utmb Health

Intellectual Property

SHOWCASE

EDITION Val

Val

Medical Devices
Diagnostics
Therapeutics
Vaccines
AI & Software

For patent information, please visit our website:

mbinnovations.co/patents

Or scan the QR code above using your phone.

utmb Health

Intellectual Property Showcase | Vaccines

EDITION
Val

TABLE OF CONTENT

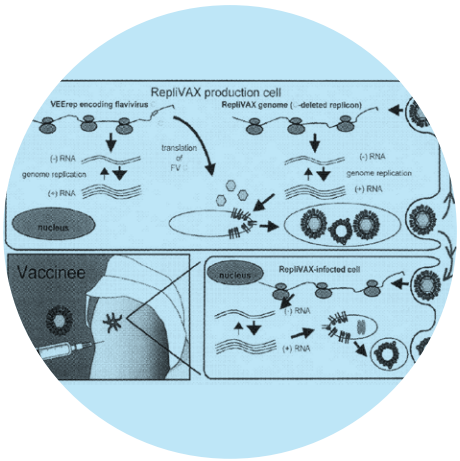
Arthropod-born Flavivirus Vaccine

PATENT TITLE

Flaviviruses Expressing the PrM, E, and NS1 Proteins of Other Flaviviruses and Uses Thereof

PATENT # US 9,499,588

INVENTORS | Peter W. Mason, Tomohiro Ishikawa



PROBLEM

The arthropod-borne flaviviruses are emerging public health crisis. These viruses also pose threats as agents of biowarfare and/or bioterrorism. Japanese encephalitis virus (JEV) is estimated to produce over 50,000 cases of CNS disease a year, about one-third of which result in death, making it the flavivirus with the highest worldwide mortality. Dengue includes a spectrum of illnesses caused by infection with one of four serotypes of Dengue virus that occur in many tropical and subtropical regions. The geographic distribution of dengue has expanded over the last 30 years to include more than 100 countries. Dengue virus is estimated to infect over 50 million per year.

There is an efficacious inactivated viral vaccine (INV) for Japanese encephalitis virus, but its production has been halted due to adverse events. Live-attenuated virus vaccines and inactivated viral vaccines for dengue are in development, but to date, no dengue vaccines have progressed beyond clinical trials, and unique aspects of immunopathogenesis of dengue are problematic for most vaccines in development.

Flavivirus vaccines in development share problems with existing vaccines. The current inactivated viral vaccine and a tick-borne encephalitis (TBE) inactivated viral vaccine in use in Western Europe require extensive purification, and are of low potency, requiring multiple vaccinations. A new flavivirus subunit vaccine candidate may suffer from similar problems. Viral-vectored vaccines, including a recently described alphavirus replicon-vectored vaccine may also suffer from problems of vector immunity that interfered with the use of vaccinia virus as a vector for a recombinant DNA-derived Japanese encephalitis virus vaccine candidate. DNA vaccines have low potency. There may also be problems with existing and new live-attenuated virus vaccines including the chimeras generated that relate to an incomplete understanding of the basis of their attenuation.

There is a critical need for new, more effective, and safer vaccines for flavivirus, especially arthopod-borne flaviviruses.

SOLUTION

This novel technology provides methods and compositions used for vaccines against flaviviruses.

POTENTIAL IMPACT

The technology overcomes the limitations of current vaccines. The new vaccines do not cause disease, even in the immunocompromised, has high potency due to in situ production of immunogens in a way that mimics viral infection, and h potentially has inexpensive production. The technology will greatly expand the preventive treatment options for controlling outbreaks.

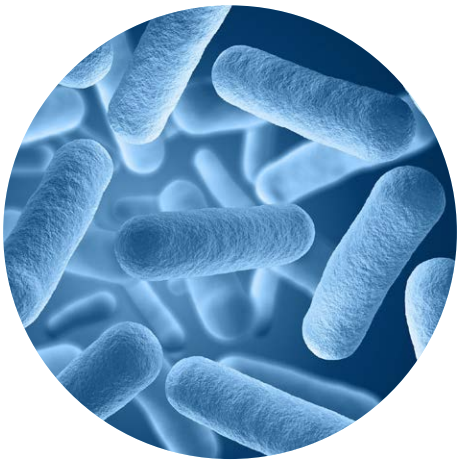
Burkholderia Vaccine

PATENT TITLE

Attenuated Burkholderia Mallei Strain Which Protects Against Pathogenic Burkholderia Infections, Vaccine Containing and Use Thereof

PATENT # US 10,213,503
 # US 9,267,947 (ASSOC.)

INVENTORS | Alfredo Torres



PROBLEM

There is an urgent need to develop effective therapeutic approaches against NIAID category B, tier 1 pathogens, such as Burkholderia mallei and Burkholderia pseudomallei, the causative agents of human glanders and melioidosis, respectively. Concern over these bacteria has heightened because of the pathogens' seemingly perfect characteristics for malicious use as a biowarfare weapon against humans. A vaccine developed to combat these bacterial agents will also have value for the immunization of at-risk populations in melioidosis endemic areas of the world.

SOLUTION

Novel Burkholderia vaccine strains have been developed that demonstrate the ability to protect against acute respiratory glanders. These vaccine strains have proven to be attenuated, safe, and effective at protecting against lethal Burkholderia mallei challenge.

POTENTIAL IMPACT

This novel technology will be useful in vaccine development for use in humans and animals. This technology can also be applicable to the development of other therapeutics providing immunoprotection against infections by NIAID category B, tier 1 pathogens, Burkholderia mallei and Burkholderia pseudomallei. In doing so, the risk of infection from the causative agents of human glanders and melioidosis will be greatly reduced. These efforts will also reduce the danger of these bacteria being used as biowarfare weapons.

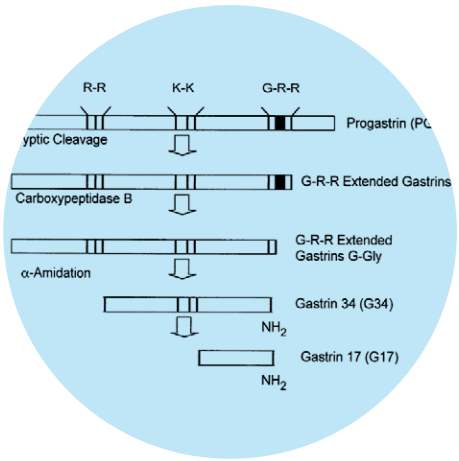
Colorectal Cancer Vaccine

PATENT TITLE

Immunogenic Compositions Comprising Progastrin and Uses Thereof

PATENT # US 10,335,470

INVENTORS | Pomila Singh, Gurpreet Singh



PROBLEM

Colorectal cancers are becoming increasingly common and deadly. Advances in molecular genetics have led to better risk assessment and earlier diagnosis, but it remains deadly due to a lack of effective adjuvant treatments. Such adjuvants are likely to arise from a better understanding of factors that regulate proliferation of colonocytes and colon cancer cells. Just as genetic instability due to the inheritance of specific genetic defects plays a dominant role in initiation and progression of familial cancers, hyperproliferation is likely to play a permissive role in the initiation and progression of sporadic cancers. Hyperproliferation is recognized as a risk factor that can initiate dysplastic growth, resulting in accumulation of genetic defects and progression to colorectal cancer. Gastrins represent a group of growth factors that play a prominent role in proliferation.

The gastrin gene is normally expressed and processed in the brain and in the antral stomach. The full length progastrin peptide undergoes enzymatic deletions at the C and N terminal ends, to generate the fully processed C-terminally amidated gastrin peptides. G17 and G34 amino acid gastrin peptides stimulate acid secretion and growth of the gastrointestinal (GI) tract. Although the colon cancer cells express the gastrin gene, they do not process the progastrin peptides. Thus, patients with colorectal cancers (CRCs) are positive for significant levels of progastrin-like peptides. Studies have reported the presence of elevated levels of progastrin peptides but not gly-extended gastrin or gastrins in patients with colorectal cancers.

A significant percentage of human colon cancer (HCC) cells have been shown to require the expression of progastrin-like peptides for maintaining in vitro and in vivo growth. Downregulation of the gastrin gene resulted in the attenuation of the growth of gastrin dependent HCCs. A processing intermediate, gly-extended gastrin (GG) was reported to exert potent growth factor effects on several target cells including normal and cancerous intestinal epithelial cells.

SOLUTION

This novel technology provides methods and compositions that can be useful as a vaccine to treat cancers that produce progastrin ectopically or are dependent on progastrin.

POTENTIAL IMPACT

The technology overcomes the limitations of current vaccines by not producing vector specific immunity, not having quality assurance and control complexities, and producing higher targeted immunity. The technology will greatly expand access to care.

