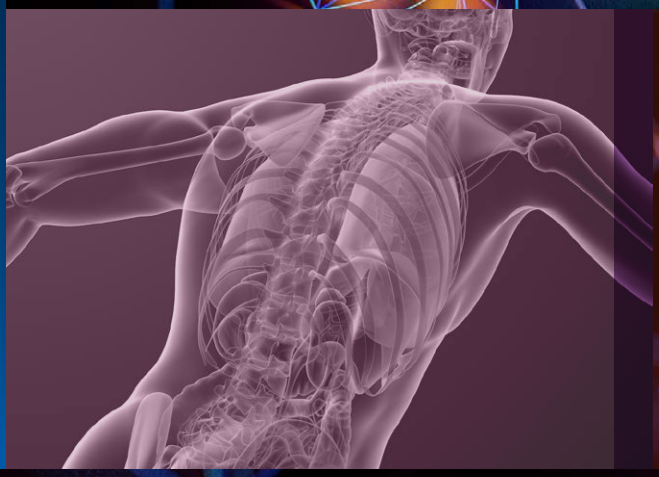
utmb Health

Intellectual Property

SHOWCASE

EDITION Di1



Di1

Medical Devices
Diagnostics
Therapeutics
Vaccines
AI & Software

utmb Health

Intellectual Property Showcase | Diagnostics

EDITION Di1

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Ehrlichia Detection

PATENT TITLE

Methods for detecting Ehrlichia infection

PATENT # US 9,568,473 | # US 8,685,406 (asso.)
 # US 9,151,755 (asso.)

INVENTORS | David Walker, Sunil Thomas

PROBLEM

Ehrlichia chaffeensis causes human monocytic ehrlichiosis which can be fatal to the immune-compromised and elderly. As the laboratory tests that detect Ehrlichiosis are often not effective during the first week of illness, physicians base early patient treatment decisions on the signs, symptoms, and patient history, not on laboratory results.

Serologic assays are the most frequently used methods for confirming cases of Ehrlichiosis. Serologic tests can be used to detect either IgG or IgM antibodies. Blood samples taken early (acute) and late (convalescent) in the disease are the preferred specimens for evaluation.

Most patients demonstrate increased IgM titers by the end of the first week of illness, but IgM assays may be falsely elevated due to other bacterial infections.

The most rapid diagnostic assays for Ehrlichiosis rely on molecular methods like PCR which can detect DNA present in a whole blood or tissue sample. However, the timing of these rapid tests can be compromised by initial antibiotic treatment.

SOLUTION

It was recently discovered that heat shock protein (Hsp60/GroEL) is the major antigenic protein of Ehrlichia. As a result of this discovery, a Ehrlichia specific Hsp60 peptide was designed in silico and used to raise antibodies. The antibodies raised against Hsp60 peptide can detect proteins of 100 kD, 70 kD, 60 kD, 45 kD, 30 kD and 15 kD in different species of Ehrlichia. As the peptide can induce network cross reactivity, it can be used in several applications that enhance the specificity and speed of diagnosis.

POTENTIAL IMPACT

In addition to providing a new target for Ehrlichia detection and diagnosis, this new peptide can be utilized for vaccine development and to develop probes for more specific detection of Ehrlichia in humans and animals by ELISA or PCR.

PATENT DETAILS

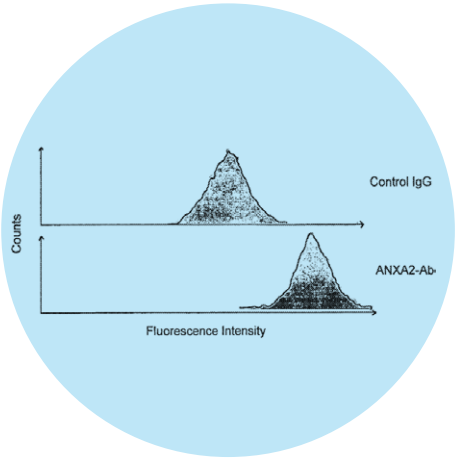
Benign and Malignant Differentiation

PATENT TITLE

Diagnosis of Benign and Cancerous Growths by Measuring Circulating Tumor Stem Cells and Serum AnnexinA2

PATENT # US 10,067,134

INVENTORS | Pomila Singh



PROBLEM

Early stages of epithelial cancers are defined as cancerous tumors limited to their tissues of origin while later stages of cancer represent metastatic growths either within the lymph nodes or at distant sites away from the primary cancerous growth.

With the advent of sophisticated proteomics, investigators discovered that AnnexinA2 (ANXA2) is increasingly expressed by epithelial tumors proportional to stage of the disease. AnnexinA2 is normally present intracellularly and performs important functions of cellular trafficking. However, rapidly proliferating tumor cells express membrane-associated extracellular, cell surface associated AnnexinA2 (CS-ANXA2).

Surface-associated ANXA2 (CS ANXA2) is increasingly expressed by many solid tumors, including colorectal (CRCs) and pancreatic cancers. ANXA2 lacks transmembrane domains and is tethered to the cell surface by binding to a 26Kda transmembrane protein. Surface-associated ANXA2 was significantly increased in colorectal adenomas and adenocarcinomas vs the corresponding normal colonic mucosa.

Measuring circulating tumor cells in the blood of patients is a relatively new concept for diagnosing cancer. The presence of circulating tumor cells likely predicts metastasis and can be useful for monitoring recurrence of the disease, post-treatment. Circulating tumor cells are detected by using many different methods, including immunocytochemistry (IHC) and RT-PCR.

Significant levels of AnnexinA2 are present in the serum of patients with breast, hepatocellular, and lung cancers. While one can potentially diagnose and predict the presence of cancerous tumors for either circulating tumor cells or cancer specific antigens, no diagnostic tests have been described to predict the presence of pre-cancerous, benign tumors. There is a critical need for technologies that detect the presence of benign pre-cancerous tumors before they convert into cancerous growths.

SOLUTION

This novel technology provides methods for distinguishing the presence of benign, pre-cancerous tumorous growths by measuring the amount of AnnexinA2, in the blood or serum, in combination with measuring the presence of circulating tumor stem cells.

POTENTIAL IMPACT

The technology overcomes limitations in the current testing methods while providing the first-in-class diagnostic prognostic for the presence of benign, pre-cancerous tumorous growths in the individual, in the absence of cancerous tumors.

