| Title | Journal | Year Published | Study type | Model used | Vaccine against | Type of phage used | Immune response | Vacination schedule (doses and | Vaccine including adjuvant | Aim of study | Methods | Key Findings | Why is this relevant to vaccines? | Response Type | Outcome |
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| Phage idiotype vaccination: first phase I/II clinical trial in patients with multiple myeloma. | Journal of Translational Medicine | 2014 | Phase I/II clinical trial | Human patients | Multiple myeloma | N/A | Utilized serum M gradientand 24-hour light chain excretion measurement | Ix intradermal immuniza-tions with the phage-conjugated Id protein vaccine at day 1, 7, 14 and week 4, 8 and 12 | No | Examine the therapeutic feasibility and tolerability of the chemically linked Id-phage in patients with advanced multiple myeloma (MM) | Using phage particles as immunological carriers to employ a novel chemically linked idiotype vaccine in a clinical phase I/II trial including 15 patients with advanced multiple myeloma. Vaccines composed of purified paraproteins linked to phage were manufactured successfully for each patient. Patients received six intradermal immunizations with phage idiotype vaccines in three different dose groups. | Phage idiotype was well tolerated by all study participants. A subset of patients (80% in the middle dose group) displayed a clinical response indicated by decrease or stabilization of paraprotein levels. Patients exhibiting a clinical response to phage vaccines also raised idiotype-specific immunoglobulins. Induction of a cellular immune response was demonstrated by a cytotoxicity assay and delayed type hypersensitivity tests. This highlights a simple, time- and cost-efficient phage idiotype vaccination strategy, which represents a safe and feasible patient-specific therapy for patients with advanced multiple myeloma and produced promising anti-tumor activity in a subset of patients. | Myeloma Id paraproteins chemically conjugated to phage particles appear to be suitable for use as vaccines and capable of evoking tumor-specific immune responses. The current study demonstrates the feasibility to rapidly create tumor-specific phage vaccines for each individual patient. | Humoral | |
| Development of a Biosafety Enhanced and Immunogenic Salmonella Enteritidis Ghost Using an Antibiotic Resistance Gene Free Plasmid Carrying a Bacteriophage Lysis System | PLOS ONE | 2013 | Original artic | Chicken Model | Salmonella | Lysis system derived from the bacteriophage PhiX174. The PhiX174 lysis gene E is integrated into the vaccine to create a "ghost" or inactivated form of S. Enteritidis | Measurement of plasma immunoglobulin G (IgG) and intestinal secretory immunoglobulin A (sIgA) levels in vaccinated chickens as well as lymphocyte proliferation assay | Chickens were primed and boosted with the S. Enteritidis ghost vaccine at two and six weeks of age, respectively. Different combinations of oral and intramuscular immunizations were used. | No | Develop a safer and more effective vaccine against Salmonella Enteritidis. This involves creating a genetically inactivated vaccine that does not use antibiotic resistance genes, thereby reducing biosafety hazards. The research focuses on constructing a novel lysis plasmid using the balanced lethal system and evaluating its immunogenic potential in chickens, aiming to protect against virulent Salmonella Enteritidis infections. | This method involves harnessing the lytic ability of bacteriophages to disrupt the bacterial cell wall, resulting in the formation of bacterial ghosts. These ghosts are empty cell envelopes that retain the immunogenic properties of the bacteria but are non-viable, thus ensuring safety and effectiveness as a vaccine. The use of phage technology in this context is pivotal for the successful creation of a biosafety-enhanced vaccine candidate. | The key findings of this paper in relation to phage technology include the successful construction of a novel lysis plasmid incorporating a bacteriophage lysis system, leading to the creation of Salmonella Enteritidis bacterial ghosts. This method proved effective in generating non-viable bacterial cells that retained their immunogenic properties, thus providing a safer and effective vaccine candidate against Salmonella Enteritidis. | The study demonstrates the potential of phage technology in developing biosafety enhanced vaccines without relying on antibiotic resistance genes. reducing potential biosafety hazards. The resulting bacterial ghosts maintain the immunogenic properties of the bacteria, ensuring the vaccine's effectiveness in stimulating an immune response. This innovative method can significantly impact how vaccines are developed, making them safer and potentially more effective in preventing diseases. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Hybrid phage displaying SLAQVKYTSASSI induces protection against Candida albicans challenge in BALB/c mice | Hum Vaccin Immun | 2014 | Original artic | Mouse Model | Candida albicans | A hybrid phage displaying the epitope SLAQVKYTSASSI was used | Measured through antibody levels (total IgG) and cytokine production in splenocytes, as well as through survival rates after challenge with C. albicans. | Mice were immunized at weeks 0, 2, 4, and 6 with either 25 µg of the recombinant phage or control substances. | No | Explore the potential of a hybrid phage displaying the epitope SLAQVKYTSASSI as a vaccine candidate against Candida albicans infections. The study focuses on assessing the efficacy of this phage in stimulating immune responses and providing protection against lethal C. albicans challenges in a mouse model. The research investigates both cellular and humoral immune responses to evaluate the vaccine's effectiveness. | The methods in this study involve constructing a hybrid phage displaying the SLAQVKYTSASSI epitope. The research assesses the phage's ability to induce immune responses in BALB/c mice. This includes evaluating both cellular and humoral immunity by analyzing antibody titers, cytokine production, and survival rates following lethal Candida albicans challenges. The study uses a mouse model to test the effectiveness of the phage as a vaccine candidate, providing insights into its potential for inducing protective immunity against C. albicans infections. | The key findings of the paper reveal that the hybrid phage displaying the SLAQVKYTSASSI epitope effectively induces an immune response in BALB/c mice against Candida albicans. The study shows significant increases in specific antibody titers and cytokine production, indicating robust humoral and cellular immunity. Importantly, vaccinated mice demonstrated enhanced survival rates following lethal challenges with C. albicans, underscoring the potential of this phage as an effective vaccine candidate for combating C. albicans infections. | This study is significant for phage technology in vaccines as it demonstrates the potential of phage-displayed epitopes in eliciting a strong immune response against infections, in this case, Candida albicans. The successful use of a hybrid phage displaying a specific epitope to induce protective immunity in a mouse model highlights the versatility and efficacy of phage technology in vaccine development. This opens up new avenues for creating targeted, effective vaccines against various pathogens using phage display techniques. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Cancer immunotherapy by a recombinant phage vaccine displaying EGFR mimotope: an in vivo study | Immunopharmacol I | 2014 | Original article - lab based | Mouse Model | Epidermal Growth Factor Receptor (EGFR) | The M13 bacteriophage was used to display the EGFR mimotope | The immune response was evaluated by measuring antibody levels against the EGFR mimotope in mice, using ELISA. | Mice were immunized subcutaneously with approximately 10^12 plaque-forming units (pfu) of the EGFR mimotope displaying phages. Booster injections were given three times with 10-day intervals. Blood samples were collected for analysis three days after the last injection. | No | recombinant phage vaccine displaying an EGFR mimotope in cancer immunotherapy. The research focuses on assessing the vaccine's ability to stimulate an immune response against cancer cells expressing the epidermal growth factor receptor (EGFR), a common target in cancer treatment. The study tests the vaccine's efficacy in an in vivo setting, using a mouse model to understand its potential as a therapeutic tool in the fight against cancer. | The methods of this study involve the development of a recombinant phage vaccine displaying an EGFR mimotope. The vaccine's efficacy is tested in a mouse model with established EGFR-expressing tumors. The study evaluates the immune response elicited by the vaccine, including antibody production and cytotoxic T cell activity. Additionally, the impact of the vaccine on tumor growth and survival rates in the mice is assessed, providing insights into the vaccine's potential as a therapeutic agent in cancer treatment. | The key findings of the study include that the recombinant phage vaccine displaying an EGFR mimotope effectively stimulates an immune response in a mouse model. This response includes the production of antibodies and activation of cytotoxic T cells targeting EGFR-expressing tumor cells. The vaccine showed a significant impact in reducing tumor growth and improving survival rates in the mice. These results indicate the potential of this phage-based vaccine as a promising approach for cancer immunotherapy, especially in targeting cancers that overexpress EGFR. | This study's relevance to phage technology in vaccines lies in its demonstration of a novel application: using a phage-display system for cancer immunotherapy. By showcasing the effectiveness of a phage vaccine displaying an EGFR mimotope in eliciting an immune response against cancer cells, the research highlights the versatility and potential of phage technology in developing targeted therapeutic vaccines. This opens up new possibilities for using phage display in creating vaccines against complex diseases like cancer, extending beyond traditional infectious disease targets. | Humoral | Antibody titre |
| Genetically Engineered Virus Nanofibers as an Efficient Vaccine for Preventing Fungal Infection | Adv Healthc Materials | 2016 | Original article - lab based | Mouse Model | Canidia Albicans yeast | The vaccine utilizes filamentous phage to display an epitope peptide of Sap2 (EPS with a sequence of Val-Lys-Tyr-Thr-Ser) | Measured through antibody response against rSap2 and CA, using methods like Western blotting and immunofluorescence | Mice were immunized intraperitoneally with 25 µg of the vaccine three times, with intervals between doses intraperitoneally. | Yes, Freund's complete adjuvant for the first dose, followed by Freund's incomplete adjuvant for subsequent doses | Evaluate the efficacy of engineered virus nanofibers displaying an epitope peptide of Sap2 (EPS) as a subunit vaccine against Candida albicans infection. | The study involved immunizing mice with the engineered nanofibers and then assessing humoral and cellular immune responses, fungal loading in kidneys, survival rates, and antibody production. | The engineered virus nanofibers induced strong immune responses, decreased fungal loading in kidneys, improved survival rates, and were cost-effective to produce. These nanofibers displayed the EPS on their surface, mimicking the native protein's immunogenic properties. | This study illustrates the potential of using virus nanofibers as a platform for developing subunit vaccines against fungal infections, highlighting their efficiency in eliciting immune responses and their cost-effectiveness for mass production. | Humoral | Antibody titre |
| Lambda phage-based vaccine induces antitumor immunity in hepatocellular carcinoma | Heliyon | 2017 | Original article - lab based | Mouse Model | Cancer | Bacteriophage λ (lambda) | Measurement of antitumor activity, activation and proliferation of antigen-specific CD4+ and CD8+ lymphocytes, and the production of Th1 and Th2 cytokines. | Mice received prophylactic immunizations three times (on days -14, -7, and 0) with 1 × 10^10 pfu of phage particles. Booster immunizations were given every 7–10 days after tumor inoculation. Injected at base of tail | No | Investigate the efficacy of a lambda (λ) phage-based vaccine in inducing antitumor immunity against hepatocellular carcinoma (HCC). The study specifically focuses on evaluating the therapeutic effects of nanoparticle lambda phage vaccine constructs against ASPH expressing murine liver tumors, aiming to establish ASPH as a potential antigenic target for immunotherapy. The research examines the generation of antigen-specific cellular immune responses and the identification of tumor-infiltrating lymphocytes to assess the antitumor activity of the vaccine. | The methodology of the study involves constructing a lambda phage-based vaccine targeting the aspartate β-hydroxylase (ASPH) antigen, expressed in hepatocellular carcinoma (HCC). The