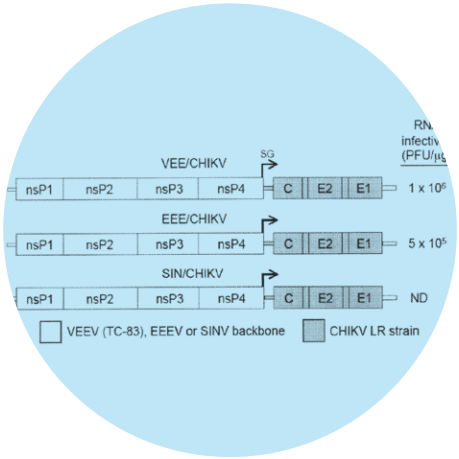
Chikungunya Vaccine

PATENT TITLE

Chimeric Chikungunya Virus and Uses Thereof

PATENT # US 8,343,506

INVENTORS | Ilya V. Frolov, Scott C. Weaver, Eryu Wang



PROBLEM

Chikungunya virus has for decades been an important etiologic agent of human disease in Africa and Asia. However, cases are grossly underestimated because Chikungunya virus infections usually cannot be distinguished clinically from dengue virus. Typically, Chikungunya virus causes a severely incapacitating, self-limited disease characterized by fever, rash, and severe joint pains. Recent outbreaks included many fatal cases, raising the possibility that Chikungunya virus has become more virulent. Chikungunya virus may spread into the Western Hemisphere through the movements of infected travelers from Asia and Africa or through introduction of infected mosquitoes carried from epidemic sites. The dramatic spread of dengue viruses throughout tropical America, via the same vectors and human hosts, serves as a precedent. If introduced into the New World, Chikungunya virus could cause millions of additional cases of severe and possibly fatal disease. In addition to its enormous potential as an emerging virus, Chikungunya virus is also underestimated as a potential biological weapon.

Despite the importance as an emerging virus and potential as a biological weapon, there are no licensed vaccines or therapeutics. Several experimental human and licensed veterinary vaccines have been produced by inactivation of wild-type or attenuated alphaviruses, but all are poorly immunogenic and require multiple vaccinations and frequent boosters. Other candidates exhibited high rates of reactogenicity, and many people failed to seroconvert.

SOLUTION

This novel technology provides an attenuated recombinant chimeric chikungunya virus (CHIKV) and methods of use as vaccines and in serological and diagnostic assays.

POTENTIAL IMPACT

The technology overcomes the limitations of other vaccine candidates while providing promise of an effective vaccine that will offer millions of people in endemic areas protection from a truly horrible and debilitating disease. The technology will also limit the potential for use as a biological weapon.

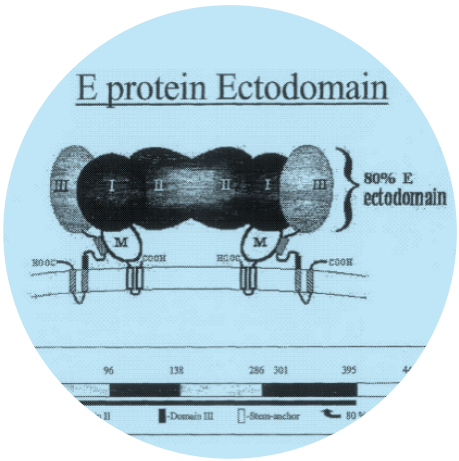
Enhances Flavivirus Detection

PATENT TITLE

Compositions and Methods Related to Flavivirus Envelope Protein Domain III Antigens

PATENT # US 7,785,799

INVENTORS | Alan Barrett, David Beasley, Michael Holbrook



PROBLEM

The United States has experienced several epidemics of West Nile (WN) virus in humans and animals over an expanding geographical range. Outbreaks of WN with neurological manifestations have also been reported in Europe and Africa.

Other members of the serocomplex include Japanese encephalitis (JE) virus, St. Louis encephalitis (SLE) virus, and Murray Valley encephalitis (MVE) virus. These viruses are antigenically like WN virus, and their co-circulation in several regions of the world has complicated the specific diagnosis of infections by these viruses. Current protocols for the serological diagnosis of WN virus infection rely primarily on preliminary screening for WN virus-reactive IgM/IgG antibody by capture ELISA and confirmation by plaque reduction neutralization test (PRNT), a process which results in considerable delays in the reliable reporting of accurate case numbers and requires a confirmatory testing.

Current diagnostic assays utilize either ELISA or dipstick formats for identification of flavivirus infection. Several assays are available for the detection of dengue virus infection. These assays utilize antigen capture and antibody based ELISAs and dipsticks for detection of virus specific IgG or IgM. The recent utilization of subviral particles (SVP) in an ELISA-based diagnostic test for tick borne encephalitis TBE infection shows promise. Since this assay uses intact viral M and E proteins it is likely that the pitfalls that affect the use of complete viral antigen may impede its employment.

The use of RT-PCR is also a potential method for diagnosis. However, RT-PCR assays have the significant limitation of requiring advanced techniques, equipment, and reagents. In addition, RT-PCR detects the presence of virus in patient serum which is, unfortunately, not beneficial as most patients go to the hospital at the onset of symptoms, at which time the virus has already been cleared. There is a critical need to improve the current reagents used for diagnosis.

SOLUTION

This novel technology provides methods and compositions for antibodies directed to, and antigens derived from, flavivirus envelope protein domain III for detection of various members of the genus flavivir.

POTENTIAL IMPACT

The technology overcomes the complexities associated with current serological based testing and RT-PCR based testing. The technology provides increased stability and will limited testing issues due to reagent control requirements. The technology will greatly expand the access to testing and associated treatments, while reducing costs of the testing.

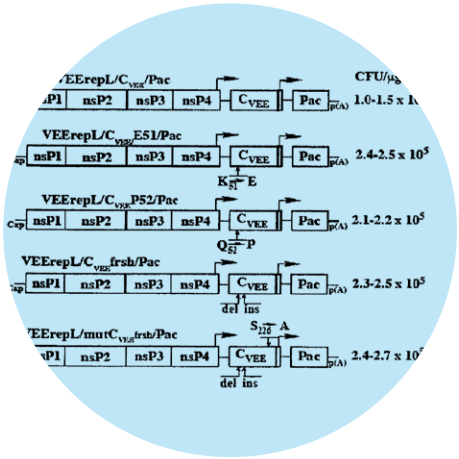
Enhanced Alphavirus Vaccine

PATENT TITLE

Attenuation of Encephalitogenic Alphavirus and Uses Thereof

PATENT # US 8,614,082

INVENTORS | Ilya V. Frolov, Elena Frolova, Scott C. Weaver



PROBLEM

The Alphavirus genus in the Togaviridae family includes several important human and animal pathogens. Alphaviruses are currently classified into 6 antigenic complexes and are globally distributed. They are efficiently transmitted by mosquitoes, in which they cause a persistent, lifelong infection that does not noticeably affect biological functions of the vectors. In vertebrates, the infection is acute and characterized by high-titer viremia, rash, fever, and encephalitis until the death of the infected host or clearance of the virus by the immune system. The encephalitogenic alphaviruses, including Venezuelan (VEEV), eastern (EEEV) and western equine encephalitis (WEEV) viruses, represent a continuous public health threat.

During VEEV epizootics, equine mortality can reach 83%, and, in humans, this virus produces a severe temporary immunodeficiency and a greatly debilitating and sometimes fatal disease. The VEEV genome is represented by a single-stranded RNA molecule of positive polarity of almost 12-kb. It mimics the structure of cellular mRNA, in which it contains a Cap at the 5' terminus and a poly(A) tail at the 3' end of the RNA.

The current vaccine (TC-83) against VEEV infection was developed four decades ago. Presently, TC-83 is still the only available vaccine for laboratory workers and military personnel. Of those vaccinated, 40% develop a disease with some symptoms typical of natural VEEV infection, including a febrile, systemic illness and other adverse effects. No effective antivirals have been developed against this virus as well.

SOLUTION

This novel technology provides a method to attenuate encephalitogenic alphaviruses, including VEEV, EEEV and WEEV. The attenuated phenotype is irreversible and thus, can be effective as human and/or veterinary.

POTENTIAL IMPACT

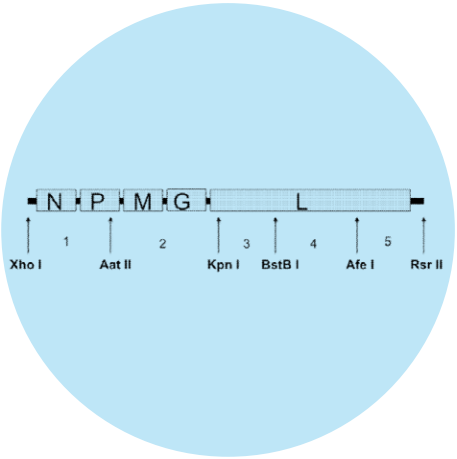
The technology overcomes the use of other alpha viruses as surrogate models for VEEV vaccine and antiviral drug discovery. The technology will help provide the promise of a more effect and tolerable VEEV vaccine that helps prevent the unnecessary spread of such a horrible disease.

Enhanced Isfahan Viral Vectors

PATENT TITLE

Recombinant Isfahan Viral Vectors

PATENT # US 9,932,564



INVENTORS | Demetrius Matassov , Rodion V. Gorchakov, Stefan Hamm, Rebecca Nowak, Robert L. Seymour, John H. Eldridge, Robert B. Tesh, David K. Clarke, Theresa E. Latham, Scott Weaver, Farooq Nasar

PROBLEM

Recombinant vesicular stomatitis virus (rVSV) has been developed as a vector platform for a range of human pathogens, and an optimized rVSV vector expressing HIV-1 gag protein has completed clinical evaluation. Despite these advances, challenges remain in the development of the rVSV vector platform, including potential immunity generated against vector proteins that may interfere with subsequent boosting immunizations. This potential problem may be overcome when rVSV vectors are used in heterologous prime-boost immunization with other immunologically distinct vectors. Serotype switching of rVSV vectors, achieved by swapping the surface G protein with that of a different vesiculovirus serotype, also enhances immunogenicity. However, cross-reactivity of cellular immune responses directed towards rVSV core proteins may limit this approach.