PATENT DETAILS

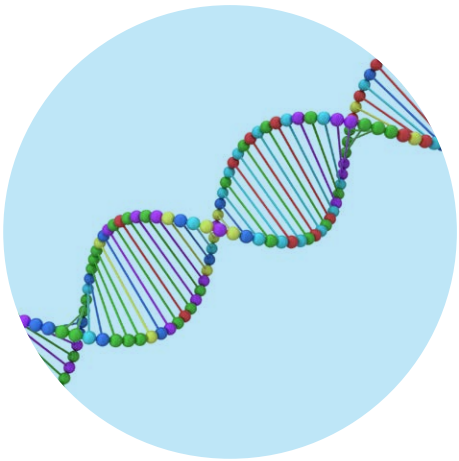
Autoimmune Disease Risk

PATENT TITLE

Method to Identify Subjects at Higher Risk to Develop an Autoimmune Disease Based on Genetic and/or Phenotypic Screening for Epistatic Variants in DDX39B (RS2523506) And IL7R (RS6897932)

PATENT # US 10,961,581

INVENTORS | Mariano A. Garcia-Blanco, Gaddiel Galarza-Munoz, Simon G. Gregory, Farren B. S. Briggs, Lisa F. Barcellos, Shelton S. Bradrick, Irina Evsyukova, Dennis C. Ko



PROBLEM

Multiple Sclerosis (MS) is a chronic autoimmune disorder characterized by self-reactive T cell-mediated damage to neuronal myelin sheaths in the central nervous system (CNS) that leads to axonal demyelination, neuronal death, and progressive neurological dysfunction. There is no cure for the disease and available treatments can only slow down disease progression, often by suppressing the immune system. Unfortunately, patients are normally diagnosed after the manifestation of clinical symptoms, at which time the patient has suffered substantial neuronal damage that cannot be reverted with current treatments. Therefore, there is a critical need for early detection and diagnosis.

The breach of immunological tolerance that leads to MS is thought to originate from complex interactions between environmental and genetic factors. The genetic background of an individual can generate an environment permissive for the survival of self-reactive lymphocytes, which could be subsequently activated by the presence of an environmental trigger, usually in the form of viral or bacterial infection. Accordingly, methods for genetic screening of variants associated with increased MS risk could provide a valuable tool to identify individuals at higher risk to develop MS.

SOLUTION

This novel technology provides enhanced methods for detection and diagnosis of MS and other autoimmune diseases by measuring the expression levels of the soluble isoform of the Interlenkin-7 Receptor (sIL7R) in combination with other protein makers.

POTENTIAL IMPACT

The technology provides a truly pioneering approach to detection and diagnosis of MS and other autoimmune diseases. Detection and diagnosis can now occur before the onset of symptoms and irreversible neural damage. The technology will help reduce both clinical treatment costs and society costs associated with MS.

PATENT DETAILS

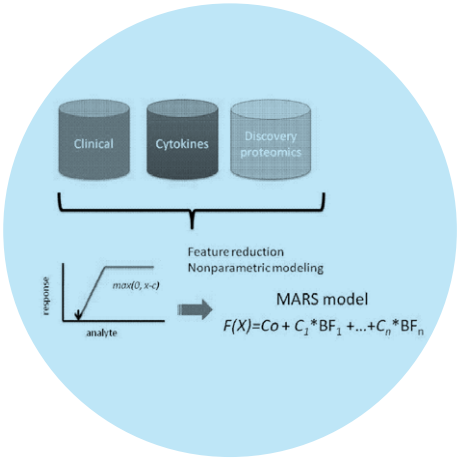
Dengue Hemorrhagic Fever Detection

PATENT TITLE

Method and Biomarkers for the Detection of Dengue Hemorrhagic Fever

PATENT # US 10,168,337

INVENTORS | Allan Brasier, Adrian Recinos, John E. Wiktorowicz, Heidi Spratt, Hyunsu Ju, Nikos Vasilakis, Ernesto E. T. Marquez, Marli Tenorio, Laura H. V. G. Gil, Eduardo Nascimento



PROBLEM

Dengue fever is a widespread mosquito born illness that can potentially affect up to one half the world's population. A secondary infection is one of the risk factors for the development of Dengue Hemorrhagic Fever (DHF). The initial clinical presentation of the two diseases (DF and DHF) are difficult for the clinician to distinguish, however the distinction is important because DHF has a mortality of up to 20%. This mortality rate can be reduced by intensive supportive care. Accurate early detection of people at risk of DHF can be used to apply clinical resources more effectively. Combinations of proteins, cytokines and complement factors that can be used in predictive models accurately identify DHF and identify those subjects in need of supportive care.

While DHF fatality rates can exceed 20%, early and intensive supportive therapy has reduced it to less than 1%. Therefore, early detection and differentiation of dengue disease types can be used for the prognosis and treatment of patients presenting with dengue-like symptoms.

SOLUTION

This novel technology provides methods of determining risk of developing Dengue Hemorrhagic Fever (DHF). The methods include measuring biomarkers including FactorD/FactorH, desmoplakin, IL2, and high molecular weight albumin.

POTENTIAL IMPACT

The technology enhances existing diagnostic methods for the identification of Dengue Hemorrhagic Fever and provides early differentiation from other stages of Dengue infection. This risk assessment is critical for determining the types and duration of therapeutic measures needed to reduce the mortality rate. The technology will help improve health outcomes and reduce overall costs.

PATENT DETAILS

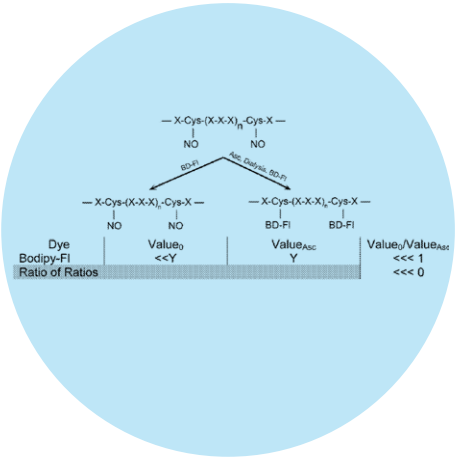
Chagas Disease Detection

PATENT TITLE

Biomarkers for Chagas Disease Related Cardiomyopathy

PATENT # US 9,696,323

INVENTORS | Allan Brasier, John E. Wiktorowicz, Hyunsu Ju, Nisha Jain Garg



PROBLEM

Chagas disease, transmitted by Trypanosoma cruzi through the bite of an insect vector, is designated as the most important emerging disease in developed countries, with approximately 16-18 million cases of infection in Latin America with 120 million people (~25% of the population) more at risk of infection. In 30-40% of the infected individuals, the disease may progress to irreversible cardiomyopathy, with infected individuals serving as carriers of the organism while exhibiting considerable morbidity and high risk of mortality.