vaccine's efficacy is evaluated in mouse models with ASPH-expressing liver tumors. The study measures the immune response, focusing on antigen-specific cellular immunity and the presence of tumor-infiltrating lymphocytes. Additionally, the impact of the vaccine on tumor growth and survival rates in the mice is assessed to determine its potential as a therapeutic agent against HCC. | The key findings of the study are that the lambda phage-based vaccine targeting the aspartate β-hydroxylase (ASPH) antigen effectively induces an antitumor immune response in a hepatocellular carcinoma (HCC) mouse model. The vaccine demonstrated the ability to generate ASPH-specific cellular immunity and increased the presence of tumor-infiltrating lymphocytes. Importantly, this resulted in significant tumor growth inhibition and improved survival rates in the treated mice, indicating the vaccine's potential as a promising therapeutic strategy against HCC. | This study is important for phage vaccine development as it showcases the potential of lambda phage-based vaccines in cancer immunotherapy, specifically against hepatocellular carcinoma (HCC). By demonstrating that a phage vaccine can effectively target cancer-specific antigens like ASPH and induce a strong antitumor immune response, the research opens new avenues for using phage technology in cancer treatment. This approach could lead to more targeted, effective cancer vaccines, expanding the scope of phage vaccines beyond traditional infectious disease applications. | Cellular | Antibody titre and T cell activation markers |
| A prokaryotic-eukaryotic | Science Advances | 2019 | Original article - lab based | Mouse Model | Flu and Pneumonia | Utilized bacteriophage T4 in combination with adeno-associated virus (AAV) to create a T4-AAV hybrid vector | Measured by evaluating the elicitation of robust antibody responses and protection efficacy against lethal challenges in animal models | Mice were immunized with T4-AAV nanoparticles, but the specific dosing schedule and route of administration are not detailed in the provided text. | No | To develop a hybrid viral vector capable of delivering large cargos of genes and proteins into human cells, potentially transforming human therapies and personalized medicine. | Creation of a hybrid viral vector (T4-AAV), delivery of large molecular payloads into mammalian cells, and evaluation of immune responses in mice models. | The T4-AAV hybrid vector efficiently delivered genes and proteins into mammalian cells, eliciting strong and durable immune responses without specifying the need for adjuvants, and provided complete protection against lethal pneumonic plague challenge | Demonstrates the potential of using hybrid viral vectors for developing effective vaccines against infectious diseases, offering a novel platform for the delivery of complex molecular cargos and eliciting robust immune responses. | Humoral | Antibody titre |
| Generation of multiepitoj | Immunology | 2020 | Original article - lab based | Mouse Model | Breast cancer | Utilized recombinant M13 phage | Measured the proliferation of splenocytes, the cytotoxic activity of CTLs against target cells, cytokine production analysis (IFN-γ and IL-4), and the detection of specific antibodies in serum. | Mice received three doses, administered intradermally at two-week intervals | No | To overcome immune tolerance by employing mutated cancer antigens to stimulate a broad immune response, particularly activating CD8+ T cells, which is crucial for effective cancer immunotherapy. | The methods included the construction of VELs from survivin, incorporation into M13 phage for vaccine formulation, and vaccination of mice. Tumor challenge with the 4T1 cell line followed vaccination, with subsequent measurement of tumor growth and metastasis. Immune responses were assessed by analyzing splenocyte proliferation, CTL activity, cytokine production, and specific antibody levels in serum. | The key findings of the study demonstrated that the vaccination with VELs derived from survivin significantly inhibited tumor growth and suppressed lung metastasis in a murine model of breast cancer. It also elicited a strong cellular immune response, evidenced by the activation of CD8+ T cells, increased cytokine production, and the generation of specific antibodies. These results highlight the potential of using mutated antigen libraries to overcome immune tolerance and stimulate a broad and effective immune response against cancer, providing a promising approach for cancer vaccine development. | The study's relevance to vaccine development lies in demonstrating the potential of VEL-based vaccines to induce a strong and broad immune response against cancer, offering a new strategy for cancer vaccine design. | Humoral and Cellular | Antibody titre and T cell activation markers |

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| **Analysis of the Consol** | Microorganisms | 2020 | Original article - lab based | Mouse model | Prototype Alzheim | Filamentous bacteriophage | Measured by assessing the IgG antibody titers against the displayed epitope AEFRH of β-amyloid, in both primary and secondary IgG responses. | Mice were immunized intraperitoneally, with a primary dose followed by a recall dose 9 months later. Additional booster doses were given 1, 2, or 3 weeks after the primary dose. | Yes, Freund's complete adjuvant for the first dose, followed by Freund's incomplete adjuvant for subsequent doses | To determine if a similar consolidation phase of immunological memory observed in previous studies occurs in the IgG response to a B cell epitope displayed on a filamentous bacteriophage. | Immunizing mice with a filamentous bacteriophage displaying a specific epitope, measuring IgG antibody titers to assess the immune response, and analyzing the impact of booster doses on the consolidation phase of immunological memory. The study utilized intraperitoneal injections of the phage mixed with Freund's adjuvant. Antibody titers were determined at various time points to evaluate the primary and secondary immune responses, with statistical analyses conducted to understand the effects of booster timing on immunological memory development. | booster dose given 15 days after priming significantly reduced the ratio between the magnitude of the secondary and primary IgG response to β-amyloid, confirming a consolidation phase in immunological memory for the phage-based vaccine. | The study contributes to understanding how timing of booster doses can affect the development of immunological memory, which is crucial for designing effective vaccination strategies, especially for diseases like Alzheimer's where immune memory plays a key role. | Humoral | Antibody titre |