In view of these observations and potential limitations, there is a critical need for additional heterologous vectors for use either alone, or in conjunction with, rVSV vectors.

SOLUTION

This novel technology provides methods and compositions related to utilizing vesiculoviruses, such Isfahan virus (ISFV) alone or in combination with vesicular stomatitis virus (VSV), as therapeutic and/ or prophylactics treatments. The methods and compositions can include native, recombinant, and chimeric viruses.

POTENTIAL IMPACT

The technology overcomes the limitations of the other therapeutics being developed in that this solution does not produce non-specific immunity within the host. These innovative improvements will help yield more effective and safer vaccines while helping to expand access to treatment.

Enhanced Vaccines (Zika)

PATENT TITLE

Vaccine with Reduced Enhancement of Viral Infection

PATENT # US 10,322,171

INVENTORS | Slobodan Paessler, Veljko Veljkovic

PROBLEM

Zika is a disease caused by Zika virus, which is spread to people primarily through the bite of infected mosquitos. The most common symptoms of Zika are fever, rash, joint pain, and conjunctivitis. The illness is usually mild, with symptoms appearing 2 to 7 days after being bitten and lasting for several days to a week. There have been reports of serious birth defects, namely microcephaly, and other poor pregnancy outcomes. There have also been cases of Guillain-Barre syndrome (GBS) reported in patients following Zika virus infection. GBS is a rare autoimmune disorder, causing muscle weakness and sometimes, paralysis. These symptoms can last anywhere from a few weeks to several months or become permenant.

Zika virus is a member of the virus family Flaviviridae, and is related to Dengue, Yellow fever, Japanese encephalitis, and West Nile viruses. Like other members of the Flavivirus genus, Zika contains a positive single-stranded genomic RNA, encoding a polyprotein that is processed into three structural proteins and seven nonstructural proteins. There is currently no available vaccine to prevent or treat Zika infection. Accordingly, there is a critical need to identify novel antigens that can elicit an immune response against Zika to provide protection against infection.

SOLUTION

This novel technology relates to the development of a vaccine capable of providing protection against viral infection associated with antibody-dependent enhancement (ADE) of infection, such as Zika, Dengue and Ebola infections or other viruses where viral antigens may elicit ADE, as well as the production of antibodies to treat or prevent such infections.

The technology can be used of an information spectrum method (ISM) to identify novel peptides that possess sufficient structural homology with Zika envelope glycoprotein (GP1) to be suitable for use as an antigen to elicit an immune response and antibody production.

POTENTIAL IMPACT

The technology provides the promise of developing the first Zika virus vaccine and antiviral therapy which is effective and free from unwanted side effects. The technology will provide frontline protection for health workers and help to reduce the risk of pandemics. The technology will also help reduce clinical and society costs.

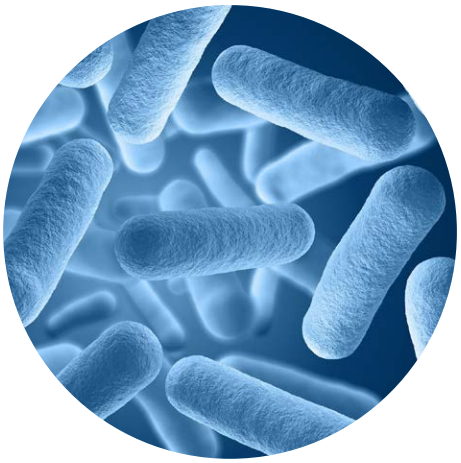
Escherichia coli Vaccine

PATENT TITLE

Compositions and Methods for Enterohemorrhagic Escherichia Coli (EHEC) Vaccination

PATENT # US 10,226,520
 # US 9,579,370 (ASSOC.)

INVENTORS | Alfredo Torres



PROBLEM

Enterohemorrhagic Escherichia coli (EHEC) O157:H7 strains are major human food-borne pathogens, responsible for bloody diarrhea and hemolytic uremic syndrome (HUS). The discovery of cattle reservoirs shedding high levels of EHEC O157:H7, which has been associated with the transmission between animals and across the human-animal interface, strongly supports the idea that adoption of vaccination for livestock and/or susceptible individuals will have significant public health benefits, preventing substantial numbers of human EHEC O157:H7 cases. Therefore, further discovery for EHEC-specific antigens needs to be completed to develop novel vaccines.

SOLUTION

Because the EHEC-associated disease is complex and many molecular and cellular processes affected during infection are not fully understood, it is plausible to propose that some EHEC-encoded virulence-associated proteins could have important yet unveiled roles in the immune/protective process. Therefore, to bypass the bias towards assaying a limited number of known virulence factors as components of a vaccine against O157:H7, the inventors of this novel technology performed a genome-wide in silico search for proteins most likely to be effective as immunogenic/protective antigens.

By comparative genomics, EHEC-specific antigens were identified with high probability to be exposed to the host during infection. Using an immunoinformatics approach, the candidates were further grouped into high, medium, and low-priority groups based on their putative antigenicity and screened as vaccine candidates in a murine model of gastrointestinal infection. Candidates were selected and evaluated as DNA vaccines for their capacity to induce an EHEC immune response and to reduce bacterial colonization in the murine intestine.

POTENTIAL IMPACT

An effective E. coli O157:H7 vaccine would prevent countless food-born illnesses around the world. Vaccination of livestock populations would help prevent wholesale destruction of stocks after an infection is detected, potentially saving billions of dollars annually.

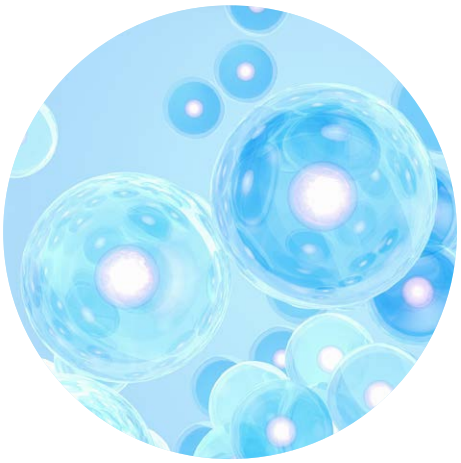
Exosome Delivery System

PATENT TITLE

Exosomes and Methods of Making and Using the Same

PATENT # US 10,590,171

INVENTORS | Jesus Silvas, Patricia Aguilar, Vsevolod Popov



PROBLEM

Bunyavirales is a broad order of viruses that cause significant morbidity and mortality around the world. These viruses are associated with a range of clinical symptoms characterized by febrile illness, severe fatal hepatitis, hemorrhagic fever, and neurological manifestations. One example of an emerging virus within this order is Severe Fever with Thrombocytopenia Syndrome (SFTS) Virus. Fatality rates for this new virus have been reported as high as 30%. The recent discovery of person-to-person transmission makes this virus and others within the order extremely dangerous. There is a critical need to develop vaccines and therapeutic treatments to combat a potential public health emergency akin to the COVID pandemic.

SOLUTION

This novel technology employs an engineered exosome and delivery method that can be used to deliver therapeutic agents such as vaccines or other immunogenic agents for the treatment of these viruses. These exosomes can be packaged with nonstructural (NS) viral proteins, glycoproteins, fusion proteins, RNA or DNA to customize the clinical requirements of the virus outbreak.

POTENTIAL IMPACT

The viral exosomes and delivery system can become effective candidates for large scale vaccine and therapeutics development. These innovations can play a critical role in reducing the spread of various viruses within the order by providing new and novel therapeutic options for increasingly harmful and deadly diseases. This expanded use of exosomes for vaccine delivery will add to the already established use of exosomes in disease diagnostics, cancer treatment, and regenerative medicine.

Ehrlichia Vaccine

PATENT TITLE

Vaccine to Protect Against *Ehrlichia* Infection

PATENT # US 10,335,476

INVENTORS | Sunil Thomas, David H. Walker

PROBLEM

Human monocytic ehrlichiosis (HME) caused by Ehrlichia chaffeensis was first reported in 1987. The clinical symptoms of HME include fever, headache, lymphadenopathy, malaise, myalgia, rash, and nausea. Illness due to ehrlichiosis can be so mild that no medical care is sought, or the illness can be severe and sometimes fatal, particularly in the immune compromised and elderly. Symptoms are generally non-specific, and other diagnoses may be considered. Because the laboratory tests that detect ehrlichiosis are often not positive in the first week of illness, physicians base early patient treatment decisions on the signs and symptoms, as well as the patient's history of tick exposure. The physician also looks at specific blood tests such as blood cell counts (decreased), or elevated liver enzyme levels are often helpful, yet non-specific predictors. There is a critical need to develop a vaccine that can protect against Ehrlichia infection.

SOLUTION

This novel technology provides methods and immunogenic compositions and vaccines, as well as therapeutic methods to prevent, ameliorate, or treat Ehrlichia infection or its sequelae.

POTENTIAL IMPACT

The technology provides the promise of a first in-class vaccine against Ehrlichia infection. The technology will greatly expand treatment options, access to care, and provide frontline protection against exposure to Ehrlichia.