Unfortunately, there are few options for the treatment of Chagas disease. Benznidazole and nifurtimox can be used for treatment of acute infection but have high toxicity in adults and are ineffective in arresting or reversing the progression of the disease.

There is a critical need for additional compositions and methods for identifying subjects harboring Trypanosomes and particularly those subjects at risk of developing cardiomyopathy.

SOLUTION

This novel technology provides Chagas-specific biomarkers and methods to assess a patient's risk of developing Chagas-related complications such as cardiomyopathy. The technology can be used to stratify patients and recommended stage-specific treatment interventions.

POTENTIAL IMPACT

The technology fills a testing void for Chagas disease while providing risk stratification and stage-specific therapeutic intervention options to the patient. The technology will enhance regional screening for Chagas, improve health outcomes for those infected, and help reduce costs.

PATENT DETAILS

Colorectal Cancer Detection and Risk Stratification

PATENT TITLE

DCLK1 Short Form Specific Binding Agents

PATENT # US 9,822,184

INVENTORS | Pomila Singh, Shubhashish Sarkar, Malaney O'Connell

PROBLEM

Colorectal cancer (CRC) is one of the most lethal forms of cancer. More than 150K patients are diagnosed with CRC each year in the US, resulting in ~50K deaths. CRC develops from pre-existing adenomas (Ads), the most common neoplastic growth found during screening colonoscopies. CRCs are potentially preventable if adequate and accurate screening methods are developed and pre-malignant growths (Ads) are completely removed during the colonoscopy, followed by surveillance.

SOLUTION

DCLK1-S, a short isoform of a stem cell marker, DCLK1, is expressed by CRCs and imparts an aggressive phenotype to colon cancer cells. DCLK1-S antibodies can be used for general research, in vitro diagnostics and could prove a successful therapeutic for CRC.

POTENTIAL IMPACT

The use of the DCLK1-S antibodies will accelerate colorectal cancer research, drug development, and long-term survival. These efforts will help prevent the 150K+ new cases of CRC and 50K+ deaths annually.

PATENT DETAILS

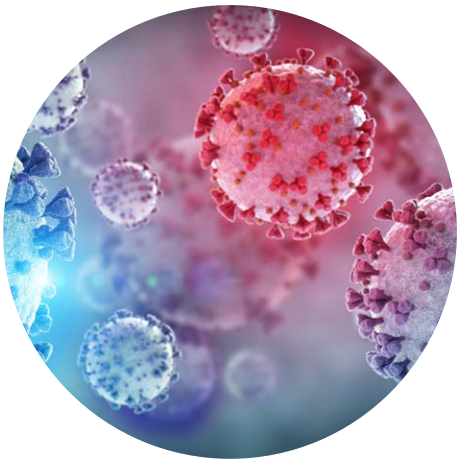
Enteroviruses Screening

PATENT TITLE

Methods and Compositions for Identifying Enterovirus

PATENT # US 9,518,303

INVENTORS | Richard B. Pyles, Aaron L. Miller



PROBLEM

Enteroviruses (EV) are responsible for between 30 million to 50 million illnesses each year in the United States. Enterovirus infections lead to 30,000 to 50,000 hospitalizations each year for aseptic meningitis, myocarditis, encephalitis, acute hemorrhagic conjunctivitis, nonspecific febrile illnesses, and upper respiratory infections. Enteroviruses are also implicated in acute flaccid paralysis in animal models, as well as in dilated cardiomyopathy and have been linked to chronic fatigue syndrome.

One of the issues in both diagnostic and epidemiological studies of enterovirus infections in children and adults is that these viruses share an extremely high degree of sequence similarity. Analysis of EV viruses by Quantitative PCR (qPCR) often results in cross-priming that can lead to misidentification of the virus present in clinical material leading to improperly connecting disease states with the wrong species of virus. It is difficult to successfully identify individuals that are suffering from co-infections with multiple EV by standard qPCR methods.

There remains a need for compositions and methods for identifying, subtyping, and/or classifying viral infections like enterovirus infections in medium to high throughput, cost-effective fashion.

SOLUTION

This novel technology provides PCR primer pairs, sequencing primers, and associated thermocycling protocols targeting a region identified within the 5' untranslated region (5'UTR) of enteroviruses (EV) for the purpose of identifying, subtyping, and classifying viruses.

POTENTIAL IMPACT

The technology provides methods for differentiation between various EVs, where other technologies cannot. The technology is scalable, cost effective, and conveniently deployable for screening large populations for EV infection.

PATENT DETAILS

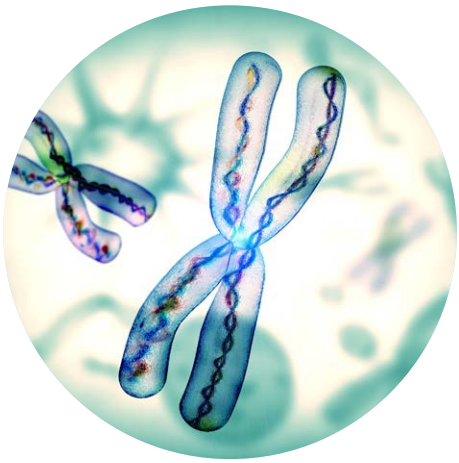
Chromosomal Inversion Detection

PATENT TITLE

Detection of Chromosomal Inversions Using Non-Repetitive Nucleic Acid Probe

PATENT # US 8,629,262

INVENTORS | Susan M. Bailey, F. Andrew Ray, Edwin H. Goodwin, Joel S. Bedford, Michael N. Cornforth



PROBLEM

Analysis of cancer cells has led to the discovery of hundreds of tumor-specific chromosome aberrations. Detailed analysis of the breakpoints involved in these structural chromosomal rearrangements has been instrumental in the discovery of many cancer-related genes. Of all possible types of structural chromosome anomalies, inversions, which represent a reversal of orientation of a DNA segment within a chromosome, are rare. Inversions can have genetic effects like the easily-detected translocations between different chromosomes seen in cancer. Both can result in effects such as disrupting regulatory sequences that control gene expression or creating genetic rearrangements like gene fusions. Inversions form through the same mechanism as translocations, the mis-repair of DNA double-strand breaks. Thus, it might be expected that translocations and inversions should be found in comparable numbers. One possible explanation for the discrepancy is that standard karyotype analyses are relatively insensitive to the detection of inversions and consequently have largely failed to find many tumor-specific chromosome aberrations of this type.

