22] lateral flow strip assays,[23] immuno-PCR[24] and fluorescence resonance energy transfer (FRET).[25] Molecules displayed on phage surface were considered as direct diagnostic agents.[26] It was reported that by using the phage display technology, scFv fragment that recognizes glycated α7 subunit of the proteasome was obtained. This antibody fragment was defined as a tool for analyzing a marker of proteasomal malfunction, cellular viability, and a potential marker of aging.[27]

Antibody phage display provides direct access to the genetic information of the binder, allowing a fast adaptation of the antibody format to the desired diagnostic assay.[12,13,17,22] The sensitivity of the diagnostic test could be increased by displaying on phage surface many copies of antibody fragments. Also the usage of the secondary antibodies with specificity for phage coat proteins could improve assay quality.

Phage display enables better understanding of the immunization process, therefore utilization of this technique in vaccine development has increased recently. This technology enables searching of immunogenic peptide sequences and constructing of novel vaccines. The phage display technology also provides new opportunities for vaccine delivery, which may lead to strengthening the effectiveness of immunization.

This review focuses on selected applications of phage display in immunization, vaccine development and investigation of allergen-antibody interactions, which can provide novel diagnostic and therapeutic agents.

Vaccine Delivery

Phage display is a powerful technique for designing novel vaccine delivery vehicles. With this method, phage display vaccine or phage DNA vaccine can be constructed. Also hybrid phage vaccine has been suggested. In the first model—the phage displayed vaccine, virions contain the antigen encoding gene which is expressed in fusion with coat protein. Antigen could be also attached to phage surface with artificial linker.[28,29] In phage DNA vaccine model, DNA vaccine that contains antigen gene cloned into eukaryotic cassette is packed within bacteriophage virion. Eukaryotic cassette is a part of vector DNA which contains three main sequences: promoter, ORF (open reading frame) and 3' untranslated region often with polyadenylation site. It was constructed to allow proper gene expression and correct folding of

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eukaryotic proteins in prokaryotic cells. The predominance of phage vaccines over standard DNA vaccines or using antigens per se is primarily the fact that virion protects the vaccine and makes it more stable for administration (especially in oral vaccines), storage and transport. Moreover, phages have been reported as the adjuvant-like particles, therefore this method allows to achieve better results at lower doses than standard vaccination.[30,31] Phage vaccines give higher and less variable immune response compared with standard vaccines. The hybrid phage vaccine is supposed to induce effectively humoral and cellular response. This model allows to display not only antigen but also targeting molecule, thus it appears to have a potentially significant advantage for goal directed therapy.[32,33]

Predominance of phage vaccines is based on fundamental properties of the virus itself such as high stability in wide range of pH, which facilitates the application and distribution in addition to a low cost of phage particle production. Moreover, phages are unable to proliferate in eukaryotic cells, thereby their application is safe. Also phage vaccine application does not cause side effects,[34] although there are some disadvantages of using prokaryotic viruses as vaccine delivery vehicles. The main problem is to display correctly folded, active epitope in a concentration sufficient to elicit an immune response. Also the administration route of the vaccine must be considered because there is a risk that after oral distribution phages will infect intestinal flora.[35] There are several strategies that could lead to enhance the oral administration of phage vaccines. First, the use of non-lytic phage may reduce the risk of infection and the destruction of the natural intestinal flora. Moreover, virions with damaged tail fibers are incapable of infection, but still can serve as a vaccine delivery vehicle. Phages that are stable in the gastro-intestinal tract could be successfully used in oral administration. although it is still more common to provide vaccines by subcutaneous or intramuscular injections.

Anti-cancer vaccines. To date, many anti-cancer vaccines based on phage display technology have been reported.[36-38] In phage DNA vaccines, cytokines, chemokines, costimulatory molecules and pathogen genes could prime the immune system. It was reported that the domain I fragment of pIII protein expressed as a fusion with an scFv can enhance T helper 1 humoral and cell-mediated antigen-specific immune response.[39] Moreover, $CD8^+$ cytotoxic T-lymphocytes (CTL), that recognize tumor-associated antigenic epitopes expressed by human leukocyte antigen (HLA) class I molecules on the cancer cells, can be primed by vaccination.[40] The best target antigens are proteins such as telomerase, tyrosinase, gp100, MAGE, Melan-A/MART, MUC1, CEA, p53, Her-2/neu, survivin or Ras, which level is significantly different in cancer cells than in healthy tissue.[41] The melanoma antigen MAGE-A1 is expressed in more than 50% of hepatocellular carcinoma, metastatic melanoma, non-small cell lung carcinoma, esophageal squamous cell carcinoma. Interestingly, phage vaccination with protein pVIII fused epitope of tumor-specific antigen ($MAGE\text{-}A1_{161–169}$) prevents and suppresses melanoma tumor growth and also enhances the NK cells activity.[42] Moreover, vaccination with heat shock protein Hsp70-peptide complexes can induce protective immune responses. The method for identification of mimetics of this protein has been described. By the use of biopanning of a random phage display library, peptides that bind to Hsp70-peptide complexes from human breast carcinoma cells were identified. These peptides were used to identify Hsp70 mimetics, which could be used as modulators of the immune response against tumors.[43]

Anti-viral vaccines. Phages have been also investigated as anti-viral vaccine delivery vehicles.[32,44] Cytotoxic T-lymphocyte (CTL) is an important factor not only in anti-cancer but also in anti-virus strategies,[45,46] including HIV infection control.[47] Thereby, ability of CTL phage displayed epitope to induce specific CTL response has been widely investigated.

In the recent study, phage display has been used to isolate and enhance a T-cell antigen receptor (TCR) from the infected person's CTL. This TCR was specific for the SL9 peptide, an immunodominant HLA-A*02-restricted, HIVgag-specific SLYNTVATL sequence. It is noteworthy that the obtained high-affinity TCRs have targeted HIV-infected cells and have recognized all common escape variants of this epitope.[47]

Interestingly, the DNA fragment encoding a hepatitis B virus epitope $S_{28–39}$ was packed into phagemid vector pC89. Hybrid phage containing a pVIII gene with the CTL epitope insert was constructed using the VASM13 helper phage and the BALB/c (H-2d) mice were immunized. After 8 d of immunization a MHC class I restricted hepatitis B specific CTL response occurred.[48] The phage lambda display system has been used for construction and characterization of cDNA expression library of human hepatitis C virus (HCV). Several proteins displayed as fusion to the carboxy terminus of the phage lambda capsid protein D were accessible for interaction and affinity-selection with specific antibodies.[49]

Furthermore, herpes simplex virus 1 (HSV-1) glycoprotein D is essential for the virus attachment and entry. It was shown that inoculation of BALB/c mice with phage DNA vaccine containing (HSV-1) glycoprotein D cassette results in enhanced both humoral and cellular immune responses.[50]