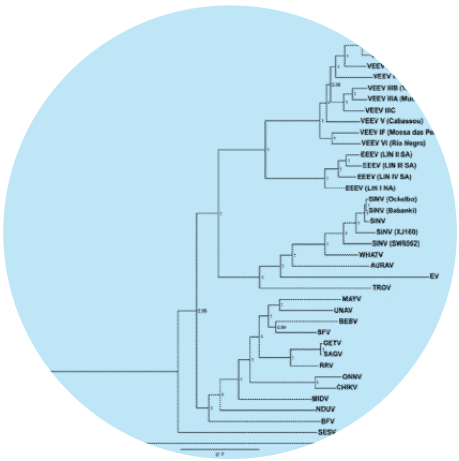
Functional Alphavirus Phylogenetics

PATENT TITLE

Alphavirus Compositions and Methods of Use

PATENT # US 9,422,529

INVENTORS | Farooq Nasar, Jesse Erasmus, Scott C. Weaver



PROBLEM

Current classification of the genus Alphavirus includes 29 species that can be further classified into nine complexes based on antigenic and/or genetic similarities. Barmah Forest, Ndumu, Middelburg, and Semliki Forest complexes consist of almost exclusively Old World viruses whereas Venezuelan equine encephalitis (VEE), Eastern equine encephalitis (EEE), and Trocara complexes are comprised of New World viruses. Western equine encephalitis (WEE) complex contains both Old World and New World viruses as well as recombinant viruses. The latter viruses are decedents of a recombinant virus that obtained nonstructural and capsid genes from an EEE-like virus and the remaining genes from a Sindbis-like virus.

Most alphaviruses are maintained in natural cycles between arthropod vectors, mainly mosquitoes, and susceptible vertebrate hosts. Occasionally, these cycles can spill over into the human and animal populations and can cause disease. Human infections with Old World viruses such as Ross River (RRV), chikungunya (CHIKV), and Sindbis (SINV) are characterized by febrile illness, rash and polyarthritis. In contrast, infections with New World viruses, Venezuelan equine encephalitis (VEEV), Eastern equine encephalitis (EEEV) and Western equine encephalitis (WEEV), can cause fatal encephalitis. The ability of alphaviruses to infect both invertebrates and vertebrates facilitates a broad host range that enables the viruses to be maintained in ecological niches with sporadic outbreaks in humans and animals.

The viral factor(s) that underlie the broad host range of mosquito-borne alphaviruses are poorly understood. Host restricted viruses may provide insight into these factor(s) and provide vector delivery platforms for expression or attenuation in specific hosts.

SOLUTION

This novel technology provides methods and compositions for use of newly identified alphaviruses.

POTENTIAL IMPACT

The technology opens a new window into specific alphavirus detection, diagnosis, vaccine/ drug development, and clinical treatment. The technology will greatly expand access to care and help prevent alphavirus outbreaks.

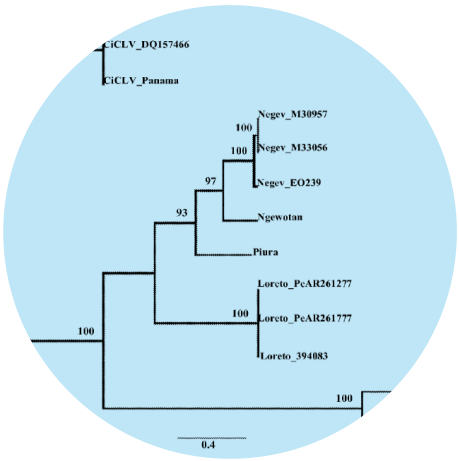
Functional Negevirus Phylogenetics

PATENT TITLE

Compositions and Methods Related to Viruses of the Genus *Negevirus*

PATENT # US 9,388,428

INVENTORS | Farooq Nasar, Rodion V. Gorchakov, Andrew D. Haddow, Robert B. Tesh, Hilda Guzman, Scott C. Weaver



PROBLEM

During the past decade, a growing number of novel insect-specific viruses have been detected in naturally infected mosquitoes. The term insect-specific was initially used to describe viruses in the genus Flavivirus (Flaviviridae) that replicate in mosquito cells but not in vertebrate cells. Although the insect-specific flaviviruses share the same genome organization and numerous amino acid motifs with the vertebrate flaviviruses, they do not infect vertebrates nor participate in the classical arthropod-vertebrate transmission cycle. Increasing numbers of non-flaviviral RNA viruses (negeviruses, bunyaviruses, alphaviruses, nidoviruses and reoviruses) have been isolated from pools of field-collected mosquitoes, suggesting that these types of agents are quite common in mosquitoes in nature.

There remains a critical need to identify additional viruses, as well as characterize and genetically engineer Negevirus for the benefit of mankind.

SOLUTION

This novel technology provides methods and compositions related to a novel group of insect specific viruses, members of the genus Negevirus, that were isolated from mosquitoes and sandflies collected in Brazil, Peru, USA, Ivory Coast, Israel, and Indonesia.

POTENTIAL IMPACT

The technology utilizes the Negevirus nucleic acids, isolated Negevirus polypeptides, and recombinant vectors incorporating Negevirus nucleic acid sequences for detection, diagnostics, therapeutic/ drug development, and clinical treatment. The technology will provide knowledge of a relatively unknown group of viruses and may lead to a method of vector population control.

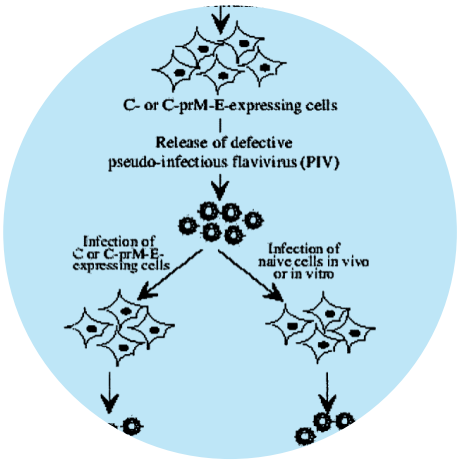
Enhanced Flavivirus Vaccine

PATENT TITLE

Pseudoinfectious Flavivirus and Uses Thereof

PATENT # US 9,273,288

INVENTORS | Peter W. Mason, Elena Frolova, Ilya Frolov



PROBLEM

The Flavivirus genus of the Flaviviridae family contains a variety of important human and animal pathogens and have been classified into four distinct antigenic complexes based on differences in reactivity in immunological tests. Generally, the flaviviruses circulate between avian or mammalian amplifying hosts and mosquito or tick vectors.

The flavivirus genome is a single-stranded capped RNA of positive polarity lacking a 3' terminal poly(A) sequence. It encodes a single polypeptide that is post-translationally processed into viral structural proteins, C, prM/M, and E, forming viral particles, and the nonstructural proteins required for replication of viral genome and its packaging into infectious virions. Virions contain a single copy of viral genomic RNA packaged into a C protein-containing nucleocapsid, surrounded by lipid envelope holding heterodimers of M and E proteins. In contrast to many other enveloped viruses, interaction between nucleocapsid and envelope spikes is not very specific and M/E-containing envelope can efficiently form around nucleocapsid derived from heterologous flavivirus, demonstrating limited level of homology in capsid sequence. Alternatively, expression of prM and E in the absence of C can lead to formation of subviral particles (SVPs), containing no RNA or C protein. PrM/M-E cassettes producing subviral particles have been the basis of several vaccine candidates. These vaccine candidates include subunit, DNA, and live-vectored vaccines. However, these vaccines have serious disadvantages.

Despite a great concern about flavivirus-associated diseases and continuing spread of the flaviviruses into new areas, antiviral therapeutics have not yet been developed for these infections, and a very limited number of approved vaccines have been produced.

SOLUTION

The technology provides replication-deficient flaviviruses or pseudoinfectious flaviviruses (PIV aka RepliVAX) for use as preventive vaccines against flavivirus-associated diseases.

POTENTIAL IMPACT

The technology overcomes limitations of current vaccines and therapeutics. Subunit vaccines are safe to use but difficult to produce large quantities. DNA vaccines are poorly immunogenic. Viral vectored vaccines suffer from lack of potency in the presence of vector immunity. Overcoming these limitations will greatly improve effective vaccines readily available to the public.

Filovirus Vaccine

PATENT TITLE

Variant Angola Marburg Virus

PATENT # US 10,466,231

INVENTORS | Joan B. Geisbert, Chad E. Mire, Thomas W. Geisbert, Robert W. Cross

PROBLEM

Serial passage of initially non-lethal Ebola virus (EBOV) in outbred guinea pigs resulted in the selection of variants with high pathogenicity. It was further found by nucleotide sequence analysis of the complete genome of the guinea pig-adapted variant Smc, that the guinea pig-adapted variant differs from wild-type virus by eight mutations; however, no mutations were identified in nontranscribed regions, including leader, trailer, and intragenic sequences.

Using a reverse genetics approach, the increase in EBOV pathogenicity is associated with amino acid substitutions in the structural protein VP24. Replication of recombinant EBOV carrying wild-type VP24, however, was impaired in primary peritoneal guinea pig macrophages and in the liver of infected animals. The substitutions in VP24 allowed EBOV to replicate in guinea pig macrophages and spread in the liver of infected animals.