| Recombinant Phage Elicits Protective Immune Response against Systemic S. globosa Infection in Mouse Model | Sci Rep | 2017 | Original article - lab based | Mouse model | Sporothrix globosa | Filamentous bacteriophage | Measured through several key parameters: quantification of specific antibodies in serum to assess humoral response, flow cytometry analyses to evaluate the proliferation and activation of specific T cell subsets (indicative of cellular immunity), cytokine profile analysis to understand the type of immune response elicited (Th1, Th2, Th17), and survival rate and fungal burden in organs | Mice were immunized intraperitoneally at weekly intervals for a total of four times with 25 μg of phage-KR in 100 μL of PBS. | No | To evaluate the effectiveness of a recombinant phage vaccine displaying an epitope peptide in generating an immune response against systemic infections caused by Sporothrix globosa. The study investigates the potential of this vaccine to induce protective immunity, focusing on both humoral and cellular immune responses in a mouse model, with the goal of developing a viable vaccine strategy against S. globosa infections. | Creating a recombinant phage vaccine displaying an epitope specific to Sporothrix globosa. This vaccine is administered to a mouse model to assess its efficacy in eliciting an immune response against S. globosa infection. The study measures both humoral and cellular immune responses, including antibody titers and cytokine production. Additionally, the effect of the vaccine on the survival rate of mice challenged with a systemic S. globosa infection is evaluated to determine its protective capacity. | The key findings of the study are that the recombinant phage vaccine displaying a specific epitope against Sporothrix globosa effectively induces a protective immune response in a mouse model. This response includes the production of significant antibody titers and a robust cellular immune response, evidenced by cytokine production. Importantly, vaccinated mice showed an increased survival rate following systemic S. globosa infection, indicating the vaccine's potential as an effective tool in preventing and managing this type of infection. | demonstrates the capability of recombinant phage technology to induce a specific and effective immune response against a fungal pathogen, Sporothrix globosa. This expands the potential applications of phage vaccine technology beyond bacterial and viral pathogens, showing its effectiveness against fungal infections as well. The success of this approach in eliciting both humoral and cellular immunity, along with improved survival rates in an animal model, highlights the versatility and potential of phage-based vaccines in addressing a wide range of infectious diseases. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Preclinical development of a vaccine against oligomeric alpha-synuclein based on virus-like particles | PLoS One | 2017 | Original article - lab based | Mouse model | Parkinson's disease | Qbeta bacteriophage virus-like particles (VLPs) conjugated with short peptides of human alpha-synuclein | Measured through the generation of high titers of antibodies against alpha synuclein, using ELISA to monitor antibody titers over time. The produced antibodies specifically targeted oligomeric and aggregated forms of alpha-synuclein, with a much greater affinity for oligomeric species over monomeric forms. | Mice were immunized with 20 μg of the vaccine intravenously or subcutaneously on day 0 and day 21. Blood was collected at regular intervals until day 70 to establish antibody production kinetics. | No | To develop a vaccine that targets alpha-synuclein oligomers, which are implicated in Parkinson's disease. The focus is on exploring the potential of using Qbeta (Qb) bacteriophage coat protein to form virus-like particles (VLPs) as a platform to present alpha-synuclein peptides to the immune system. | The methodology involves engineering VLPs to display peptides of alpha-synuclein. The Qbeta (Qb) bacteriophage coat protein interacts with RNA and spontaneously forms VLPs when expressed in E. coli. These can be used to effectively present antigens to immune effector cells and stimulate strong humoral responses.These VLPs are then used to immunize mice, followed by evaluation of the immune response. The study assesses antibody production, specificity, and affinity, particularly focusing on the ability of these antibodies to recognize and bind to alpha-synuclein oligomers. | The study's key findings include the successful induction of a specific immune response against alpha-synuclein oligomers. The antibodies generated showed a higher affinity for oligomeric forms of alpha-synuclein compared to the monomeric forms, suggesting the potential effectiveness of the vaccine in targeting pathological structures relevant to Parkinson's disease | This research is significant for phage vaccine technology as it showcases the application of phage technology to create VLPs in targeting neurodegenerative diseases, particularly Parkinson's disease. It illustrates the versatility of phage-derived systems in vaccine development, extending their use beyond traditional infectious diseases to address complex neurological disorders. | Humoral | Antibody titre |
| Phage Display-Derived Ligand for Mucosal Transcytotic Receptor GP-2 Promotes Antigen Delivery to M Cells and Induces Antigen-Specific Immune Response | SLAS Discov | 2017 | Original article - lab based | Mice | The vaccine developed in this study was not targeted against a specific pathogen but was focused on enhancing the delivery of antigens to the mucosal immune system. The study aimed to improve oral immunization efficiency by targeting glycoprotein-2 (GP-2), a receptor on M cells within the follicle-associated epithelium, which plays a crucial role in transcytosing luminal antigens. | N/A | Measured the induction of EGFP-specific serum IgG using ELISA, and assessed priming of EGFP-specific lymphocytes and the pattern of cytokine secretion. The Gb1-EGFP fusion induced both mucosal and systemic immune responses, which were measured in terms of antigen-specific serum and fecal antibodies, cytokine secretion, and lymphocyte proliferation. | | No | To enhance oral vaccine efficiency by targeting the mucosal transcytotic receptor GP-2, which is expressed on M cells in the intestinal epithelium. The goal