Other studies have described the platform for peptide display based on virus-like-particles (VLPs) of the RNA bacteriophage PP7. This platform was utilized in displaying the human papilloma virus type 16 (HPV16), minor capsid protein L2 epitope. After intramuscular injection of HPV16 L2 epitope displayed on PP7 VLPs the robust anti-HPV16 L2 serum antibodies were generated. Thus, vaccine based on this protein could provide more comprehensive protection against infection by diverse HPV types.[51-53]

Although intensive research on anti-viral vaccines is conducted, much focused on a narrow range of diseases often associated with the appearance of tumors. It should be noted that the phage display technique has been used in the research on novel therapeutics that will specifically interfere with the transcription/replication complex of negative-strand RNA viruses (NSRV). Due to the high infectivity of these viruses and the possibility of calling epidemics and pandemics, this research is particularly important. NSRV can cause respiratory diseases (influenza virus, respiratory syncytial virus, measles and mumps

viruses), encephalitis (rabies virus, Hendra and Nipah viruses; Rift Valley fever virus) or hemorrhagic fevers (Ebola and Marbug virus, Crimean-Congo hemorrhagic fever virus, Lassa virus). It is noteworthy that the transcription/replication complex is similar for all NSRV, thus broad-spectrum anti-viral therapeutics could be developed. Panning of large libraries by the phage display technique has led to the identification of five promising peptides, two of which have potentially broad-spectrum activity.[54] Furthermore, it was described that mice immunized with phage displayed vaccine that contain a protective B cell epitope of human respiratory syncytial virus gained a complete resistance to this virus.[28]

Anti-parasite vaccines. Phage display strategies for anti-parasite therapeutics have been described.[55-58] One of them is based on an iterative subtraction strategy to identify potential vaccine antigens of *Brugia malayi*—the filarial parasites that cause lymphatic filariasis (a debilitating disease affecting over 120 million people in the tropical and sub-tropical countries). The cDNA library expressed on the surface of T7 phage was screened with human sera and five antigens (ALT-2, TPX-2, VAH, COX-2 and novel cuticular collagen Col-4) were identified. Vaccination of mice and jird with recombinant ALT-2 resulted in achieving high immunity level.[59] It is noteworthy that strategies for development of malaria vaccines have been reported. The abundant merozoite surface protein-1 (MSP-1) of *Plasmodium falciparum* has been successfully used in vivo as a protective immunogen.[55] Another vaccination approach to malaria is a phage displayed SM1 peptide that specifically binds to the same surfaces that are invaded by the malaria parasite and almost completely inhibits invasion of the midgut by ookinetes and invasion of the salivary glands by sporozoites.[56] Besides, host antibody response to the ring-infected erythrocyte surface antigen (RESA) from *P. falciparum* has been characterized by phage display library.[60]

Anti-bacterial vaccines. Mimetics of polysaccharides were obtained by the phage display method. This strategy can be used for anti-bacterial vaccine development. Phage display libraries have been utilized in identification of *Neisseria meningitidis* serotypes A, B and C. Moreover, peptides selected by screening random phage library against *Staphylococcus aureus* RNAIII-activating protein were able to elicit immune responses in murine models.[61,62] The mouse monoclonal antibodies (mAbs) against *Klebsiella pneumoniae* MrkD adhesin were obtained by the hybridoma technique and screened against phage-displayed random library which resulted in (QKTLAKSTYMSA) mimotope selection that was able to mimic immunological properties of the native epitope of *K. pneumoniae* MrkD.[63] Furthermore, lambda display library of DNA fragments from *Streptococcus pneumoniae* and *Mycoplasma pneumoniae* genome was applied in identification of epitope-containing fragments. This study demonstrated that *S. pneumoniae* epitope is conserved in all *Pneumococcus* serotypes and *S. mitis* strains, while it is absent in other *Streptococcus* strains. It also allows to confirm the immunogenicity *of M. pneumoniae* adhesins P1 and P30 and to identify four novel immunogenic polypeptides.[64] Moreover, immunization of maternal mice with the phage particles displaying recombinant anti-idiotypic Ab fragments resulted in obtaining the streptococcal infection immunity by the neonatal mice.[65]

Other studies focused on *Pseudomonas aeruginosa* have led to identification of outer membrane proteins encoding genes that are potential targets for anti-*P. aeruginosa* vaccine development.[66]

Anti-fungal vaccines. Strengthening the immune response against fungal infection has been intensively investigated. Specific epitope LKVIRK of *Candida albicans* heat shock protein 90 was genetically inserted into the phage major coat protein pVIII using a phagemid vector system and investigated in vivo in C57BL/6 mice as anti-fungal vaccine. Immunization led to achieve higher titers of epitope LKVIRK-specific serum IgG as compared with those immunized with heat-killed *C. albicans* (HK-CA).[67] Protective immune responses mediated by hybrid-phage expressing *Candida albicans* heat shock protein 90 epitope (DEPAGE) in C57BL/6J mice were also evaluated. This epitope, expressed as fusion with pVIII, has been reported to induce the specific antibody response, enhance delayed-type hypersensitivity (DTH) response, natural killer (NK) cell activity and concanavalin A (ConA)-induced splenocyte proliferation.[68] Phage display based method of identification of short peptide sequences that can distinguish *C. albicans* from other closely related species has been also reported.[69,70]

Anti-drug vaccines and abuse treatment. Addictions are a major societal and health problem and the addiction syndrome is similar between different drugs of abuse and could be described as a chronic relapsing brain disorder with neurobiological changes.[71] Recently, immunopharmacotherapy treatment of drug abuse has been widely discussed and anti-drug vaccines against methamphetamine,[72] phencyclidine, opiates, nicotine[73] and cocaine,[74] have become the object of intensive research.[75,76] Moreover, phage display peptide libraries and biopanning are considered a tool for early diagnosis and prognosis of chronic alcohol consumption.[77] Antibody fragments have been applied toanti-idiotypic cocaine vaccines, cocaine-specific scFv fragments, nicotine-specific IgG and methamphetamine-specific scFv.[72-74]

Phages ability to penetrate the central nervous system (CNS) was applied to generate phage displayed cocaine-binding proteins. This anti-cocaine antibodies block the psychostymulatory effects of cocaine. One of them is GNC92H2 phage displayed protein, which delivered intranassally might serve as anti-drug therapeutic.[75] The potential of this approach has been demonstrated, however the kinetic constant of this protein is insufficient for clinical treatment. Nevertheless, phage displayed enzymes such as butyrylcholinesterase (BChE), the major cocaine-metabolizing enzyme and bacterial cocaine esterase (CocE), the most efficient cocaine degradation biocatalyst might be displayed on phage surface to enable them to access the CNS and protect them from proteolysis.[78]

Anti-sperm Contraceptive Vaccines. To date, several human scFv antibody fragments that recognize sperm antigens were described as potential contraceptives.[79] The phage display technique was used to obtain antibodies that react in a concentration-dependant manner with fertility-related sperm antigens.