Selective passages of Ebola virus in guinea pigs resulted in a guinea pig-adapted strain (GPA-P7) strain. By the 7th passage, the infection with the adapted EBOV induced a lethal disease in animals accompanied by characteristic hematological changes, leukocytosis, a pronounced deficiency in platelets, lymphocytes, monocytes, and a significant decrease in blood neutrophil's phagocytic capacity. The increased virulence is said to correlate with appearance of several nucleotide substitutions: in the genes NP, A2166G (N566S), VP24, U10784C (L147P), G10557A (M711), G10805U (R154L), and L, G12286A (V2361). It was theoretically calculated that the mutations associated with an increase in EBOV virulence alter the secondary structure of the proteins NP (C-terminal region) and full-sized VP24.

SOLUTION

This novel technology provides a uniformly lethal ZEBOV-Mayinga filovirus strain and methods of determining the effectiveness of drug candidates that impacts filovirus infection or virulence.

POTENTIAL IMPACT

The technology provides the promise of new drug candidates and therapeutics to combat filoviruses and offer frontline protection to aid workers in pandemic locations. The technology will greatly expand the access to and quality of treatments against filoviruses.

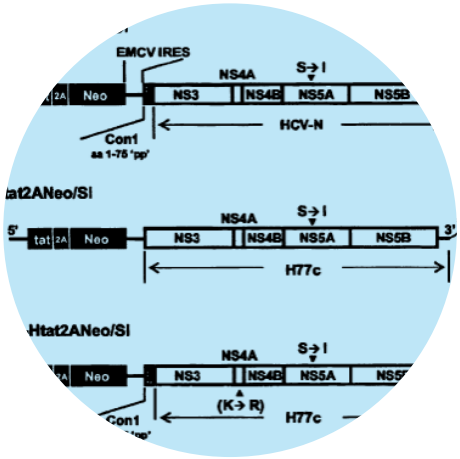
HCV Replication Platform

PATENT TITLE

Replication Competent Hepatitis C Virus and Methods of Use

PATENT # US 8,026,092

INVENTORS | Stanley M. Lemon, MinKyung Yi



PROBLEM

Hepatitis C virus (HCV) is the most common cause of chronic viral hepatitis within the United States, infecting approximately 5 million Americans and responsible for thousands of deaths annually due to progressive hepatic fibrosis leading to cirrhosis and/or the development of hepatocellular carcinoma. HCV is a single stranded, positive sense RNA virus with a genome length of approximately 9.6 kb. It is currently classified within a separate genus of the flavivirus family, the genus Hepacivirus. The HCV genome contains a single large open reading frame (ORF) that follows a 5' non-translated RNA of approximately 342 bases containing an internal ribosome entry segment (IRES) directing cap-independent initiation of viral translation. The large ORF encodes a polyprotein which undergoes posttranslational cleavage, under control of cellular and viral proteinases. This yields a series of structural proteins which include a core or nucleocapsid protein, two envelope glycoproteins, and at least six nonstructural proteins.

Except for the 5' non-translated RNA, there is substantial genetic heterogeneity among strains of HCV. Phylogenetic analyses have led to the classification of HCV strains into a series of genetically distinct genotypes, each of which contains a group of genetically related viruses. The genetic distance between some of these genotypes is large enough to suggest that there may be significant serotypic differences.

There is little understanding of the extent to which infection with a virus of any one genotype might confer protection against viruses of a different genotype. The currently available therapy of interferon in combination with ribavirin has poor response rate against most prevalent strains of HCV. Establishment of selectable sub-genomic replicon systems has advanced the study of HCV RNA replication. However, only replicons of genotype 1b strains are readily available, and extension of replicon systems to other genotypes has been largely unsuccessful. Extension of the replicon system to other genotypes are also necessary to understand the mechanism of HCV RNA replication.

SOLUTION

This novel technology provides methods and compositions for replication-competent polynucleotides for HCV drug/ vaccine discovery.

POTENTIAL IMPACT

The technology provides a truly enhanced drug discovery screening platform that considers both genotype and serotype variations. The technology will help expand access to HCV testing, drug/ vaccine discovery, and treatment options.

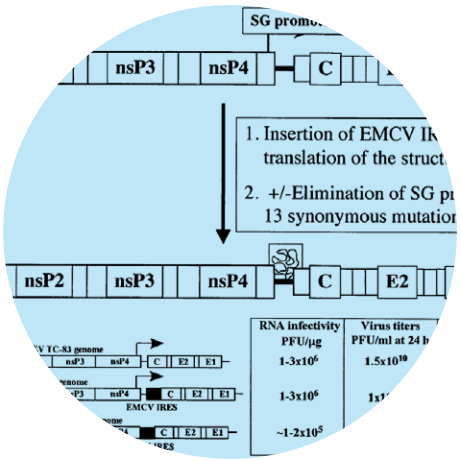
Incompetent Mosquito Alphavirus

PATENT TITLE

Attenuated Recombinant Alphaviruses Incapable of Replicating in Mosquitoes and Uses Thereof

PATENT # US 9,580,690

INVENTORS | Scott C. Weaver, Ilya V. Frolov, Elena Frolova



PROBLEM

The Alphavirus genus in the Togaviridae family contains several significant human and animal pathogens. These viruses are widely distributed on all continents except Antarctica and represent a significant public health threat. Most of the alphaviruses are transmitted by mosquitoes, in which they cause a persistent, life-long infection that has little effect on it's biological functions. In vertebrates infected by mosquitoes during their blood meal, alphaviruses cause an acute infection, characterized by a viremia that is a prerequisite of infection of new mosquitoes and its circulation in nature.

Venezuelan equine encephalitis virus (VEEV) is one of the most pathogenic members of the alphavirus genus. It continuously circulates in South, Central and North America and causes sporadic epidemics. The human disease caused by VEEV is characterized as a febrile illness with chills, severe headache, myalgia, somnolence, and pharyngitis. Young and old individuals develop a reticuloendothelial infection with severe lymphoid depletion, followed by encephalitis.

Presently, TC-83 is the only available vaccine for laboratory workers and military personnel; however, nearly 40% of all vaccinated patients develop disease with some symptoms typical of natural VEE, including fever, systemic illness, and other adverse effects. Because of the alphavirus' very high mutation rate, the reversion of TC-83 to a pathogenic phenotype remains a great concern. VEEV TC-83 is capable of replicating in mosquito cells, and infecting mosquitoes following vaccination; therefore, its transmission by mosquitoes remains possible. Ideally, live vaccine strains should not be transmissible by arthropod vectors, because circulation among reservoir hosts could lead to unforeseen changes that might include increased virulence.

SOLUTION

This novel technology provides methods and compositions using recombinant alphaviruses having mosquito infection incompetence. The technology is developed for vaccine screening and treatment.

POTENTIAL IMPACT

The technology provides for new and more effective Alphavirus vaccines. The viral genomes have been engineered to contain RNA elements that would be functional only in cells of vertebrate, but not insect, origin. The technology greatly expands treatment options for those at risk of contracting the disease. The technology will help reduce both the clinical and societal costs associated with VEEV infection.

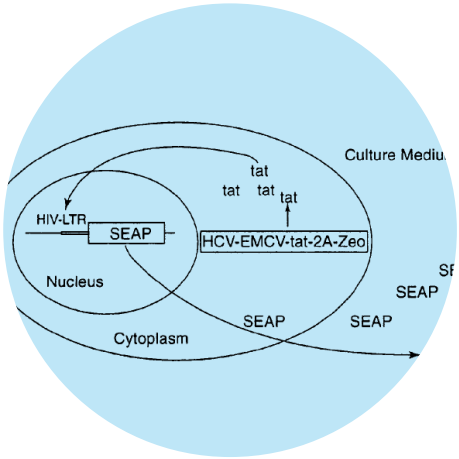
Inhibition of HCV

PATENT TITLE

Replication Competent Hepatitis C Virus and Methods of Use

PATENT # US 8,367,401

INVENTORS | Stanley M. Lemon, MinKyung Yi



PROBLEM

Hepatitis C virus (HCV) is the most common cause of chronic viral hepatitis within the United States, infecting approximately 5 million Americans and responsible for thousands of deaths annually due to progressive hepatic fibrosis leading to cirrhosis and/or the development of hepatocellular carcinoma. HCV is a single stranded, positive sense RNA virus with a genome length of approximately 9.6 kb. It is currently classified within a separate genus of the flavivirus family, the genus Hepacivirus. The HCV genome contains a single large open reading frame (ORF) that follows a 5' non-translated RNA of approximately 342 bases containing an internal ribosome entry segment (IRES) directing cap-independent initiation of viral translation. The large ORF encodes a polyprotein which undergoes posttranslational cleavage, under control of cellular and viral proteinases. This yields a series of structural proteins which include a core or nucleocapsid protein, two envelope glycoproteins, and six nonstructural proteins.

Several types of interferon have proven effective in the treatment of HCV, either alone as monotherapy, or in combination with ribavirin. However, treatment with interferon-ribavirin carries a high risk of treatment failure, either primary failure of virus elimination or relapse of the infection upon cessation of therapy. These therapeutic agents are relatively toxic and are associated with a high frequency of adverse reactions. The development of better (more effective and safer) antiviral agents capable of suppressing or eliminating HCV infection has been hindered by the fact that this virus replicates with very low efficiency. The absence of a highly permissive cell culture system that can support robust replication of the virus has prevented the development of high throughput antiviral screens for use in the development of inhibitors of viral replication and has delayed the investigation of the virus and relevant aspects of its molecular and cellular biology. It has also stymied efforts at vaccine development and the immunologic characterization of the virus, the human response HCV, and the diseases associated with infection.