is to improve antigen delivery to mucosal immune sites using phage display-derived ligands. | The research involved biopanning a phage display library to identify peptide ligands binding to GP-2. Selected peptides were fused to enhanced green fluorescent protein (EGFP) and administered orally to mice. The study assessed the uptake of these peptides by M cells and measured the resulting mucosal and systemic immune responses. | One peptide, Gb-1, showed high affinity for GP-2 and significantly increased EGFP uptake by M cells. Mice orally administered with the Gb1-EGFP fusion exhibited strong mucosal and systemic immune responses, with elevated antigen-specific serum and fecal antibodies, cytokine secretion, and lymphocyte proliferation. | This study demonstrates the potential of phage display technology to develop targeted mucosal vaccines. By identifying ligands that can specifically target mucosal receptors, it opens new avenues for designing more efficient oral vaccines, crucial for combating pathogens that enter through mucosal surfaces. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Immunogenicity of T7 bacteriophage nanoparticles displaying G-H loop of foot-and-mouth disease virus (FMDV) | Vet Microbiol | 2017 | Original article - lab based | Pigs | Foot-and-mouth disease virus (FMDV). | T7 bacteriophage | Immune response was measured by antibody titers, lymphocyte proliferation tests, and detection of neutralizing antibodies against FMDV. | Pigs were single immunized via the intramuscular route with the T7-GH phage vaccine. | Yes, included the adjuvant Montanide ISA206 | To evaluate the immunogenicity of T7 bacteriophage nanoparticles displaying the G-H loop of FMDV in developing a vaccine against foot-and-mouth disease. | The methodology includes cloning the G-H loop gene into T7 bacteriophage, large-scale amplification, and purification of the T7-GH phage. Pigs were immunized with these nanoparticles, and the immune response was assessed through antibody titers, lymphocyte proliferation tests, and detection of specific neutralizing antibodies against FMDV. | The T7-GH phage nanoparticles were effective in eliciting antigen-specific immune responses in pigs, comparable to commercial FMDV vaccines. The vaccine induced significant antibody responses and specific lymphocyte responses, with a notable proportion of immunized pigs protected from a virulent homologous virus challenge. | This study is important as it demonstrates the potential of T7 bacteriophage nanoparticles in developing effective vaccines against viral diseases like foot-and-mouth disease, highlighting the versatility and efficacy of phage-based vaccine platforms. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Phage-Based Anti-HER2 Vaccination Can Circumvent Immune Tolerance against Breast Cancer | Cancer Immunol Re | 2018 | Original article - lab based | Mice | D16HER2, a splice variant of the HER2 protein, associated with breast cancer | Filamentous bacteriop | The immune response was measured by evaluating the anti-D16HER2 humoral response. | N/A | No | To develop phage-based vaccines targeting D16HER2, a splice variant of the HER2 protein, to overcome immune tolerance and treat HER2-positive breast cancers. | The research involved engineering bacteriophages to display immunogenic epitopes of D16HER2 on their surface. These phage-based vaccines were tested in a mouse model for their ability to induce an immune response against HER2-positive breast cancer. | The study found that these phage-based vaccines were successful in breaking immune tolerance, triggering a protective anti-D16HER2 humoral response. This indicates their potential efficacy as immunotherapy against HER2-positive breast cancers. | This research is crucial for phage vaccine development as it shows the potential of phage-based vaccines in cancer immunotherapy, particularly in overcoming immune tolerance, which is a significant challenge in cancer treatment. | Humoral | Antibody titre |
| Phage vaccines displaying YGKDVKDLFDYAQE epitope induce protection against systemic candidiasis in mouse model | Vaccine | 2018 | Original article - lab based | Mice | Candida albicans infections | Filamentous bacteriophage | The immune response was assessed through antibody production, cytokine levels, and survival rates post-infection. | Mice were immunized intraperitoneally at two-week intervals. | No | To develop a phage-based vaccine displaying the epitope YGKDVKDLFDYAQE for protection against systemic Candida albicans infections. | The study involved constructing filamentous phage variants displaying the epitope on coat proteins, immunizing mice with these recombinant phages, and assessing the immune response and protection against C. albicans. | The phage-based vaccine induced strong humoral and cellular immune responses, reduced fungal burden in mice, and improved survival rates, indicating its efficacy against C. albicans infections. | This research demonstrates the potential of phage display technology in developing vaccines against fungal infections, expanding the applicability of phage vaccines beyond bacterial and viral diseases. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Immunostimulation of Cyprinus carpio using phage lysate of Aeromonas hydrophila | Fish Shellfish Immunol | 2019 | Original article - lab based | Carp Model | Aeromonas hydrophila | Lytic bacteriophage p | Antibody titers, indicating humoral immunity, were assessed using serum agglutination assays. Cellular immunity was evaluated through the expression of immune-related genes, such as interleukin-1 beta (IL-1β), tumor necrosis factor alpha (TNF-α), lysozyme C, and serum amyloid A (SAA), using quantitative PCR (qPCR) analysis. | Intraperitoneal injection of vaccine formulations in carp. | Yes, used PLGA encapsulation for antigen delivery | The study aims to develop a vaccine against Aeromonas hydrophila in common carp using phage lysate (PL) as an antigen, assessing its efficacy and immune stimulation. | The vaccine was prepared using the lytic bacteriophage pAh 6-c to generate phage lysate of A. hydrophila. Common carp were immunized with different formulations, including PLGA-encapsulated phage lysate, to assess immune response. | The vaccine elicited a robust immune response, with higher survival rates in vaccinated fish compared to controls. High-dose phage lysate showed better efficacy, particularly when encapsulated with PLGA. | This demonstrates phage lysate's potential as an effective vaccine antigen, expanding the scope of phage vaccine applications in aquaculture. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Self-destructing Salmonella via temperature induced gene E of phage PhiX174 improves influenza HA DNA vaccine immune protection against H1N1 infection in mice model | J Immunol Methods | 2019 | Original article - lab based | Mice | H1N1 influenza virus | PhiX174 phage gene E was used for inducing lysis in the Salmonella carrier | Immune response was measured by assessing HA-specific antibody responses, cytokine production, and protection against H1N1 challenge in mice. | Mice were immunized intraperitoneally at two-week intervals. Immunizations occurred on week 0, week 2, and week 4 | No | To enhance the efficacy of an influenza HA DNA vaccine using a novel delivery system based on temperature-induced lysis of Salmonella by phage PhiX174 gene E. | Involved constructing a lysis plasmid with phage PhiX174 gene E and an influenza HA DNA vaccine, delivered using a modified Salmonella strain. The immune response and protective efficacy against H1N1 were tested in mice. | The modified Salmonella delivery system improved the immunogenicity of the HA DNA vaccine, demonstrating enhanced humoral and cellular responses and better protection against H1N1 infection in mice. | This study illustrates the potential of integrating phage elements (PhiX174 gene E) into bacterial vaccine carriers, offering a novel approach to enhancing DNA vaccine delivery and efficacy | Humoral and Cellular | Antibody titre and T cell activation markers |
| Targeted phage display- | Med | 2021 | Original article - lab based | Mice | N/A, just focuses on the methodology of pulmonary delivery using phage display technology and its potential for targeted vaccine delivery, rather than on a specific infectious agent. | Unspecified bacteriophage | A systemic humoral immune response was elicited, measured through the presence of phage particles in the bloodstream and the generation of specific antibodies (IgG, IgA) against the phage and the CAKSMGDIVC peptide | Mice and non-human primates were administered with the targeted phage particles via the intratracheal route, following a specific dosing schedule that included two serial doses of 10^12 Transducing Units (TU). | No | To investigate and demonstrate the feasibility of a novel immunization strategy involving targeted pulmonary delivery of phage particles displaying the ligand peptide CAKSMGDIVC | The study involved in vivo selection of a phage display library, identification and validation of the CAKSMGDIVC ligand and its receptor α3β1 integrin, pharmacokinetic modeling, and evaluation of humoral immune responses in mice and non-human primates. | The targeted phage particles successfully crossed the pulmonary barrier, were transported to the systemic circulation, and induced a robust and specific systemic humoral response. | Demonstrates a novel approach for targeted pulmonary vaccine delivery, potentially applicable to various diseases, highlighting the versatility and translational potential of phage display technologies in vaccine development. | Humoral | Antibody titre |

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| A Recombinant RBD-Based Phage Vaccine Report: A Solution to the Prevention of New Diseases? | Vaccines | 2023 | Original article - lab based | Mice | SARS-CoV-2 (COVID-19) | M13 filamentous bacteriophage | antiphage antibodies, Anti-P1 protein antibodies and presence of CD4+ and CD8+ T lymphocytes | Mice received booster dose given 2 weeks after first injection and bloods collected 2 weeks aftter booster dose | Yes, one group received 50 µg of spike protein with aluminium salts | To investigate whether mice could be effectively immunized against COVID-19 by using recombinant phages displaying the P1 spike protein on their surfaces. Combination with Purified P1 Protein: Additionally, the study explored whether adding purified P1 protein to the inoculation with recombinant phages could enhance the immune response in the mice. | First, recombinant M13 phages were engineered to display a truncated spike protein (P1), and mice were immunized with these phages. Second, mice were injected with purified P1 protein along with recombinant or helper phages. The immune responses, including the production of anti-phage and anti-P1 antibodies, as well as the activation of CD4+ and CD8+ T cells in the lung tissue, were assessed. | Mice that received recombinant phages were immunized against the phage particles but did not generate anti-P1 IgG antibodies. In contrast, the group that received a combination of P1 protein and recombinant phage showed immunization against the P1 protein. Both groups exhibited the presence of CD4+ and CD8+ T cells in the lung tissue, suggesting activation of the immune system. Number of antigens on phage body is crucial in stimulating immue system. While the recombinant phage was immunogenic enough to elicit an immune response against the phage particles, the addition of purified P1 protein was necessary to induce an immune response specifically against the target spike protein. | exploring the potential of bacteriophages as a vaccine platform for COVID-19, considering their safety, immunogenicity, and potential cost-effective production. The study provides insights into the efficacy of different strategies for stimulating the immune system against the virus. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Development of Klebsiell | Front Immunol | 2022 | Original article - lab based | Mice | Klebsiella pneumoniae | Unspecified bacteriophage | Induction and persistence of antibodies against CPS in mice. Bactericidal activities of antibodies induced by the vaccines. Survival rates of mice challenged with K. pneumoniae after vaccination. Protection against subsequent infection of K. pneumoniae by the respective capsular type. | Booster dose given at 1 and 2 weeks after intial dose | Yes, used glycolipid adjuvant C34 | To develop effective vaccines against Klebsiella pneumoniae, a pathogen associated with nosocomial and community-acquired infections, especially due to antibiotic resistance. The focus was on serotypes K1 and K2, known for causing invasive infections, using a novel approach involving phage-derived depolymerases for vaccine development. | Phages were isolated to identify capsule depolymerases for K1 and K2 serotypes. These depolymerases were then used to cleave the capsule polysaccharides (CPS) of K. pneumoniae into oligosaccharides with intact immunogenic modifications. The resulting K1 and K2 oligosaccharides were conjugated with a carrier protein to create CPS-conjugated vaccines. Mice were immunized, and their immune responses and protective efficacy were evaluated. | The study successfully developed K1 and K2 CPS-conjugated vaccines using phage depolymerases. Immunization with these vaccines induced high levels of anti-CPS antibodies, resulting in significant bactericidal activity. The vaccines provided effective protection against subsequent K. pneumoniae infection in a mouse model, demonstrating promising potential for human vaccine development. | This research is relevant due to the increasing antibiotic resistance of K. pneumoniae, making vaccine development crucial. The study's innovative use of phage depolymerases to obtain immunogenic CPS modifications addresses previous challenges in vaccine preparation. The successful demonstration of vaccine efficacy in a mouse model suggests a promising strategy for developing vaccines against K. pneumoniae infections, which have become a global health concern. | Humoral | Antibody titre |