The contraceptive effect of cFA-1,[80] YLP_{12},[81] P10G,[82] A9D,[83] and SP56[84] peptides has been investigated in vivo in murine

model. All vaccines show maximum 75% reduction in mice fertility, however, this result cannot be directly related to the effectiveness of the vaccine in humans.[85] Furthermore, an immunocontraceptive vaccine for men was considered.[86] Phage display libraries were used to select several peptides of 7 and 12 amino acids with binding specificity to canine zona pellucida (ZP) glycoprotein, one of the key proteins in the sperm-oocyte binding process. The NNQSPILKLSIH peptide was found to induce an immune response and to stimulate anti-sperm antibodies production.[87] Studies on the contraceptive effect of sperm antigens include also LDH-C4, 80 kDa HSA, Eppin and Izumo, however they have not led to clinical trials.[88]

Investigation of Allergen-Antibody Interactions

Cloning and characterization of diverse types of allergens is essential for investigating the allergen-IgE interactions. Phage display is an advanced technology that can lead to development of novel diagnostic and therapeutic agents. Fab fragments with high affinity for the IgE-binding epitope of the allergen could be applied to neutralize allergens in vivo and to prevent binding of IgE to FcεRI receptor and thereby block histamine release. The obtained mimotopes could serve as anti-allergic vaccines and might be safer than the currently used natural allergens, which evoke IgE responses.[89]

Screening of random phage libraries allows mapping of allergen epitopes and leads to obtain a variety of allergen mimetics. Phage display has been used to generate IgE Fab library, which allows to select four Fab clones that were specific for the *Phleum pratense* grass (timothy-grass) allergen Phl p 5.[90] The CDR3 region was rich in aromatic amino acids which increase the allergen cross-reactivity of specific IgE.[91] The rPhl p 5a domain contains several IgE epitopes in a configuration optimal for efficient effector cell activation, interacts with serum IgE from 76% of grass pollen-allergic patients and reveals an extremely high allergenic activity in basophil histamine release as well as skin test experiments.[92] The selection of anti-idiotypic antibodies against Phl p 5a-specific IgE directly from the B-cell repertoire of a grass pollen allergic individual had led to identification of five different Fab clones with anti-idiotypic specificity for anti-Phl p 5a-IgE. It was reported that phagemid DNA was used to produce two soluble recombinant anti-idiotypic Fab clones in *E. coli*, both of which induced anti-Phl p 5a-specific antibodies in immunized BALB/c mice.[93]

Recently, phage display has been used to characterize the epitopes and identify the mimotopes for antibodies to the *Lolium* (ryegrass) pollen allergen Lol p 2,[94] *Betula* (birch) pollen allergen Bet v 1,[95] *Prunus dulcis* (almond) allergen,[96] *Charybdis feriatus* allergen (crab)[97] and to the *Dermatophagoides pteronyssinus* (home dust) allergen Der p 1.[98] Moreover, the cDNA display libraries based on pJuFo phagemid were utilized to define fungal (*Aspergillus fumigatus*),[99] peanut (*Arachis hypogaea*) and wheat (*Triticum aestivum L.)* protein allergens.[100] For instance, a panel of six *Arachis hypogaea* allergens was isolated by the phage display technology. Two of them were previously described as major peanut allergens (Ara h 1[101] and Ara h 2[102]), allergens Ara h 4, Ara h 6 and Ara h 7 have been shown to contain similar sequence to seed storage proteins and the last one, Ara h 5 was similar to a well-known plant allergen profilin. Phage display can offer solutions in allergen studies that will certainly affect the development of novel diagnostic tools and therapeutic agents.

Development of New Vaccine and Diagnostic Candidates

Several novel vaccines and diagnostic candidates, developed by the use of phage display were described earlier.[51,72-74] Recently, the usage of the phage display technique to identify new potential vaccines and diagnostic candidates has been described. This technique was utilized to identify three antigens: a conserved hypothetical protein (MSC_0636), a glycosyl transferase (MSC_0108), and an acyl carrier protein phosphodiesterase (MSC_0029), that could serve as diagnostic agents in Contagious Bovine Pleuropneumonia caused by *Mycoplasma mycoides*. Interestingly, the prototype of the diagnostic test resulted in 100% sensitivity and specificity.[103] Also, phage display allowed to identify novel immunogenic proteins and generate antibodies against *Salmonella typhimurium*. These proteins could be used to establish a diagnostic kit with very high specificity in comparison to commonly used methods.[104] It was suggested that MAP-31, a four-branch multiple antigen peptide, may be a novel vaccine candidate against *Staphylococcus aureus*.[105] A novel mechanism of marking morbillivirus vaccines, using rinderpest virus (RPV) has been recently described. Moreover, this method was considered to be utilized in development of marked vaccines for peste des petits ruminants virus (PPRV).[106] It was shown that immunogens carrying large combinatorial libraries of mutated epitope variants (VELs) induce potent, broad and long lasting $CD8^+IFN\text{-}\gamma^+$ T-cell response. This VELs with structural composition RGPGXAXXXX or XGXGXAXVXI, where X is any of 20 natural amino acids, could serve as vaccines against antigenically variable pathogens including HIV-1 virus.[107] Also the immunogenicity of different conjugates of epitope EC26–2A4 localizing to the membrane proximal external region (MPER) of the HIV-1 transmembrane protein gp41 has been studied. This EC26-2A4 MPER epitope was reported as a promising vaccine candidate for HIV-1 virus.[108]

Conclusion

Since its creation in 1985, phage display has become a technology of great importance in medicine and biotechnology. With this inspiring technology, mechanisms of many diseases can be investigated, which may lead to development and improvement of diagnostic methods and therapies. Moreover, through phage display new drugs and vaccines may be available on the market, allowing treatment and protection against many diseases such as autoimmune and cancer diseases or life-threatening infections. Further research should focus on studying the immune response, which may lead to improvement of the method for rapid antibody selection and development of new therapies. It can be concluded that the role of phage display in diagnostic and medical applications within the next decades will continue to increase.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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References