SOLUTION

This novel technology provides methods for identifying compounds that inhibits replication of an HCV RNA.

POTENTIAL IMPACT

The technology provides the platform for better understanding of HCV molecular and cellular biology. In doing so, the technology can be utilized to develop more effective and safer antiviral drugs and vaccines against specific HCV strains. This will provide patients with better treatment options and reduce both clinical and societal costs associated with HCV.

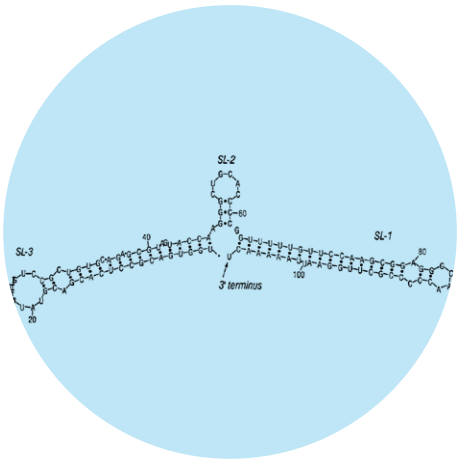
HCV Surrogate Model

PATENT TITLE

Chimeric GB Virus B (GBV-B)

PATENT # US 7,473,772

INVENTORS | Annette Martin, David V. Sangar, Stanley M. Lemon, Rene Rijnbrand



PROBLEM

Chronic hepatitis C (HCV) is a major threat to public health. Serologic surveys suggest that 5+ million Americans are chronically infected with the hepatitis C virus. These individuals are at increased risk of developing progressive hepatic fibrosis leading to cirrhosis, loss of hepatocellular function, and hepatocellular carcinoma. The course of chronic hepatitis C is typically lengthy, often extending over decades, with an insidious clinical progression usually occurring in the absence of symptoms. Nonetheless, liver disease due to HCV results in the death of thousands of Americans annually, and chronic hepatitis C is the most common cause of liver transplantation in the U.S.

There is a critical need to better understand the virus and develop better treatments. Unfortunately, technical difficulties in working with HCV have made it necessary to use infectious surrogate viruses in efforts to develop treatments and vaccines for HCV. Presently, those who are working on HCV treatment and prevention are employing an infectious chimeric virus of sindbis and HCV and/or an infectious clone of pestiviruses as surrogate virus models in HCV drug discovery efforts. Alternatively, they are using isolated proteins or RNA segments of HCV for biochemical and structural studies. This approach precludes functional studies

GBV-B is a hepatotropic flavivirus that has a unique phylogenetic relationship to human HCV and strong potential to serve as a surrogate virus. GBV-B virus is much closer in sequence and biological properties than currently used surrogates. It will be easier to make biologically relevant chimeras between HCV and GBV-B than by using more distantly related viruses. Unfortunately, the use of GBV-B as a surrogate or model for HCV has not been possible in the past, because no infectious molecular clone of GBV-B virus genome could be prepared. It is now known that this obstacle was encountered because the GBV-B genome was believed to be 259 nucleotides shorter than its actual length.

SOLUTION

This novel technology provides a 259 nucleotide 3' sequence for GBV-B that allows for the construction of a chimera virus to act as a surrogate for HCV.

POTENTIAL IMPACT

The technology provides methods and composition to utilize GBV-B as an improved surrogate for HCV discovery and treatment development. The technology overcomes the restrictive limitations of using HCV directly for this work and provides a much closer relative to act as the surrogate. The technology will provide a mechanism to greatly develop and expand treatments for HCV.

Neutralizing Ebola Antibodies

PATENT TITLE

Antibody-Mediated Neutralization of Ebolaviruses

PATENT # US 11,054,423

INVENTORS | James Crowe, Andrew Flyak, Alexander Bukreyev, Philipp Ilinykh

PROBLEM

Ebola viruses are members of the family Filoviridae, which infect humans and non-human primates causing a hemorrhagic fever with mortality rates up to 90%. Recent outbreaks in Western African nations have taken a heavy toll on the local populations and pose a threat for a greater outbreak and possible future pandemic. Unfortunately, there is no approved treatment for the disease.

SOLUTION

New neutralizing antibodies have been developed that have been utilized for enhanced detections techniques and represent promising candidates for vaccines and therapeutics that would be the first frontline treatment for this extremely deadly hemorrhagic fever.

POTENTIAL IMPACT

The development of neutralizing antibodies to Ebola promises to bring an end to the recurring endemic outbreaks in Western African countries and provides hope for prevention of larger pandemics. Successful vaccines and/or therapeutics can also limit the opportunity for, and associated damage caused by, Ebola being used as a bioweapon.

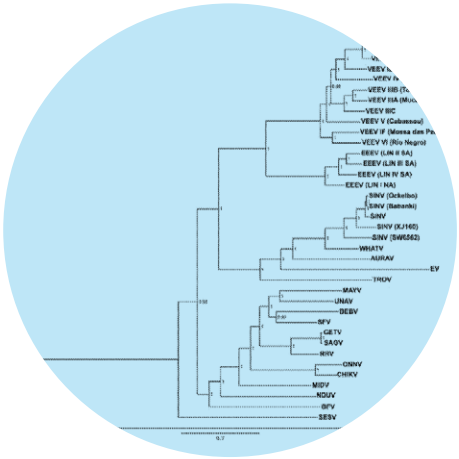
Mosquito-only Alphavirusv

PATENT TITLE

Alphavirus Compositions and Methods of Use

PATENT # US 9,683,244

INVENTORS | Scott C. Weaver, Farooq Nasar, Rodion V. Gorchakov, Hilda Guzman, Naomi Forrester, Gustavo Palacios, Ian W. Lipkin, Robert B. Tesh



PROBLEM

The genus Alphavirus includes 29 species that are classified into nine complexes based on antigenic and/or genetic similarities. Barmah Forest, Ndumu, Middelburg, and Semliki Forest complexes consist of almost exclusively Old World viruses whereas Venezuelan equine encephalitis (VEE), Eastern equine encephalitis (EEE), and Trocara complexes are comprised of New World viruses. Western equine encephalitis (WEE) complex contains, Old World, New World, and recombinant viruses.

Most alphaviruses are maintained in natural cycles between arthropod vectors and susceptible vertebrate hosts. Occasionally, these cycles can spill over into the human and animal populations and can cause disease. Human infections with Old World viruses such as Ross River (RRV), chiknngunya (CHIKV), and Sindbis (SINV) are characterized by febrile illness, rash, and polyarthritis. In contrast, infections with New World viruses, Venezuelan equine encephalitis (VEEV), Eastern equine encephalitis (EEEV) and Western equine encephalitis (WEEV), can cause fatal encephalitis. The ability of alphaviruses to infect both invertebrates and vertebrates facilitates a broad host range that enables the viruses to be maintained in ecological niches with sporadic outbreaks.

Viral factor(s) that underlie the broad host range of mosquito-borne alphaviruses are poorly understood. Host restricted viruses may provide insight into these factor(s) and provide vector delivery platforms for expression or attenuation in specific hosts.

SOLUTION

This novel technology provides a new alphavirus, Eilat virus including nucleic acid compositions, protein compositions, viral compositions, and methods of use for detection, diagnostics, vaccine/ drug discovery, and clinical treatment. The technology represents the first mosquito-only alphavirus.

POTENTIAL IMPACT

The technology enables new methods of virus and vaccine discovery. This will open new opportunities for more effective and safer vaccines and antiviral treatments. The technology will expand the access to care and help reduce costs.

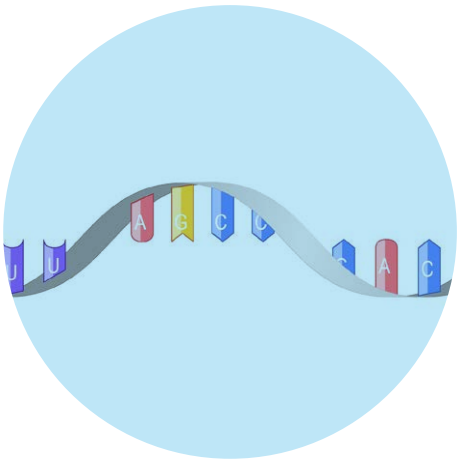
Plague Vaccine

PATENT TITLE

Live-Attenuated Vaccine Against Plague

PATENT # US 10,328,139

INVENTORS | Ashok Chopra, Jian Sha



PROBLEM

Yersinia pestis is the causative agent of plague and can be transmitted to humans via an infected flea bite or by direct inhalation of the aerosolized coccobacilli from an infected person or an animal. Plague manifests itself in three major forms in humans, namely bubonic, septicemic, and pneumonic. Pneumonic plague is the most feared form due to its rapid onset and associated high mortality rate.

Y. pestis has been responsible for at least three pandemics in the past, which killed more than 200 million people. The emergence of multi-antibiotic resistant Y. pestis strains from plague patients, and the potential of malicious dissemination of recombinantly engineered bacteria as an airborne bioweapon, necessitates the development of an effective pre-exposure and/or post-exposure prophylaxis treatment.