| Adaptive antitumor immu | J Exp Clin Cancer R | 2022 | Original article - lab based | Mice | hepatocellular carcinoma (HCC) and triple-negative breast cancer (TNBC) | Bacteriophage λ (lambda) | Tumor Growth and Survival: Tumor size, weight, and overall survival of mice were measured. Cytotoxic T Cell Activity: In vitro cytotoxicity of splenocytes derived from vaccinated mice against target tumor cells (BNL or 4T1) was assessed. T Cell Activation: Antigen (ASPH) specific CD4+ and CD8+ T cell activation was measured by the upregulation of IFN-γ. Antibody Response: Anti-ASPH antibody titers in serum were evaluated. Tumor Microenvironment: Histological features, the number of tumor-infiltrating lymphocytes (TILs), and the presence of tertiary lymphoid structures (TLSs) were assessed. Overall Immune Response: Various immune parameters, including cytokine secretion, were measured. | Immunised weekly for varying durations | No | To investigate the therapeutic potential of an aspartate β-hydroxylase (ASPH)-based λ phage vaccine in murine models of hepatocellular carcinoma (HCC) and triple-negative breast cancer (TNBC). The research sought to evaluate the vaccine's impact on tumor growth, immune response activation, and overall survival. | The study utilized a murine model with immunocompetent BALB/c mice. The λ phage vaccine was engineered to display ASPH peptides and administered via subcutaneous injections. The experiment included tumor inoculation, vaccination, and, in some groups, programmed cell death protein 1 (PD-1) blockade. Various assays, including tumor size measurements, cytotoxicity assays, and immune cell activation assessments, were employed to evaluate the vaccine's efficacy. | The combination of the ASPH-based λ phage vaccine with PD-1 blockade demonstrated substantial anti-tumor effects in both HCC and TNBC models. The combination therapy led to enhanced cytotoxic T cell activity, increased T cell activation, and the development of tertiary lymphoid structures within the tumors. The vaccine induced a significant anti-ASPH antibody response, indicating a robust immune reaction against the target antigen. The study revealed a favorable impact on the tumor microenvironment, with increased infiltration of CD3+ and CD8+ T cells. | This research is relevant as it proposes a novel therapeutic approach using a bacteriophage-based vaccine targeting ASPH in cancer models. The findings suggest the potential effectiveness of this vaccination strategy, particularly in combination with immune checkpoint blockade, offering insights into future immunotherapeutic interventions for hepatocellular carcinoma and triple-negative breast cancer. | Cellular | T cell activation markers |
| A universal bacteriophag | Sci Adv | 2021 | Original article - lab based | Mice and Rabbits | SARS-CoV-2 (COVID-19) | Bacteriophage T4 nanoparticle | antibody titers, virus neutralization titers, ACE2 blocking titers, and survival rates against SARS-CoV-2 challenge in mice. the generation of balanced TH1- and TH2-derived antibody responses against different CoV-2 antigens. | N/a | No | To develop a versatile vaccine platform using bacteriophage T4 nanoparticle and CRISPR engineering for the rapid generation of vaccine candidates against emerging and pandemic pathogens, with a specific focus on SARS-CoV-2. | This study employed CRISPR genome engineering, utilizing both type II Cas9 and type V Cas12a nucleases, to create recombinant phages containing SARS-CoV-2 gene insertions | The T4-CRISPR platform successfully generated a pipeline of SARS-CoV-2 vaccine candidates in a matter of weeks, demonstrating efficiency in design and selection. The resulting vaccine, delivered by the T4 nanoparticle, elicited robust immune responses, including strong virus neutralization titers and ACE2 blocking titers in mice and rabbits. Importantly, the vaccine induced balanced TH1- and TH2-derived antibody responses against multiple CoV-2 antigens, without the need for an adjuvant. The T4-COVID vaccine was found to be safe in preclinical animal studies, showing no significant adverse reactions across various administration routes. | presents a novel and alternative vaccine design platform capable of rapidly generating vaccine candidates against emerging pathogens. The versatility of the T4-CRISPR platform, its ability to induce broad immune responses, and the absence of the need for an adjuvant highlight its potential as a cost-effective and safe alternative for large-scale vaccine production, particularly in pandemic situations. The findings contribute to the ongoing efforts to develop effective vaccines with broader protection against evolving pathogens. | Humoral | Antibody titre |