1. Juillerat A, Gronemeyer T, Keppler A, Gendreizig S, Pick H, Vogel H, et al. Directed evolution of O6-alkylguanine-DNA alkyltransferase for efficient labeling of fusion proteins with small molecules in vivo. Chem Biol 2003; 10:313-7; PMID:12725859; http://dx.doi.org/10.1016/S1074-5521(03)00068-1.
2. Xia G, Chen L, Sera T, Fa M, Schultz PG, Romesberg FE. Directed evolution of novel polymerase activities: mutation of a DNA polymerase into an efficient RNA polymerase. Proc Natl Acad Sci USA 2002; 99:6597-602; PMID:12011423; http://dx.doi.org/10.1073/pnas.102577799.
3. Hekim C, Leinonen J, Närvänen A, Koistinen H, Zhu L, Koivunen E, et al. Novel peptide inhibitors of human kallikrein 2. J Biol Chem 2006; 281:12555-60; PMID:16527822; http://dx.doi.org/10.1074/jbc.M600014200.
4. Scholle MD, Kriplani U, Pabon A, Sishtla K, Glucksman MJ, Kay BK. Mapping protease substrates by using a biotinylated phage substrate library. Chembiochem 2006; 7:834-8; PMID:16628754; http://dx.doi.org/10.1002/cbic.200500427.
5. Varadarajan N, Gam J, Olsen MJ, Georgiou G, Iverson BL. Engineering of protease variants exhibiting high catalytic activity and exquisite substrate selectivity. Proc Natl Acad Sci USA 2005; 102:6855-60; PMID:15867160; http://dx.doi.org/10.1073/pnas.0500063102.
6. Kay BK, Kasanov J, Yamabhai M. Screening phage-displayed combinatorial peptide libraries. Methods 2001; 24:240-6; PMID:11403573; http://dx.doi.org/10.1006/meth.2001.1185.
7. Fischer N, Riechmann L, Winter G. A native-like artificial protein from antisense DNA. Protein Eng Des Sel 2004; 17:13-20; PMID:14985533; http://dx.doi.org/10.1093/protein/gzh002.
8. Chu R, Takei J, Knowlton JR, Andrykovitch M, Pei W, Kajava AV, et al. Redesign of a four-helix bundle protein by phage display coupled with proteolysis and structural characterization by NMR and X-ray crystallography. J Mol Biol 2002; 323:253-62; PMID:12381319; http://dx.doi.org/10.1016/S0022-2836(02)00884-7.
9. Meyer T, Stratmann-Selke J, Meens J, Schirrmann T, Gerlach GF, Frank R, et al. Isolation of scFv fragments specific to OmpD of Salmonella Typhimurium. Vet Microbiol 2011; 147:162-9; PMID:20708859; http://dx.doi.org/10.1016/j.vetmic.2010.06.023.
10. Pitaksajjakul P, Lekcharoensuk P, Upragarin N, Barbas CF 3rd, Ibrahim MS, Ikuta K, et al. Fab MAbs specific to HA of influenza virus with H5N1 neutralizing activity selected from immunized chicken phage library. Biochem Biophys Res Commun 2010; 395:496-501; PMID:20382115; http://dx.doi.org/10.1016/j.bbrc.2010.04.040.
11. Schütte M, Thullier P, Pelat T, Wezler X, Rosenstock P, Hinz D, et al. Identification of a putative Crf splice variant and generation of recombinant antibodies for the specific detection of Aspergillus fumigatus. PLoS ONE 2009; 4:e6625; PMID:19675673; http://dx.doi.org/10.1371/journal.pone.0006625.
12. Chakravarthy B, Ménard M, Brown L, Atkinson T, Whitfield J. Identification of protein kinase C inhibitory activity associated with a polypeptide isolated from a phage display system with homology to PCM-1, the pericentriolar material-1 protein. Biochem Biophys Res Commun 2012; 424:147-51; PMID:22732405; http://dx.doi.org/10.1016/j.bbrc.2012.06.093.
13. Bugli F, Paroni Sterbini F, Graffeo R, Caridi F, Iantomasi R, Torelli R, et al. Effective use of nitrocellulose-blotted antigens for phage display monoclonal antibody selection. New Microbiol 2011; 34:281-6; PMID:21811748.
14. Filfil R, Paul-Roc B, Cantin C, Iqbal U, Tolkatchev D, Vinogradova A, et al. Molecular imaging of breast tumors using a near-infrared fluorescently labeled clusterin binding peptide. Int J Cancer 2012; 131:E681-92; PMID:22119929; http://dx.doi.org/10.1002/ijc.27368.
15. Nilvebrant J, Alm T, Hober S. Orthogonal protein purification facilitated by a small bispecific affinity tag. J Vis Exp 2012; In Press; PMID:22297419; http://dx.doi.org/10.3791/3370.
16. Miller SJ, Lee CM, Joshi BP, Gaustad A, Seibel EJ, Wang TD. Targeted detection of murine colonic dysplasia in vivo with flexible multispectral scanning fiber endoscopy. J Biomed Opt 2012; 17:021103; PMID:22463021; http://dx.doi.org/10.1117/1.JBO.17.2.021103.
17. Angenendt P, Wilde J, Kijanka G, Baars S, Cahill DJ, Kreutzberger J, et al. Seeing better through a MIST: evaluation of monoclonal recombinant antibody fragments on microarrays. Anal Chem 2004; 76:2916-21; PMID:15144205; http://dx.doi.org/10.1021/ac035357a.
18. Chang WJ, Kishikawa-Kiyama M, Shibata Y, Lee SY, Abiko Y. Inhibition of Porphyromonas gingivalis hemagglutinating activity by synthetic peptides derived from phage display selection using MAb against the recombinant outer membrane protein. Hybrid Hybridomics 2004; 23:352-6; PMID:15684661; http://dx.doi.org/10.1089/hyb.2004.23.352.