SOLUTION

This novel technology provides materials and methods for an enhanced process of detecting chromosomal inversions that be used for diagnostic and therapeutic purposes.

POTENTIAL IMPACT

The technology is an improvement over the current standards and is effective in detection of inversions that can play key roles in the development of cancer and other diseases. Accurate detection of these chromosomal aberrations can accelerate treatment and result in better health outcomes.

PATENT DETAILS

Ehrlichiosis Diagnosis and Treatment

PATENT TITLE

Diagnosis and Treatment of Ehrlichiosis

PATENT # US 8,492,103

INVENTORS | Sunil Thomas, David H. Walker

PROBLEM

Ehrlichia causes human monocytic ehrlichiosis (HME) and is transmitted by the bite of infected ticks. The clinical symptoms of HME include fever, headache, malaise, myalgia, rash, lymphadenopathy, and nausea. Symptoms are generally non-specific and consequently, easily misdiagnosed. As laboratory tests for 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. The physician also looks at specific blood tests to help determine the likelihood of ehrlichiosis. Clues such as a low platelet count, low serum sodium levels, abnormal white blood cell counts, or elevated liver enzyme levels are often helpful predictors.

Serologic assays are the most frequently used methods for confirming cases of ehrlichiosis. The indirect immunofluorescence assay (IFA) is generally considered the standard. Other assays include ELISA, latex agglutination, and dot immunoassays. All have significant limitations.

The most rapid and specific diagnostic assays for ehrlichiosis rely on molecular methods like PCR that can detect DNA present in a whole blood or tissue sample. PCR on whole blood specimens taken early during illness have been shown to be a very effective tool to diagnose ehrlichiosis. Immunostaining procedures can also be performed on formalin-fixed tissue samples. Ideally, whole blood or skin biopsy specimens used for diagnosis should be taken before or within the first 48 hours after doxycycline treatment is started. After antibiotic therapy has been started, it becomes more difficult to detect the organisms by these methods.

Techniques using PCR to evaluate for the presence of the organism itself not antibodies, to date, does not distinguish between live and dead organisms. For this reason, antibody tests are used to make a diagnosis, which can be limited by low sensitivity. There is no vaccine for ehrlichiosis currently. Thus, new methods and compositions are needed to diagnose and treat ehrlichiosis.

SOLUTION

This novel technology provides Ehrlichia diagnostics and therapeutics specific to the outer membrane P28-19 and heat shock proteins.

POTENTIAL IMPACT

The technology overcomes the time limitations associated with the serological test while being able to differentiate live and dead organisms. This approach tests for active virus and the patient's immune response.

PATENT DETAILS

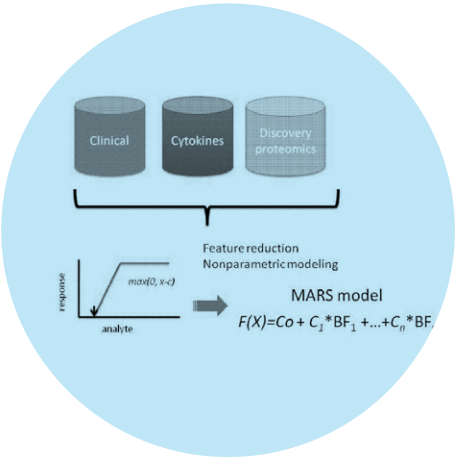
Dengue Detection

PATENT TITLE

Method for the Detection of an Albumin Isoform

PATENT # US 10,126,309

INVENTORS | John E. Wiktorowicz



PROBLEM

Dengue is an international public health problem affecting urban populations in tropical and sub-tropical regions, where ~2.5 billion people are at risk. Dengue virus is a single positive-stranded RNA virus which is transmitted among humans by mosquitoes. Dengue infection can produce diseases of a wide spectrum of severity, from asymptomatic to flu-like dengue fever (DF), to life-threatening dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS).

There are four serotypes of dengue virus, and often a region may have more than one circulating serotype. Epidemiological studies have found a 40 to 80-fold increased risk of DHF after a second infection with a different serotype. This observation has led to the antibody-dependent enhancement theory, which hypothesizes that neutralizing antibodies generated during the adaptive immune response cross-react, but do not neutralize, a second infecting dengue serotype.

Currently, there is no drug therapy or vaccine for DHF. Early therapy to treat individual symptoms can reduce mortality. Typical dengue treatments include transfusion of fresh blood or platelets, intravenous (IV) fluids and electrolytes to correct electrolyte imbalances and dehydration, and oxygen therapy. Therefore, detection and differentiation of dengue disease severity early in the course of infection is critical for the prognosis and treatment of patients.

Recent advances in global scale proteomics technologies enable the detection of candidate protein biomarkers. These biomarkers include proteins, peptides, or metabolites whose measurement alone (or in a combination) can be used to reliably indicate a disease outcome.

SOLUTION

This novel technology provides methods for identifying patients with dengue-like symptoms who are at risk of developing dengue hemorrhagic fever. The methods involve measurements of various biomarkers in plasma including IL-10 and seven proteins comprised of tropomyosin, complement 4A, immunoglobulin V, fibrinogen, and three isoforms of albumin to determine the likelihood of DHF.

POTENTIAL IMPACT

The technology overcomes the limitations of other testing methods and provides a quick, low-cost method for dengue serotype identification and differentiation. This will pave the way for new therapeutic interventions leading to better health outcomes for patients.

PATENT DETAILS

Flavivirus Diagnostic

PATENT TITLE

Molecular Typing System for Flavivirus Diagnostics

PATENT # US 9,771,623

INVENTORS | Aaron Miller, Richard Pyles

PROBLEM

Sensitive and accurate diagnostic testing is crucial for early viral detection, as evidenced by the recent Zika epidemics, and associated impacts upon fetal development and viability. Because Flaviviruses share a high degree of sequence similarity and are prone to base changes that negate primer binding for commonly targeted viral genes, currently recommended qPCR assays for specific family members (e.g., Zika) often result in cross-priming leading to misidentification (false positives) of the virus present in the sample. Further, the loss of specific sequence leads to a lack of detection and misdiagnosis (false negatives).

SOLUTION

A novel technology has been developed to use nested amplification and next-generation sequencing of a broadly conserved region of the family of flaviviruses including family members often misdiagnosed as Zika. The technology accurately and specifically discriminates among members of the family confirming the identification of the correct virus, adding a further degree of confidence beyond positive qPCR results currently being used.