| Infectious bronchitis viru | Antiviral Res | 2021 | Original article - lab based | Chicken Model | Infectious Bronchitis Virus | Unspecified bacteriophage | The immune response in the study was assessed using quantitative real-time PCR (qRT-PCR) to measure the reduction in virus yield and indirect immunofluorescence assay (IFA) for visualizing the virus in chicken embryo kidney cells (CEKs). High-affinity peptides were found to reduce infectious bronchitis virus (IBV) proliferation in CEKs and in vivo in chickens. The study measured both humoral and cellular immune responses by detecting specific IBV S1 antibodies and IBV neutralizing antibodies in vaccinated chickens, indicating the activation of humoral immunity. | Chickens immunized at 7, 14, 21, and 28 days old with the corresponding phages (phage H, phage T, or non-affinity phage) by intramuscular injection. After immunization, chickens were infected with the virus at 42 days old. | No | To develop a vaccine against Infectious Bronchitis Virus (IBV) using specific-phage display technology targeting the glycosylated aminopeptidase N (gAPN) protein. The goal was to evaluate the immune response and antiviral efficacy of the developed vaccine in chickens. | SPF chicken embryos, chickens, and chicken embryo kidney cells (CEKs) were utilized. The gAPN gene was cloned and expressed, and phage display technology was employed for biopanning to identify peptides with high affinity for gAPN. High-affinity peptides were then tested for their ability to inhibit IBV in vitro using ELISA, virus yield reduction assay, and immunofluorescence assays. In vivo experiments involved immunizing chickens with selected phages and assessing their immune response and protection against IBV infection. | The study identified high-affinity peptides that effectively bound to the gAPN protein. In vitro experiments demonstrated that these peptides had antiviral activity, reducing IBV titers and showing potential in inhibiting virus replication in chicken cells. In vivo, vaccinated chickens exhibited an immune response with increased IBV-specific antibodies, resulting in reduced virus replication and milder pathological changes after IBV infection. | This research is relevant as it presents a novel approach to developing a vaccine against IBV in chickens. The use of phage display technology to identify high-affinity peptides targeting the gAPN protein represents a promising strategy. The findings suggest potential applications for controlling IBV infections in poultry, addressing a significant concern in the poultry industry and contributing to the development of effective vaccines against viral diseases in animals. | Humoral and Cellular | Antibody titre and T cell activation markers |
| The Effect of Immunosu | Front Immunol | 2021 | Original article - lab based | Mice | Type 1 diabetes | Recombinant GAD65 phage vaccine | Blood glucose levels and body weight to assess the effect of the vaccine on hyperglycemia and diabetes. Serum antibodies, including IgG1 and IgG2a, were measured by ELISA to evaluate the humoral immune response. Cytokines (IL-2, IL-4, IL-10, IFN-γ, TGF-β1) in the serum were examined using electrochemiluminescence. T cell proliferation in response to GAD65 was assessed. Dendritic cell maturation was analyzed by flow cytometry. The proportion of CD4+CD25+Foxp3+ Treg cells in spleen lymphocytes was evaluated. | Mice were subcutaneously immunized with the GAD65 phage vaccine alone or co-immunized with Kyn (kynurenine, an immunosuppressive adjuvant). The immunization schedule involved injections at weeks 10 and 12. | Yes, used kynurenine | To enhance the preventive efficacy of GAD65 vaccination for autoimmune diabetes by using kynurenine (Kyn) as an immunosuppressive adjuvant. The goal is to induce regulatory T cells (Tregs) and tolerogenic responses in a NOD mouse model. | Utilized a phage-displayed vaccine containing specific GAD65 sequences and co-immunized NOD mice with Kyn. They assessed the impact on hyperglycemia development, weight loss, Treg induction, dendritic cell maturation, and immune response modulation. RNA and miRNA sequencing were performed on mouse spleen lymphocytes stimulated by Kyn. | Subcutaneous administration of GAD65 phage vaccine + Kyn prevented hyperglycemia in 60% of NOD mice. No significant weight loss or deaths were observed, suggesting safety. Kyn enhanced the induction of GAD65-specific Tregs and inhibited dendritic cell maturation. The immune response shifted from a diabetogenic Th1 response to a regulatory Th2 response. miRNA and mRNA analysis suggested a role for Kyn in immune regulation, impacting pathways related to metabolism and immune function. | This study provides insights into an effective approach for preventing autoimmune diabetes by combining GAD65 vaccination with Kyn as an adjuvant. The findings highlight the potential of Kyn in inducing immune tolerance and modulating the immune response, offering a novel strategy for autoimmune disease treatment. | Humoral and Cellular | Antibody titre and T cell activation markers |
| Vaccination with cathepsi | Parasitol Int | 2021 | Original article - lab based | Mice | SARS-CoV-2 (COVID-19) | Recombinant phage | The immune response was assessed by measuring the ability of vaccine candidates to induce SARS-CoV-2 Spike S1 protein-specific antibodies in mice. Enzyme-linked immunosorbent assays (ELISAs) were performed to quantify the antibody response. | Mice were immunized with BaDAS and DEaDAS vaccine candidates, and the vaccination schedule involved intraperitoneal injections with boosts administered 2–3 weeks after the initial inoculation. Some mice received a third dose after 4 weeks. | No | To explore the potential of mycobacteriophages, such as Bxb1 and its derivatives, as platforms for phage-based vaccines against SARS-CoV-2. Specifically, the focus was on displaying immunogenic epitopes on the phage surface and investigating their adjuvant properties. | The researchers genetically manipulated mycobacteriophages to display SARS-CoV-2 epitopes, creating vaccine candidates known as BaDAS and DEaDAS. They assessed the immune responses in mice, particularly examining the ability of the displayed peptides to induce neutralizing antibodies. The study also investigated the limitations and opportunities of peptide display on phage capsid subunits. | Mycobacteriophages can be genetically engineered to display SARS-CoV-2 epitopes and serve as potential DNA vaccine delivery systems. BaDAS and DEaDAS vaccine candidates induced immune responses, but there was variation in individual mice responses to the displayed epitopes. Despite antibody binding to the displayed peptide, neutralization of SARS-CoV-2 was not observed, possibly due to conformational limitations of the displayed epitope. C-terminal extensions on capsid and tail tube proteins influenced the immune response, indicating their potential role as immunogenic decoys. Challenges include constraints on antigen size, genome capacity, and conformational suitability of displayed peptides for inducing neutralizing responses. | The study addresses the urgent need for diverse strategies in COVID-19 vaccine development. Phage-based vaccines offer advantages such as low cost, ease of production, and potential adjuvant properties. Understanding the immune responses and limitations of mycobacteriophage-based vaccines contributes to the broader exploration of vaccine platforms against SARS-CoV-2. | Humoral | Antibody titre |