19. Lillo AM, Ayriss JE, Shou Y, Graves SW, Bradbury AR, Pavlik P. Development of phage-based single chain Fv antibody reagents for detection of Yersinia pestis. PLoS ONE 2011; 6:e27756; PMID:22174746; http://dx.doi.org/10.1371/journal.pone.0027756.
20. Pai S, Ellington AD, Levy M. Proximity ligation assays with peptide conjugate 'burrs' for the sensitive detection of spores. Nucleic Acids Res 2005; 33:e162; PMID:16237122; http://dx.doi.org/10.1093/nar/gni150.
21. Schlingemann J, Leijon M, Yacoub A, Schlingemann H, Zohari S, Matyi-Tóth A, et al. Novel means of viral antigen identification: improved detection of avian influenza viruses by proximity ligation. J Virol Methods 2010; 163:116-22; PMID:19751768; http://dx.doi.org/10.1016/j.jviromet.2009.09.008.
22. Chen L, Wang Y, Cheng D, Dou S, Liu X, Liu G, et al. Comparing two TAG-72 binding peptides previously identified by phage display as potential imaging agents. Nucl Med Commun 2011; 32:920-4; PMID:21876403; http://dx.doi.org/10.1097/MNM.0b013e328348fc64.
23. Mashayekhi F, Chiu RY, Le AM, Chao FC, Wu BM, Kamei DT. Enhancing the lateral-flow immunoassay for viral detection using an aqueous two-phase micellar system. Anal Bioanal Chem 2010; 398:2955-61; PMID:20865404; http://dx.doi.org/10.1007/s00216-010-4213-7.
24. Guo YC, Zhou YF, Zhang XE, Zhang ZP, Qiao YM, Bi LJ, et al. Phage display mediated immuno-PCR. Nucleic Acids Res 2006; 34:e62; PMID:16682441; http://dx.doi.org/10.1093/nar/gkl260.
25. Ozers MS, Marks BD, Gowda K, Kupcho KR, Ervin KM, De Rosier T, et al. The androgen receptor T877A mutant recruits LXXLL and FXXLF peptides differently than wild-type androgen receptor in a time-resolved fluorescence resonance energy transfer assay. Biochemistry 2007; 46:683-95; PMID:17223690; http://dx.doi.org/10.1021/bi061321b.
26. Ueberberg S, Meier JJ, Waengler C, Schechinger W, Dietrich JW, Tannapfel A, et al. Generation of novel single-chain antibodies by phage-display technology to direct imaging agents highly selective to pancreatic beta- or alpha-cells in vivo. Diabetes 2009; 58:2324-34; PMID:19592622; http://dx.doi.org/10.2337/db09-0658.
27. Gonzalez-Dosal R, Sørensen MD, Clark BF, Rattan SI, Kristensen P. Phage-displayed antibodies for the detection of glycated proteasome in aging cells. Ann N Y Acad Sci 2006; 1067:474-8; PMID:16804029; http://dx.doi.org/10.1196/annals.1354.068.
28. Bastien N, Trudel M, Simard C. Protective immune responses induced by the immunization of mice with a recombinant bacteriophage displaying an epitope of the human respiratory syncytial virus. Virology 1997; 234:118-22; PMID:9234952; http://dx.doi.org/10.1006/viro.1997.8632.
29. Kobayashi N, Oyama H, Nakano M, Kanda T, Banzono E, Kato Y, et al. "Cleavable" hapten-biotin conjugates: preparation and use for the generation of anti-steroid single-domain antibody fragments. Anal Biochem 2009; 387:257-66; PMID:19454256; http://dx.doi.org/10.1016/j.ab.2009.01.004.
30. Hashiguchi S, Yamaguchi Y, Takeuchi O, Akira S, Sugimura K. Immunological basis of M13 phage vaccine: Regulation under MyD88 and TLR9 signaling. Biochem Biophys Res Commun 2010; 402:19-22; PMID:20875795; http://dx.doi.org/10.1016/j.bbrc.2010.09.094.
31. Peachman KK, Li Q, Matyas GR, Shivachandra SB, Lovchik J, Lyons RC, et al. Anthrax vaccine antigen-adjuvant formulations completely protect New Zealand white rabbits against challenge with Bacillus anthracis Ames strain spores. Clin Vaccine Immunol 2012; 19:11-6; PMID:22089245; http://dx.doi.org/10.1128/CVI.05376-11.
32. Ledón T, Ferrán B, Pérez C, Suzarte E, Vichi J, Marrero K, et al. TLP01, an mshA mutant of Vibrio cholerae O139 as vaccine candidate against cholera. Microbes Infect 2012; In Press; PMID:22546527; http://dx.doi.org/10.1016/j.micinf.2012.04.004.
33. Ulivieri C, Citro A, Ivaldi F, Mascolo D, Ghittoni R, Fanigliulo D, et al. Antigenic properties of HCMV peptides displayed by filamentous bacteriophages vs. synthetic peptides. Immunol Lett 2008; 119:62-70; PMID:18538862; http://dx.doi.org/10.1016/j.imlet.2008.04.004.
34. Bruttin A, Brüssow H. Human volunteers receiving Escherichia coli phage T4 orally: a safety test of phage therapy. Antimicrob Agents Chemother 2005; 49:2874-8; PMID:15980363; http://dx.doi.org/10.1128/AAC.49.7.2874-2878.2005.
35. Riemer AB, Hantusch B, Sponer B, Kraml G, Hafner C, Zielinski CC, et al. High-molecular-weight melanoma-associated antigen mimotope immunizations induce antibodies recognizing melanoma cells. Cancer Immunol Immunother 2005; 54:677-84; PMID:15565329; http://dx.doi.org/10.1007/s00262-004-0632-7.
36. Coomber DW, Ward RL. Isolation of human antibodies against the central DNA binding domain of p53 from an individual with colorectal cancer using antibody phage display. Clin Cancer Res 2001; 7:2802-8; PMID:11555596.