SOLUTION

Genetically modified Y. pestis strains have been developed that include three alterations compared to a control Y. pestis. The first alteration includes decreased mRNA, decreased protein, or a combination encoded by a lpp coding region. The second alteration includes decreased mRNA, decreased protein, or a combination encoded by a msbB coding region. The third alteration is selected from an alteration of an intergenic region and decreased mRNA, decreased protein, or a combination encoded by a ail coding region.

POTENTIAL IMPACT

The development of this novel genetically modified Y. pestis will provide the key component to manufacture a vaccine for plague. This will offer the first of its kind therapeutic to treat Y. pestis and its associated bacteria. In doing so, the risk of a mass pandemic or bioweapon cataclysm may be prevented.

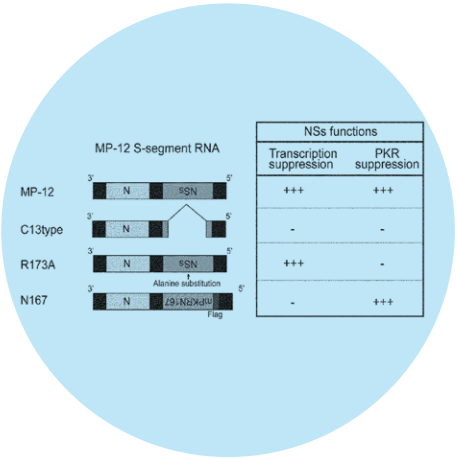
Rift Valley Fever Vaccine

PATENT TITLE

Recombinant Rift Valley Fever Virus Encoding a Dominant-Negative Inhibitor of DSRNA-Dependent Protein Kinase in The NSs Region

PATENT # US 9,144,605

INVENTORS | Tetsuro Ikegami, Birte Kalveram, Sabarish Indran, Olga Lihoradova, Alexander Freiberg



PROBLEM

Rift Valley fever (RVF) is a mosquito-borne zoonotic disease that is caused by the Rift Valley fever virus (RVFV), a member of the family Bunyaviridae, genus Phlebovirus. RVFV causes abortion and fetal malformation in animals, while it causes acute febrile illness in humans. Some human patients also develop complications such as neurological disorders, blindness, or lethal hemorrhagic fever. RVFV is classified as an NIAID category A priority pathogen because of the impact on human health and agriculture.

RVFV has a tripartite negative-stranded RNA genome containing a S, M, and L genome segment. The S-segment encodes the N and NSs proteins with the NSs protein encoded in an ambisense manner. The M-segment encodes Gn, Ge, 78-kD, and NSm proteins. The L-segment encodes an RNA-dependent RNA polymerase. The MP-12 strain of RVFV is one of the most promising vaccine candidates for Rift Valley fever. MP-12 is attenuated having mutations in the M and L segments, while the S segment retains virulence by encoding a functional NSs protein. NSs suppresses host transcription, including interferon-beta (INF) mRNA synthesis, and promotes degradation of dsRNA dependent protein kinase (PKR).

SOLUTION

This novel technology provides methods and compositions for an enhanced Rift Valley fever vaccine and/or therapeutic treatments.

POTENTIAL IMPACT

The technology employs deletions and/or inactivating mutations of NSs resulting in attenuation of the virus. However, maintenance of the PKR inhibition function enhances stimulation of an immune response to the virus. Thus, the incorporation of PKR inhibition in a NSs inactive virus results in an attenuated virus with an enhanced ability to induce an immune response. The technology will greatly expand the development of more effective and tolerable vaccines and therapeutics. This will provide frontline protection against this terrible disease.

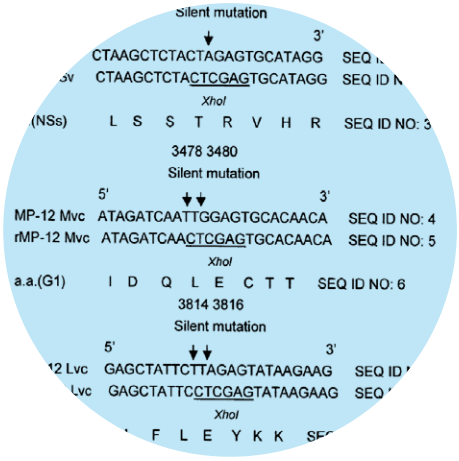
Rift Valley Genetics

PATENT TITLE

Reverse Genetic System for Rift Valley Fever Virus and Uses Thereof

PATENT # US 8,084,248

INVENTORS | Shinji Makino, Tetsuro Ikegami, Clarence J. Peters, Sungyong Won



PROBLEM

Rift Valley fever virus (RVFV) causes an endemic disease of sub-Saharan Africa that has emerged in explosive mosquito-borne epidemics resulting not only in massive economic loss in herds of sheep and cattle but also causing hemorrhagic fever, encephalitis, retinal vasculitis, and lesser disease in humans. The possibilities of introduction in many different countries and of its use as a bioterrorist agent demand the availability of effective protective measures for humans and domestic animals.

It is likely that the disease can only be controlled by an effective live attenuated vaccine for livestock and certainly the control activities will necessitate protection of humans, most likely by vaccination. Another major barrier to the development of vaccine for Rift Valley fever virus is the lack of understanding of the molecular virology of Bunyaviridae and of its medically important genus Phlebovirus.

There is a critical need for a Rift Valley fever virus expression system that can be used to develop vaccines for Rift Valley fever virus, screen antivirals and develop markers for Rift Valley fever virus.

SOLUTION

This novel technology provides methods and compositions for a reverse genetic system for Rift Valley fever virus.

POTENTIAL IMPACT

The technology will provide for detailed understanding of these types of viruses, large scale screening of antivirals, development of RVFV specific markers, and development and testing of critically needed vaccine candidate. The technology will provide the promise of new therapeutic to treat humans and livestock and reduce the risk of the virus being used as a bioweapon.

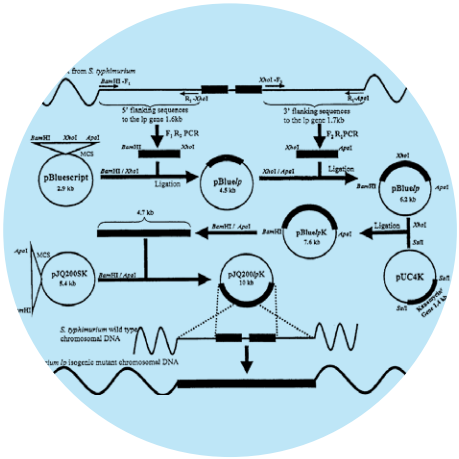
Safer Vaccines and Vectors

PATENT TITLE

Methods and Compositions for Vaccination Against or Involving Enterobacteriaceae Bacteria

PATENT # US 7,655,241

INVENTORS | Gary R. Klimpel, David W. Niesel, Ashok Chopra, Jian Sha



PROBLEM

Host immune responses include both the humoral immune response, involving antibody production, and the cell-mediated immune response. Protective immunization by vaccine has usually been designed to induce the formation of humoral antibodies directed against infectious agents. Control of certain diseases characterized by the presence of tumor cells or by chronic infection of cells with infectious agents, often requires a cell-mediated immune response either in place of, or in addition to the generation of antibody. While the humoral immune response may be induced using live infectious agents and agents which have been inactivated, a cellular immune response is most effectively induced using live agents as vaccines.

Although the potential broad use of attenuated bacteria as a vaccine or vaccine vector for the prevention and treatment of infectious disease and cancer has significant advantages over other vaccines, the issue of safety during use of attenuated bacteria are not trivial. The use of an attenuated strain of Listeria monocytogenes is accompanied by potentially severe side effects. One group of individuals that might benefit from the use of an attenuated bacteria as a vaccine or vaccine vector are individuals who are infected with HIV. However, because these individuals are severely immunocompromised, the use of attenuated bacteria as a vaccine or vaccine vector are undesirable unless the bacteria are fully and irreversibly attenuated.

There is a critical need for the development of bacterial strains for use as vaccines and vaccine vectors that are attenuated to the extent that they are unable to cause disease in an individual into whom it is inoculated, but still able to develop cell mediated immune responses.

SOLUTION

This novel technology provides methods and compositions for vaccination against bacteria in the family Enterobacteriaceae, as well as methods and compositions for vaccination against any heterologous peptide or polypeptide expressed by a bacterium in the family Enterobacteriaceae

POTENTIAL IMPACT

The technology can produce a superior vaccine lacking a functional lipoprotein gene yet is still capable of generating humoral and cell-mediated immune response without negative side effects seen with other vaccines.

Treatment for Plague

PATENT TITLE

Methods for Treating Plague

PATENT # US 10,076,562

INVENTORS | Ashok Chopra, Vladimir Motin, Eric Rothe

PROBLEM

Yersinia pestis is the causative agent of plague and can be transmitted to humans via an infected flea bite or by direct inhalation of the aerosolized coccobacilli from an infected person or an animal. Plague manifests itself in three major forms in humans, namely bubonic, septicemic, and pneumonic. Pneumonic plague is the most feared form due to its rapid onset and associated high mortality rate.

Y. pestis has been responsible for at least three pandemics, which killed more than 200 million people. The emergence of multi-antibiotic resistant Y. pestis strains from plague patients, and the potential of malicious dissemination of recombinantly engineered bacteria as an airborne bioweapon, necessitates the development of an effective pre-exposure and/or post-exposure prophylaxis treatment.