POTENTIAL IMPACT

It is important to identify the serotype or subtype of a flavivirus infection. Knowledge of the infecting flavivirus(es) can provide useful guidance to a physician in determining a course of treatment. Additionally, an understanding of the geographic and chronological development of a flavivirus infection in a population can influence preventive measures among the members of the population to minimize the spread of the disease or infection. Furthermore, it is useful from a broader perspective to track the incidence and distribution of a flavivirus disease from an epidemiological point of view.

PATENT DETAILS

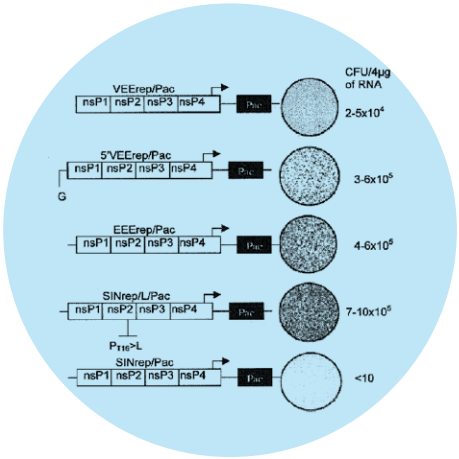
Improved Viral Replicons

PATENT TITLE

Venezuelan Equine Encephalitis Virus Replicons with Adaptive Mutations in the Genome and Uses Thereof

PATENT # US 7,332,322

INVENTORS | Ilya Frolov, Elena Frolova



PROBLEM

Alphavirus replicons are self-replicating RNAs that are useful for directing the expression of heterologous gene products. Replicons mimic the structure of cellular mRNAs. Upon delivery into cells, they are used by cellular translational machinery as cellular mRNAs, and viral nonstructural proteins are translated to form replicative complexes. Replicon RNAs are used as templates for the synthesis of full-length, minus-strand intermediates that serve as templates for production of large quantities of positive strand genomic and sub-genomic RNAs. This process has made alphavirus-based replicons such as those derived from Venezuelan Equine Encephalitis Virus (VEEV) very attractive for large-scale production of heterologous proteins.

A main disadvantage of the previous generation of alphavirus replicons is their cytotoxicity and/or sensitivity to type I interferon (IFN), an immune mediator produced by the host in response to viral presence.

The major known phenomena during replication of alphaviruses and alphavirus-based replicons are transcriptional and translational shutoffs in the infected or transfected cells. Inhibition of both transcription and translation of cellular mRNAs is aimed at suppressing activation of cellular reaction developed in response to replication of virus specific RNAs. These events downregulate expression and release cytokines that induce an antiviral state. Inhibition of transcription and translation of cellular genes are the critical components of alphavirus-specific cytopathic effect. Development of cytopathic effect is one of the disadvantages of the previously designed Sindbis virus, Venezuelan equine encephalitis virus, and Semliki Forest virus-based vectors, and long-term expression could not be achieved.

There is a lack of suitable alphavirus, specifically VEEV, replicon-based vectors with lowered cytotoxicity and/or sensitivity to IFN-alpha.

SOLUTION

This novel technology provides recombinant vectors comprising of Venezuelan equine encephalitis virus replicons useful for directing the expression of heterologous gene products.

POTENTIAL IMPACT

The technology overcomes the cytotoxic effects from the previous generation of alpha-virus vectors and provides an improved method for screening for an inhibitory compound of eastern equine encephalitis virus replication.

PATENT DETAILS

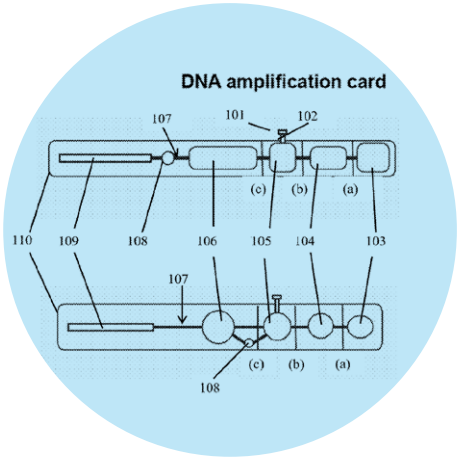
Isothermal Diagnostic Platform

PATENT TITLE

Point of Care Isothermal Diagnostic

PATENT # WO 2018071296

INVENTORS | Bruno Travi, Alejandro Castellanos, Scott Moen, Peter Melby, Omar Saldarriaga



PROBLEM

Infectious diseases, such as leishmaniasis and malaria, have a massive impact on human health. Morbidity and mortality from infectious diseases particularly affect the world's poorest populations. These diseases cause chronic disability with impaired development in children and reduced economic capacity in adults.

Despite the huge burden of these diseases, diagnostic tests are not always available, particularly tests that are affordable and can be implemented in resource-poor regions of the world. Infectious agents are currently diagnosed using conventional tests developed for reference health centers or tertiary care facilities such as quantitative PCR, serology, and microscopy. These conventional tests require expensive equipment, trained personnel, and relatively complex laboratory facilities beyond the capability of health infrastructures of resource-limited endemic areas.

Molecular diagnostic tools like PCR and quantitative PCR are sensitive and specific but are costly and require technological expertise. Detection of antibodies against the pathogens can be variable and persist after the pathogen is cleared, giving false positive results.

There remains a need for additional point-of-care (POC) devices and methods for detecting pathogens or disease in resource challenged locations.

SOLUTION

A low-cost, field-applicable diagnostic device has been developed that can be used at the point-of-care (POC) and is sensitive and specific. The novel technology can be used to perform sensitive, field-applicable diagnostic tests. This technology is configurable to genetic and proteomic targets and is indispensable for programs to eliminate specific diseases.

POTENTIAL IMPACT

These sensitive diagnostic tests can lead to the reduction of disease burden by increasing the ability to diagnose carriers of the disease and direct treatment to more of those that need it and less to those that do not. This technology can enable more accurate definitions of the burden of disease in populations to directly inform those implementing disease intervention.