37. Wagner S, Hafner C, Allwardt D, Jasinska J, Ferrone S, Zielinski CC, et al. Vaccination with a human high molecular weight melanoma-associated antigen mimotope induces a humoral response inhibiting melanoma cell growth in vitro. J Immunol 2005; 174:976-82; PMID:15634921.
38. Hardy B, Raiter A. A mimotope peptide-based anticancer vaccine selected by BAT monoclonal antibody. Vaccine 2005; 23:4283-91; PMID:15919139; http://dx.doi.org/10.1016/j.vaccine.2005.04.009.
39. Cuesta AM, Suárez E, Larsen M, Jensen KB, Sanz L, Compte M, et al. Enhancement of DNA vaccine potency through linkage of antigen to filamentous bacteriophage coat protein III domain I. Immunology 2006; 117:502-6; PMID:16556264; http://dx.doi.org/10.1111/j.1365-2567.2006.02325.x.
40. Wang LF, Yu M. Epitope identification and discovery using phage display libraries: applications in vaccine development and diagnostics. Curr Drug Targets 2004; 5:1-15; PMID:14738215; http://dx.doi.org/10.2174/1389450043490668.
41. Nencioni A, Grüenbach F, Patrone F, Brossart P. Anticancer vaccination strategies. Ann Oncol 2004; 15(Suppl 4):iv153-60; PMID:15477300; http://dx.doi.org/10.1093/annonc/mdh920.
42. Fang J, Wang G, Yang Q, Song J, Wang Y, Wang L. The potential of phage display virions expressing malignant tumor specific antigen MAGE-A1 epitope in murine model. Vaccine 2005; 23:4860-6; PMID:16029917; http://dx.doi.org/10.1016/j.vaccine.2005.05.024.
43. Arnaiz B, Madrigal-Estebas L, Todryk S, James TC, Doherty DG, Bond U. A novel method to identify and characterise peptide mimotopes of heat shock protein 70-associated antigens. J Immune Based Ther Vaccines 2006; 4:2; PMID:16603084; http://dx.doi.org/10.1186/1476-8518-4-2.
44. van der Vaart JM, Pant N, Wolvers D, Bezemer S, Hermans PW, Bellamy K, et al. Reduction in morbidity of rotavirus induced diarrhoea in mice by yeast produced monovalent llama-derived antibody fragments. Vaccine 2006; 24:4130-7; PMID:16616802; http://dx.doi.org/10.1016/j.vaccine.2006.02.045.
45. Guo Z, Zhang H, Rao H, Jiang D, Cong X, Feng B, et al. DCs pulsed with novel HLA-A2-restricted CTL epitopes against hepatitis C virus induced a broadly reactive anti-HCV-specific T lymphocyte response. PLoS ONE 2012; 7:e38390; PMID:22701633; http://dx.doi.org/10.1371/journal.pone.0038390.
46. Iborra S, Izquierdo HM, Martínez-López M, Blanco-Menéndez N, Reis e Sousa C, Sancho D. The DC receptor DNGR-1 mediates cross-priming of CTLs during vaccinia virus infection in mice. J Clin Invest 2012; 122:1628-43; PMID:22505455; http://dx.doi.org/10.1172/JCI60660.
47. Varela-Rohena A, Molloy PE, Dunn SM, Li Y, Suhoski MM, Carroll RG, et al. Control of HIV-1 immune escape by CD8 T cells expressing enhanced T-cell receptor. Nat Med 2008; 14:1390-5; PMID:18997777; http://dx.doi.org/10.1038/nm.1779.
48. Wan Y, Wu Y, Bian J, Wang XZ, Zhou W, Jia ZC, et al. Induction of hepatitis B virus-specific cytotoxic T lymphocytes response in vivo by filamentous phage display vaccine. Vaccine 2001; 19:2918-23; PMID:11282203; http://dx.doi.org/10.1016/S0264-410X(00)00561-2.
49. Santini C, Brennan D, Mennuni C, Hoess RH, Nicosia A, Cortese R, et al. Efficient display of an HCV cDNA expression library as C-terminal fusion to the capsid protein D of bacteriophage lambda. J Mol Biol 1998; 282:125-35; PMID:9733645; http://dx.doi.org/10.1006/jmbi.1998.1986.
50. Hashemi H, Bamdad T, Jamali A, Pouyanfard S, Mohammadi MG. Evaluation of humoral and cellular immune responses against HSV-1 using genetic immunization by filamentous phage particles: a comparative approach to conventional DNA vaccine. J Virol Methods 2010; 163:440-4; PMID:19903497; http://dx.doi.org/10.1016/j.jviromet.2009.11.008.
51. Tumban E, Peabody J, Peabody DS, Chackerian B. A pan-HPV vaccine based on bacteriophage PP7 VLPs displaying broadly cross-neutralizing epitopes from the HPV minor capsid protein, L2. PLoS ONE 2011; 6:e23310; PMID:21858066; http://dx.doi.org/10.1371/journal.pone.0023310.
52. Caldeira JdoC, Medford A, Kines RC, Lino CA, Schiller JT, Chackerian B, et al. Immunogenic display of diverse peptides, including a broadly cross-type neutralizing human papillomavirus L2 epitope, on virus-like particles of the RNA bacteriophage PP7. Vaccine 2010; 28:4384-93; PMID:20434554; http://dx.doi.org/10.1016/j.vaccine.2010.04.049.
53. Slupetzky K, Gambhira R, Culp TD, Shafti-Keramat S, Schellenbacher C, Christensen ND, et al. A papillomavirus-like particle (VLP) vaccine displaying HPV16 L2 epitopes induces cross-neutralizing antibodies to HPV11. Vaccine 2007; 25:2001-10; PMID:17239496; http://dx.doi.org/10.1016/j.vaccine.2006.11.049.
54. Castel G, Chtéoui M, Heyd B, Tordo N. Phage display of combinatorial peptide libraries: application to antiviral research. Molecules 2011; 16:3499-518; PMID:21522083; http://dx.doi.org/10.3390/molecules16053499.
55. Ghosh AK, Moreira LA, Jacobs-Lorena M. Plasmodium-mosquito interactions, phage display libraries and transgenic mosquitoes impaired for malaria transmission. Insect Biochem Mol Biol 2002; 32:1325-31; PMID:12225923; http://dx.doi.org/10.1016/S0965-1748(02)00095-4.
56. Ghosh AK, Ribolla PE, Jacobs-Lorena M. Targeting Plasmodium ligands on mosquito salivary glands and midgut with a phage display peptide library. Proc Natl Acad Sci USA 2001; 98:13278-81; PMID:11687659; http://dx.doi.org/10.1073/pnas.241491198.