SOLUTION

A novel frontline therapeutic has been developed to treat Y. pestis and its associated viruses. The treatment is composed of a vector that has a polynucleotide encoding a fusion protein composed of a YscF protein domain, a mature F1 protein domain, and a LcrV protein domain. The therapeutic can be delivered via an intramuscular route or intranasal route.

POTENTIAL IMPACT

The development of this novel technology offers the first of its kind therapeutic to treat Y. pestis. In doing so, the risk of a mass pandemic or bioweapon cataclysm may be prevented.

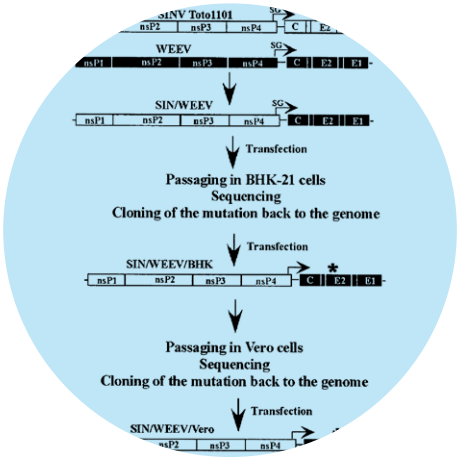
Western Equine Encephalitis Vaccine

PATENT TITLE

Chimeric Sindbis-Western Equine Encephalitis Virus and Uses Thereof

PATENT # US 8,748,591

INVENTORS | Scott C. Weaver, Ilya Frolov



PROBLEM

Western equine encephalitis virus (WEEV) is not as neuroinvasive as eastern equine encephalitis virus (EEEV). However, its transmission and pathogenesis are similar. Mosquitoes carry the virus from the wild bird reservoir to the dead-end hosts, horses, and humans. Female mosquitoes acquire the virus by taking a blood meal from an infected host.

The virus infects the epithelial cells of the midgut of the mosquito and spreads through the circulation to the salivary glands where it sets up a persistent infection. The virus enters a new host when the mosquito regurgitates virus-containing saliva into the victim's bloodstream. The virus replicates in the capillary endothelial cells, macrophages, monocytes, liver, spleen, or lymphatic tissue. Systemic symptoms (chills, fever, myalgia) occur, perhaps due to production of interferon. A secondary viremia follows the replication in the reticuloendothelial system and allows infection of the target cells in the brain.

Damage is due both to cell death following infection and to inflammation. The disease occurs only in months when mosquitoes are active. Subclinical infections greatly exceed the number of clinical cases. Although many infections do not progress beyond the systemic phase, infection of the brain (signaled by severe headache and nausea) is followed by a rapidly progressive downhill course. Although a vaccine has been developed for horses, this vaccine is not useful for the general population. Hence, it is necessary to develop vaccines that can be used for the general population since infants are particularly susceptible to CNS disease caused by this virus and survivors may have severe CNS sequelae.

SOLUTION

This novel technology provides an attenuated recombinant chimeric sindbis-western equine encephalitis virus (WEEV) and methods for use as vaccines and in serological and diagnostic assays.

POTENTIAL IMPACT

The technology overcomes the limitations of currently available vaccines. The technology will greatly expand the access to treatment while providing a new, more effect vaccine free of unwanted side effects.

Zika Virus Vaccine

PATENT TITLE

CDNA Clone-Launched Platform for High-Yield Production of Inactivated Zika Virus

PATENT # US 10,240,130

INVENTORS | Xuping Xie, Chao Shan, Pei-Yong Shi

PROBLEM

Zika virus (ZIKV) has recently caused explosive outbreaks and is unexpectedly associated with congenital microcephaly, other fetal abnormalities, and Guillain Barre Syndrome. Since 2007, ZIKV has rapidly spread across islands in the South Pacific and into the Americas. Despite urgent medical needs, neither clinically approved vaccines nor antiviral drugs are available for prevention and treatment.

SOLUTION

This novel technology includes the development of variant Zika strains, cDNA clones and mRNA transcripts that contain specific mutations in the Zika ORF, and methods for producing high yields of Zika viruses ("ZIKVs") using these variant cDNA clones, transcripts, and strains. The produced ZIKVs can be used for the manufacture of purified inactivated vaccines (PIVs), which may be useful for treating ZIKV-related diseases and for providing immunoprotection against ZIKV.

POTENTIAL IMPACT

This novel technology addresses the need for technologies that can increase the yield of virus production to improve accessibility of inactivated vaccines and reduce costs without compromising vaccine immunogenicity. In doing so, this technology will help drive successful vaccine development which will help reduce the transmission and negative clinical outcomes associated with the virus.

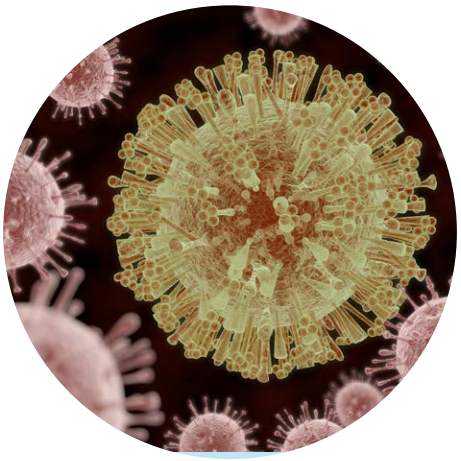
Zika Virus System – A Step Towards viable Vaccines

PATENT TITLE

Reverse Genetics System of Zika Virus

PATENT # US 10,533,997

INVENTORS | Pei-Yong Shi, Chao Shan, Xuping Xie



PROBLEM

Zika virus (ZIKV) has recently caused explosive outbreaks and is unexpectedly associated with congenital microcephaly, other fetal abnormalities, and Guillain Barr Syndrome. Diagnosis of ZIKV infection is performed through detection of viral components (e.g., viral RNA, viral proteins, or virus isolation) and detection of host immune response (e.g., antibodies against viral proteins). For viral component-based diagnosis, RT-PCR is the most popular assay because of its sensitivity and specificity. Due to the short duration of the viremic phase, the diagnostic window for detection of viral components is narrow. Therefore, host immune response-based assays play an important role, among which ELISA and PRNT are the two most common.

Conventionally, serologic diagnosis of ZIKV infection relies mainly upon ELISA which is confounded with the flaw of cross-reactivity. ELISA results typically require neutralization tests for confirmation. PRNT is time-consuming, labor-intensive, slow, low-throughput, and cost-ineffective. PRNT relies upon both virus-specific and cross-reactive epitopes of viral E protein such that the results may be inconclusive with respect to flavivirus infections. Therefore, there is a critical need to improve the accuracy and speed of serologic diagnosis for flaviviruses.

SOLUTION

Novel compositions and methods have been developed for a high-throughput assay for ZIKV and dengue virus (DENV) diagnosis that can attain at least the sensitivity and selectivity of the current PRNT assay, while exhibiting a higher dynamic range. The assays described herein are homogeneous and utilize luciferase viruses to quantify the neutralizing titers in a 96-well format.

Besides the improvement of assay throughput, the reporter virus technology has also shortened the turnaround time to less than two days. Collectively, the results suggest that, along with the viral RT-PCR assay, the reporter virus-based serologic assay could be readily used as a first-line test for clinical diagnosis of ZIKV infection.

POTENTIAL IMPACT

This technology addresses three major applications: (1) Vaccine development for both inactivated vaccine and attenuated vaccine. (2) Therapeutics development through reporter virus and high throughput screening. (3) Novel diagnostics development using reporter virus and engineered reporter virus. This technology will help diagnose ZIKV outbreaks and support the development of new therapeutics. This model can be configured for other virus orders.

Universal Flu Vaccine

PATENT TITLE

Universal Influenza Vaccine Targeting Virus/Host Recognition

PATENT # (PENDING)

INVENTORS | Velkjo Veljkovic, Slobodan Paessler

PROBLEM

Influenza, commonly called the flu, is a contagious respiratory illness caused by influenza viruses, which infect the respiratory tract. Unlike many other viral respiratory infections, such as the common cold, the flu can cause severe and life-threatening complications. Flu season usually strikes both the northern and southern hemispheres each year, resulting in three to five million cases of severe illness and up to 500,000 deaths annually.

Flu vaccines protect against the influenza viruses that research indicates will be most common during the upcoming season. Traditional flu vaccines, called trivalent vaccines, are made to protect against three or four flu viruses: However, if the selected strain(s) do not match the strains spreading in the community and/or the strain(s) mutates prior to, or during the flu season, that season's vaccine may not provide protection. The protective capability of currently available influenza vaccines is substantially limited.

SOLUTION

A method has been developed for identifying novel antigens possessing structural homology with hemagglutinin (HA) from various influenza viruses, making it capable of eliciting an immune response against different strains of the flu. Such antigens can be used as the basis for a universal flu vaccine, suitable for use alone or in combination with traditional strain-specific, seasonal flu vaccines.

POTENTIAL IMPACT

The development of a universal flu vaccine will help to reduce sickness and death during years when traditional viral strain predictions are incorrect. This method will also help streamline vaccine manufacturing and increase quality control measures.

This page is intentionally left blank.

Intellectual Property Showcase:
Vaccines

For more information, please contact:
Alexander Vo, PhD at ahvo@utmb.edu

utmb Health

301 University Boulevard; Galveston, TX 77555