PATENT DETAILS

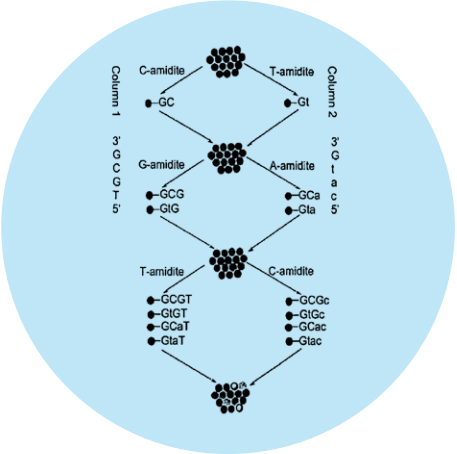
Next Generation Aptamers

PATENT TITLE

Bead Bound Combinatorial Oligonucleoside Phosphorothioate and Phosphorodithioate Aptamer Libraries

PATENT # US 7,338,762

INVENTORS | David G. Gorenstein, Xianbin Yang, Bruce A. Luxon, Norbert Herzog



PROBLEM

Virtually all organisms have nuclease enzymes that rapidly degrade foreign DNA as an important in vivo defense mechanism. The use of normal oligonucleotides as diagnostic or therapeutic agents in the presence of most bodily fluids or tissue samples is generally precluded. However, phosphoromonothioate or phosphorodithioate modifications of the DNA backbone in oligonucleotides can impart both nuclease resistance and enhance the affinity for target molecules.

Current technology is problematic for focusing on the identification and quantification of a single mRNA species and does not provide information on the most relevant levels of functional protein expression and protein-protein interactions.

SOLUTION

This novel technology utilizes thioated aptamer compositions and methods that permit the isolation of individual aptamer protein complexes without the need for repeated iterative cycles of selection and reamplification of likely binding targets. Also, included are methods for creating libraries that permit not only the isolation of a primary aptamer: protein target, but the isolation of protein(s) that may interact with the aptamer: protein target, so-called secondary interactions.

POTENTIAL IMPACT

The technology overcomes limitations of the current standard by enhancing availability and use of aptamers for screening, including high throughput screening, of primary or secondary target molecules. The technology will help reduce the cost and complexity of aptamer usage for research and clinical applications.

PATENT DETAILS

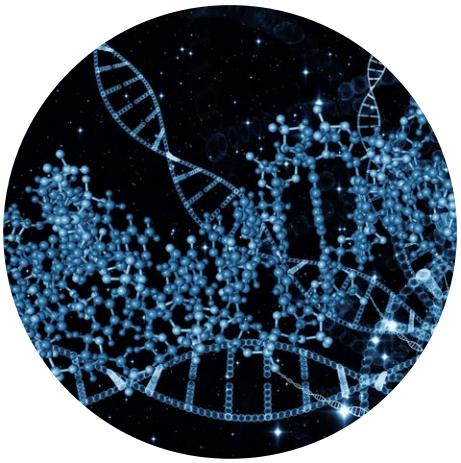
Next-Gen Sequencing

PATENT TITLE

Poly(A)-ClickSeq Click-Chemistry for Next Generation 3-End Sequencing Without RNA Enrichment or Fragmentation

PATENT # US 11,149,053

INVENTORS | Andrew Routh, Eric Wagner, Ping Ji, Elizabeth Jaworski



PROBLEM

Profiling the position of the poly(A) tail using high-throughput sequencing technologies is critical to understanding the complex interplay of poly(A) tail location with mRNA stability, degradation, and translation. Approaches have been developed that infer poly(A) tail position and abundances through computational analysis of standard RNA-seq using designer algorithms. However, these approaches have the disadvantage in that precise poly(A) site junctions are not enriched relative to the rest of the transcriptomic data and so datasets are invariably large and require high depth sequencing runs (>100M reads) as only a subset of the RNA-seq will contribute to the analysis.

SOLUTION

A novel technology has been developed with the specific goal of enriching for the junction of the encoded 3'UTR ends and the beginning of the non-templated poly(A) tail. This technology improves methods for sequencing and determining the presence of cleavage and polyadenylation sites giving rise to distinct mRNA isoforms of different lengths.

POTENTIAL IMPACT

This novel technology circumvents current techniques that entail complex experimental pipelines and purification strategies that can impart sample bias and reduce throughput capacity. These complexities limit the number of core facilities offering these types of sequencing technologies thereby limiting their application only to laboratories with more than routine experience in sequencing library preparation. The utilization of this novel technology can empower many additional researchers.

PATENT DETAILS

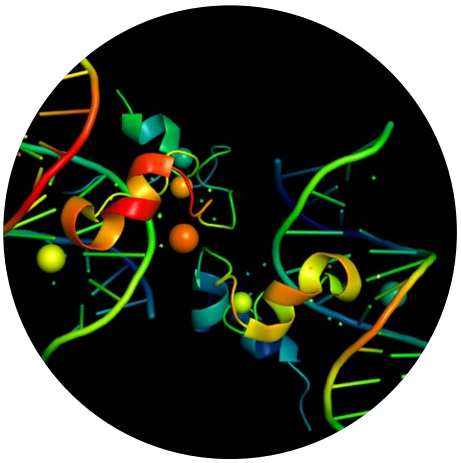
NFkB/ RelA Aptamers

PATENT TITLE

Single Stranded DNA Aptamers Binding NF-kB/RelA

PATENT # US 9,834,770

INVENTORS | Steven G. Widen, Thomas G. Wood, Allan R. Brasier, Yingxin Zhao



PROBLEM

DNA aptamers have been developed and used for a variety of therapeutic and diagnostic purposes. Signal amplification strategies have been developed for aptamer-based molecular recognition of target proteins and nucleic acids. Additionally, aptamers have been developed that incorporate a thiophosphate replacement in the phosphate backbone for improved binding efficiencies to a target. TNF-a aptamers have been developed that can specifically be bound to TNF-a and inhibit the cytoxicity of TNF-a.

The aptamers have high specificity, high affinity, quick penetration to target tissue, rapid plasma clearance, and lower immunogenicity. Aptamers have the advantages of affinity and specificity, like monoclonal antibodies, and have permeability and pharmacokinetics characteristics like small molecular polypeptides.

There is a critical need to adapt and enhance current aptamer technology to target other specific protein and nucleic acid mediators of disease and disease progression.

SOLUTION

This novel technology provides single stranded DNA aptamers that recognize NFkB/RelA, mediators of tissue inflammation or cancer.

POTENTIAL IMPACT

These aptamers bind to several distinct regions of RelA and may be useful to antagonize the DNA binding of RelA as an inhibitor of cellular inflammation, visualize the location or amount of RelA in tissues from pathological conditions, or to quantitatively measure the activated state of RelA by affinity binding. The technology will enhance cancer screening and therapeutic intervention.