57. Gazarian KG, Solis CF, Gazarian TG, Rowley M, Laclette JP. Synthetic peptide-targeted selection of phage display mimotopes highlights immunogenic features of α-helical vs non-helical epitopes of Taenia solium paramyosin: implications for parasite- and host-protective roles of the protein. Peptides 2012; 34:232-41; PMID:22015270; http://dx.doi.org/10.1016/j.peptides.2011.10.003.
58. Liu Y, Brindley PJ, Zeng Q, Li Y, Zhou J, Chen Y, et al. Identification of phage display peptides with affinity for the tegument of Schistosoma japonicum schistosomula. Mol Biochem Parasitol 2011; 180:86-98; PMID:21930161; http://dx.doi.org/10.1016/j.molbiopara.2011.09.001.
59. Gnanasekar M, Rao KV, He YX, Mishra PK, Nutman TB, Kaliraj P, et al. Novel phage display-based subtractive screening to identify vaccine candidates of Brugia malayi. Infect Immun 2004; 72:4707-15; PMID:15271932; http://dx.doi.org/10.1128/IAI.72.8.4707-4715.2004.
60. Adda CG, Tilley L, Anders RF, Foley M. Isolation of peptides that mimic epitopes on a malarial antigen from random peptide libraries displayed on phage. Infect Immun 1999; 67:4679-88; PMID:10456916.
61. Yang G, Gao Y, Dong J, Xue Y, Fan M, Shen B, et al. A novel peptide isolated from phage library to substitute a complex system for a vaccine against staphylococci infection. Vaccine 2006; 24:1117-23; PMID:16359760; http://dx.doi.org/10.1016/j.vaccine.2005.09.004.
62. Yang G, Gao Y, Dong J, Liu C, Xue Y, Fan M, et al. A novel peptide screened by phage display can mimic TRAP antigen epitope against Staphylococcus aureus infections. J Biol Chem 2005; 280:27431-5; PMID:15908434; http://dx.doi.org/10.1074/jbc.M501127200.
63. Li Y, Han WY, Li ZJ, Lei LC. Klebsiella pneumoniae MrkD adhesin-mediated immunity to respiratory infection and mapping the antigenic epitope by phage display library. Microb Pathog 2009; 46:144-9; PMID:19100827; http://dx.doi.org/10.1016/j.micpath.2008.11.006.
64. Beghetto E, De Paolis F, Montagnani F, Cellesi C, Gargano N. Discovery of new Mycoplasma pneumoniae antigens by use of a whole-genome lambda display library. Microbes Infect 2009; 11:66-73; PMID:18992837; http://dx.doi.org/10.1016/j.micinf.2008.10.004.
65. Magliani W, Polonelli L, Conti S, Salati A, Rocca PF, Cusumano V, et al. Neonatal mouse immunity against group B streptococcal infection by maternal vaccination with recombinant anti-idiotypes. Nat Med 1998; 4:705-9; PMID:9623980; http://dx.doi.org/10.1038/nm0698-705.
66. Beckmann C, Brittnacher M, Ernst R, Mayer-Hamblett N, Miller SI, Burns JL. Use of phage display to identify potential Pseudomonas aeruginosa gene products relevant to early cystic fibrosis airway infections. Infect Immun 2005; 73:444-52; PMID:15618183; http://dx.doi.org/10.1128/IAI.73.1.444-452.2005.
67. Yang Q, Wang L, Lu DN, Gao RJ, Song JN, Hua PY, et al. Prophylactic vaccination with phage-displayed epitope of C. albicans elicits protective immune responses against systemic candidiasis in C57BL/6 mice. Vaccine 2005; 23:4088-96; PMID:15963364; http://dx.doi.org/10.1016/j.vaccine.2004.07.005.
68. Wang G, Sun M, Fang J, Yang Q, Tong H, Wang L. Protective immune responses against systemic candidiasis mediated by phage-displayed specific epitope of Candida albicans heat shock protein 90 in C57BL/6J mice. Vaccine 2006; 24:6065-73; PMID:16842891; http://dx.doi.org/10.1016/j.vaccine.2006.05.022.
69. Bliss JM, Sullivan MA, Malone J, Haidaris CG. Differentiation of Candida albicans and Candida dubliniensis by using recombinant human antibody single-chain variable fragments specific for hyphae. J Clin Microbiol 2003; 41:1152-60; PMID:12624045; http://dx.doi.org/10.1128/JCM.41.3.1152-1160.2003.
70. Krishnaswamy S, Kabir ME, Miyamoto M, Furuichi Y, Komiyama T. Cloning antifungal single chain fragment variable antibodies by phage display and competitive panning elution. Anal Biochem 2009; 395:16-24; PMID:19665444; http://dx.doi.org/10.1016/j.ab.2009.08.003.
71. Meijler MM, Matsushita M, Wirsching P, Janda KD. Development of immunopharmacotherapy against drugs of abuse. Curr Drug Discov Technol 2004; 1:77-89; PMID:16472221; http://dx.doi.org/10.2174/1570163043484851.
72. Moreno AY, Mayorov AV, Janda KD. Impact of distinct chemical structures for the development of a methamphetamine vaccine. J Am Chem Soc 2011; 133:6587-95; PMID:21473576; http://dx.doi.org/10.1021/ja108807j.
73. Moreno AY, Azar MR, Warren NA, Dickerson TJ, Koob GF, Janda KD. A critical evaluation of a nicotine vaccine within a self-administration behavioral model. Mol Pharm 2010; 7:431-41; PMID:20104903; http://dx.doi.org/10.1021/mp900213u.
74. Treweek JB, Janda KD. An antidote for acute cocaine toxicity. Mol Pharm 2012; 9:969-78; PMID:22380623; http://dx.doi.org/10.1021/mp200588v.
75. Carrera MR, Kaufmann GF, Mee JM, Meijler MM, Koob GF, Janda KD. Treating cocaine addiction with viruses. Proc Natl Acad Sci USA 2004; 101:10416-21; PMID:15226496; http://dx.doi.org/10.1073/pnas.0403795101.
76. Meijler MM, Kaufmann GF, Qi L, Mee JM, Coyle AR, Moss JA, et al. Fluorescent cocaine probes: a tool for the selection and engineering of therapeutic antibodies. J Am Chem Soc 2005; 127:2477-84; PMID:15725002; http://dx.doi.org/10.1021/ja043935e.
77. Anni H, Nikolaeva O, Israel Y. Selection of phage-display library peptides recognizing ethanol targets on proteins. Alcohol 2001; 25:201-9; PMID:11839467; http://dx.doi.org/10.1016/S0741-8329(01)00164-1.
78. Dickerson TJ, Janda KD. Recent advances for the treatment of cocaine abuse: central nervous system immunopharmacotherapy. AAPS J 2005; 7:E579-86; PMID:16353936; http://dx.doi.org/10.1208/aapsj070359.

79. Naz RK. Antisperm vaccine for contraception. Am J Reprod Immunol 2005; 54:378-83; PMID:16305663; http://dx.doi.org/10.1111/j.1600-0897.2005.00331.x.
80. Naz RK, Zhu X. Recombinant fertilization antigen-1 causes a contraceptive effect in actively immunized mice. Biol Reprod 1998; 59:1095-100; PMID:9780314; http://dx.doi.org/10.1095/biolreprod59.5.1095.
81. Naz RK, Chauhan SC. Human sperm-specific peptide vaccine that causes long-term reversible contraception. Biol Reprod 2002; 67:674-80; PMID:12135913; http://dx.doi.org/10.1095/biolreprod67.2.674.
82. O'Rand MG, Beavers J, Widgren EE, Tung KS. Inhibition of fertility in female mice by immunization with a B-cell epitope, the synthetic sperm peptide, P10G. J Reprod Immunol 1993; 25:89-102; PMID:7513024; http://dx.doi.org/10.1016/0165-0378(93)90051-I.
83. Lea IA, van Lierop MJ, Widgren EE, Grootenhuis A, Wen Y, van Duin M, et al. A chimeric sperm peptide induces antibodies and strain-specific reversible infertility in mice. Biol Reprod 1998; 59:527-36; PMID:9716550; http://dx.doi.org/10.1095/biolreprod59.3.527.
84. Hardy CM, Mobbs KJ. Expression of recombinant mouse sperm protein sp56 and assessment of its potential for use as an antigen in an immunocontraceptive vaccine. Mol Reprod Dev 1999; 52:216-24; PMID:9890753; http://dx.doi.org/10.1002/(SICI)1098-2795(199902)52:2<216::AID-MRD13>3.0.CO;2-R.
85. Naz RK. Development of genetically engineered human sperm immunocontraceptives. J Reprod Immunol 2009; 83:145-50; PMID:19853924; http://dx.doi.org/10.1016/j.jri.2009.06.260.
86. O'rand MG, Widgren EE, Sivashanmugam P, Richardson RT, Hall SH, French FS, et al. Reversible immunocontraception in male monkeys immunized with eppin. Science 2004; 306:1189-90; PMID:15539605; http://dx.doi.org/10.1126/science.1099743.
87. Samoylova TI, Cox NR, Cochran AM, Samoylov AM, Griffin B, Baker HJ. ZP-binding peptides identified via phage display stimulate production of sperm antibodies in dogs. Anim Reprod Sci 2010; 120:151-7; PMID:20434854; http://dx.doi.org/10.1016/j.anireprosci.2010.04.002.
88. Naz RK. Antisperm contraceptive vaccines: where we are and where we are going? Am J Reprod Immunol 2011; 66:5-12; PMID:21481057; http://dx.doi.org/10.1111/j.1600-0897.2011.01000.x.
89. Davies JM, O'hehir RE, Suphioglu C. Use of phage display technology to investigate allergen-antibody interactions. J Allergy Clin Immunol 2000; 105:1085-92; PMID:10856140; http://dx.doi.org/10.1067/mai.2000.107040.
90. Steinberger P, Kraft D, Valenta R. Construction of a combinatorial IgE library from an allergic patient. Isolation and characterization of human IgE Fabs with specificity for the major timothy grass pollen allergen, Phl p 5. J Biol Chem 1996; 271:10967-72; PMID:8631916.
91. Droupadi PR, Varga JM, Linthicum DS. Mechanism of allergenic cross-reactions--IV. Evidence for participation of aromatic residues in the ligand binding site of two multi-specific IgE monoclonal antibodies. Mol Immunol 1994; 31:537-48; PMID:8190129; http://dx.doi.org/10.1016/0161-5890(94)90041-8.
92. Flicker S, Vrtala S, Steinberger P, Vangelista L, Bufe A, Petersen A, et al. A human monoclonal IgE antibody defines a highly allergenic fragment of the major timothy grass pollen allergen, Phl p 5: molecular, immunological, and structural characterization of the epitope-containing domain. J Immunol 2000; 165:3849-59; PMID:11034391.
93. Hantusch B, Knittelfelder R, Wallmann J, Krieger S, Szalai K, Untersmayr E, et al. Internal images: human anti-idiotypic Fab antibodies mimic the IgE epitopes of grass pollen allergen Phl p 5a. Mol Immunol 2006; 43:2180-7; PMID:16510185; http://dx.doi.org/10.1016/j.molimm.2006.01.009.
94. de Lalla C, Tamborini E, Longhi R, Tresoldi E, Manoni M, Siccardi AG, et al. Human recombinant antibody fragments specific for a rye-grass pollen allergen: characterization and potential applications. Mol Immunol 1996; 33:1049-58; PMID:9010244; http://dx.doi.org/10.1016/S0161-5890(96)00061-2.
95. Jensen-jarolim E, Leitner A, Kalchhauser H, Zürcher A, Ganglberger E, Bohle B, et al. Peptide mimotopes displayed by phage inhibit antibody binding to bet v 1, the major birch pollen allergen, and induce specific IgG response in mice. FASEB J 1998; 12:1635-42; PMID:9837853.
96. Tawde P, Venkatesh YP, Wang F, Teuber SS, Sathe SK, Roux KH. Cloning and characterization of profilin (Pru du 4), a cross-reactive almond (Prunus dulcis) allergen. J Allergy Clin Immunol 2006; 118:915-22; PMID:17030246; http://dx.doi.org/10.1016/j.jaci.2006.05.028.
97. Leung PS, Chen YC, Gershwin ME, Wong SH, Kwan HS, Chu KH. Identification and molecular characterization of Charybdis feriatus tropomyosin, the major crab allergen. J Allergy Clin Immunol 1998; 102:847-52; PMID:9819304; http://dx.doi.org/10.1016/S0091-6749(98)70027-2.
98. Furmonaviciene R, Tighe PJ, Clark MR, Sewell HF, Shakib F. The use of phage-peptide libraries to define the epitope specificity of a mouse monoclonal anti-Der p 1 antibody representative of a major component of the human immunoglobulin E anti-Der p 1 response. Clin Exp Allergy 1999; 29:1563-71; PMID:10520087; http://dx.doi.org/10.1046/j.1365-2222.1999.00686.x.
99. Kodzius R, Rhyner C, Konthur Z, Buczek D, Lehrach H, Walter G, et al. Rapid identification of allergen-encoding cDNA clones by phage display and high-density arrays. Comb Chem High Throughput Screen 2003; 6:147-54; PMID:12678710; http://dx.doi.org/10.2174/1386207033329751.
100. Bittner C, Grassau B, Frenzel K, Baur X. Identification of wheat gliadins as an allergen family related to baker's asthma. J Allergy Clin Immunol 2008; 121:744-9; PMID:18036646; http://dx.doi.org/10.1016/j.jaci.2007.09.051.
101. Burks AW, Williams LW, Helm RM, Connaughton C, Cockrell G, O'Brien T. Identification of a major peanut allergen, Ara h I, in patients with atopic dermatitis and positive peanut challenges. J Allergy Clin Immunol 1991; 88:172-9; PMID:1880317; http://dx.doi.org/10.1016/0091-6749(91)90325-I.
102. Burks AW, Williams LW, Connaughton C, Cockrell G, O'Brien TJ, Helm RM. Identification and characterization of a second major peanut allergen, Ara h II, with use of the sera of patients with atopic dermatitis and positive peanut challenge. J Allergy Clin Immunol 1992; 90:962-9; PMID:1460200; http://dx.doi.org/10.1016/0091-6749(92)90469-I.
103. Naseem S, Means J, Jores J, Heller M, Dübel S, Hust M, et al. Phage display-based identification and potential diagnostic application of novel antigens from Mycoplasma mycoides subsp. mycoides small colony type. Vet Microbiol 2010; 142:285-92; PMID:19900769; http://dx.doi.org/10.1016/j.vetmic.2009.09.071.
104. Meyer T, Schirrmann T, Frenzel A, Miethe S, Stratmann-Selke J, Gerlach GF, et al. Identification of immunogenic proteins and generation of antibodies against Salmonella Typhimurium using phage display. BMC Biotechnol 2012; 12:29; PMID:22703709; http://dx.doi.org/10.1186/1472-6750-12-29.
105. Chen Y, Liu B, Yang D, Li X, Wen L, Zhu P, et al. Peptide mimics of peptidoglycan are vaccine candidates and protect mice from infection with Staphylococcus aureus. J Med Microbiol 2011; 60:995-1002; PMID:21436375; http://dx.doi.org/10.1099/jmm.0.028647-0.
106. Buczkowski H, Parida S, Bailey D, Barrett T, Banyard AC. A novel approach to generating morbillivirus vaccines: negatively marking the rinderpest vaccine. Vaccine 2012; 30:1927-35; PMID:22265946; http://dx.doi.org/10.1016/j.vaccine.2012.01.029.
107. Charles-Niño C, Pedroza-Roldan C, Viveros M, Gevorkian G, Manoutcharian K. Variable epitope libraries: new vaccine immunogens capable of inducing broad human immunodeficiency virus type 1-neutralizing antibody response. Vaccine 2011; 29:5313-21; PMID:21600948; http://dx.doi.org/10.1016/j.vaccine.2011.05.007.
108. Zhou M, Kostoula I, Brill B, Panou E, Sakarellos-Daitsiotis M, Dietrich U. Prime boost vaccination approaches with different conjugates of a new HIV-1 gp41 epitope encompassing the membrane proximal external region induce neutralizing antibodies in mice. Vaccine 2012; 30:1911-6; PMID:22269872; http://dx.doi.org/10.1016/j.vaccine.2012.01.026.