PATENT DETAILS

Plague Killer

PATENT TITLE

Substrate Peptide Sequences for Plague Plasminogen Activator and Uses Thereof

PATENT # US 9,187,523

INVENTORS | Vladimir L. Motin, Sadhana Chauhan, Scott R. Gilbertson, Anton Agarkov, Pedro Lory

PROBLEM

Yersinia pestis, a Gram-negative bacterium is the causative agent of plague, an acute and lethal disease. Although plague is a zoonotic infection, it can be transmitted to humans via a bite from a flea that previously fed on an infected rodent. Typically, flea transmission of Yersinia pestis causes a form of disease referred to as bubonic plague. From the initial site of infection, bacteria disseminate to the draining lymph node, causing swelling of this lymph node to form a bubo, from which, if left untreated, can spread into the circulation, eventually causing bacteremia and the second form of the disease, septicemic plague. Sometimes septicemic disease occurs even without the development of buboes and is characterized by elevated temperature, chills, headache, malaise, and gastrointestinal disturbances.

Pneumonic plague can result if the lungs become infected. Pneumonic plague is the most feared form of the disease that arises due to colonization of the alveolar spaces and can also be caused by bacterial spread from an infected person (or animal) to a healthy individual by the aerosol route. Pneumonic plague develops rapidly (1-3 days), results in a high mortality rate in infected individuals (approaching 100%), and spreads rapidly from human-to-human. Yersinia pestis is responsible for at least three pandemics in the past, killing 200+ million people. For that reason, and because plague is characterized as an emerging infectious disease, the CDC has classified it as a Category A biological agent. For these reasons, the development of highly effective anti-plague treatments, particularly to combat Yersinia pestis resistant to traditional drugs, is an immediate public health priority.

SOLUTION

This novel invention provides substrates and inhibitors of plague plasminogen activators and their use in detecting Yersinia pestis and controlling the associated infection.

POTENTIAL IMPACT

The technology provides a new and unique set of tools to detect and fight infections caused by Yersinia pestis. The technology can dramatically reduce the risk of infections and spread of this disease that has killed millions over the years.

PATENT DETAILS

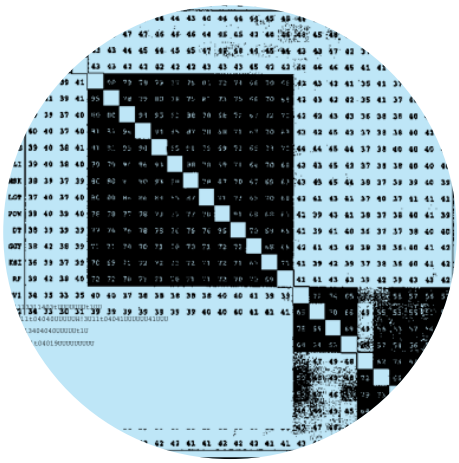
Physiochemical Sequence Analysis

PATENT TITLE

Physicochemical (Pcp) Based Consensus Sequences and Uses Thereof

PATENT # US 8,900,596

INVENTORS | Catherine H. Schein, Petr Danecek



PROBLEM

Conserved sequences within protein families usually maintain the structure of the protein and the primary functions. The second characteristic is variance. Variance can arise at specific positions in a random fashion or can represent a true change that may correlate with alteration in phenotype or activity. The problem in dealing with biological datasets, such as sequences for viral or microbial genomes, is that they often have a pronounced bias due to inequivalent distribution. This unequal distribution can arise from non-uniform sampling.

Unbiased data reduction methods are needed to make practical use of large volumes of sequence data. Conventional methods for calculating consensus sequences cannot account for dataset bias, as they determine the amino acid that occurs most frequently, thus eliminating information on variants at a given position. Even when such averaging is done over a closely related series of sequences, numerical averaging can eliminate important information on the functional importance of substitutions that conserve the physicochemical properties at a position that may be essential for the function or fold of the protein. While some calculation methods consider amino acid groupings according to charge, size, or hydrophobicity, one dimensional averaging method cannot deal with highly variant positions.

SOLUTION

This novel technology provides a method to extract functional information from aligned protein sequences that can identify functional variance even in biased datasets.

POTENTIAL IMPACT

The technology can be applied to design of multivalent vaccines, targets for drug design, novel enzymes, and diagnostic kits for differentiating infectious organisms. The technology can shorten the time to vaccine production and distribution while reducing development costs.

PATENT DETAILS

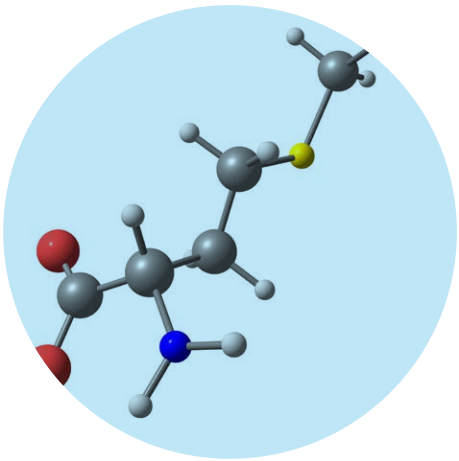
Protein Structure & Function

PATENT TITLE

Physical-Chemical Property Based Sequence Motifs and Methods Regarding Same

PATENT # US 7,424,369

INVENTORS | Werner Braun, Venkatarajan S. Mathura, Catherine H. Schein



PROBLEM

Determining the similarity of sequences in databases to that of proteins of known function is one of the most direct computational ways of deciphering codes that connect molecular sequences of protein structure and function. However, sequence data analysis methods range from very sensitive, but computationally intensive algorithms, to relatively rapid, but less sensitive analysis methods.

The ability to truly analyze such sequence data depends significantly on the development of advanced computational tools for rapid and accurate annotation of sequences as to the probable structure and function of the proteins they encode. There is a critical need for methods that use functional information (e.g., physical-chemical property information) to effectively extract useful information from sequence data being searched.

SOLUTION

This novel technology provides enhanced methods to analyze protein physical-chemical property (PCP) data in conjunction with sequence data (e.g., DNA, RNA, amino acids).

POTENTIAL IMPACT

The technology provides functional annotation to a sequence thereby improving assessment and selection of potential drug candidates. The enhanced method can provide critical insight into drug development and help refine candidates in turn speeding up development and reducing associated costs.

PATENT DETAILS

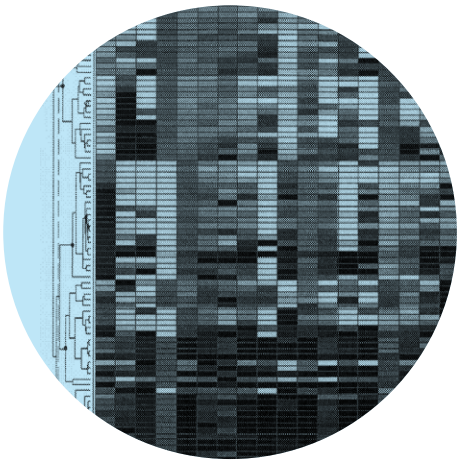
Rapid Asthma Testing

PATENT TITLE

Molecular Phenotyping of Severe Asthm

PATENT # US 8,053,199

INVENTORS | Allan R. Brasier, William J. Calhoun, Gary D. Boetticher



PROBLEM

Asthma is a chronic inflammatory disease of the airways characterized by recurrent episodes of systematic airflow obstruction and various degrees of airway hyperreactivity. The recognition that this disease has a chronic inflammatory component has directed interventions towards early use of inhaled glucocorticoids, typically producing significant reductions in inflammatory markers, and improvement in pulmonary function. However, there is a subset of patients (5-7%) with severe, or refractory asthma that do not respond to glucocorticoids. These patients account for 40-50% of asthma related health care costs and incur significant morbidity and reductions in quality of life.

Severe asthmatics have distinct inflammatory processes suggesting that they may also express distinct airway cytokine profiles compared to those with responsive asthma. However, severe asthma diagnostics still lack an objective method for distinguishing clinically significant subtypes.

There is a need for diagnostic assays that will allow medical personnel to rapidly identify individuals who may benefit from more intensive treatment of their asthma, thereby reducing morbidity and improving quality of life for those affected.

SOLUTION

This novel technology provides a method for rapid identification of individuals by identifying cytokine patterns for subtypes of asthma and predictors of methacholine hyper-responsiveness.

POTENTIAL IMPACT

This rapid identification of asthmatic phenotypes based on molecular profiles may facilitate clinical investigation on the etiology, pathogenesis, and intervention for asthma. The technology will directly reduce the costs associated with severe refractory asthma.

PATENT DETAILS

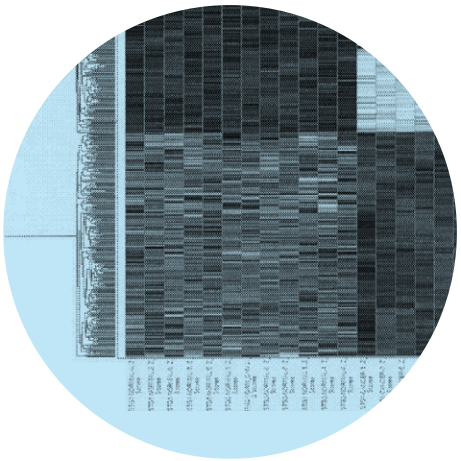
Renal Cancer Therapy

PATENT TITLE

Methods for Detecting, Diagnosing and Treating Human Renal Cell Carcinoma

PATENT # US 8,361,721

INVENTORS | John A. Copland, Bruce A. Luxon, Christopher G. Wood



PROBLEM

Renal cell carcinoma (RCC) represents a major health issue. The American Cancer Society predicts >30,000 new cases annually in the United States, with ~12,000 people dying of the disease. When clinically localized or even locally advanced, renal cell carcinoma can be surgically resected using a variety of approaches. With metastatic progression however, renal cell carcinoma is incurable, and existing systemic therapies are largely ineffective in impacting disease response or patient survival. The lack of effective systemic therapy for metastatic renal cell carcinoma is due to a fundamental lack of understanding of the molecular events that result in cellular transformation, carcinogenesis, and progression in the human kidney.

The advent of gene array technology has allowed classification of disease states at the molecular level by examining changes in all mRNAs expressed in cells or tissues. Gene expression fingerprints representing large numbers of genes may allow precise and accurate grouping of renal cell carcinomas. Moreover, large scale gene expression analysis has the potential of identifying several differentially expressed genes in renal cell carcinoma compared to normal renal epithelial cells. These genes or markers may be further tested for clinical utility in the diagnosis and treatment of renal cell carcinoma.

SOLUTION

This novel technology provides methods of gene expression profiling for human renal cell carcinoma. The technology identifies genes with a differential pattern of expression between different subtypes of renal cell carcinomas and normal renal epithelium. These genes and their products can be used to develop novel diagnostic and therapeutic markers for the treatment of renal cell carcinomas.

POTENTIAL IMPACT

The technology overcomes limitations of current technology by accessing the molecular differences between renal cell carcinoma and normal renal epithelium. The technology can be used to develop precision personalized medicine for later stage renal cancer patients, giving hope to many.

PATENT DETAILS

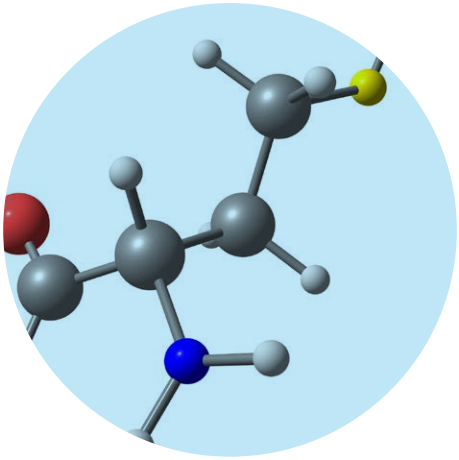
Theoretical Protein Analysis

PATENT TITLE

Ensemble-Based Analysis of the pH-Dependence of Stability of Proteins

PATENT # US 7,027,969

INVENTORS | Vince Hilser, Steven T. Whitten



PROBLEM

The solution behavior of a protein is a direct result of its chemical composition in coordination with the various conformational states it may adopt in the aqueous solvent. Enumerating these states and their free energy differences provide the information required to interpret stability, binding, allosteric effects, cooperative interactions, and function in terms of structure.

Structural and energetic cataloging of states other than the native structure observed in crystallographic and NMR studies has proved elusive and exceedingly difficult to obtain by experiment due to the overwhelming free energy domination of the native state. But many observed protein phenomena are difficult to understand without postulating the existence and population of partially folded states.

Proton titration offers an ideal experimental technique to probe the local stability of various regions of a protein. Theoretical interpretation of proton binding curves is particularly informative because 1) protons bind non-homogeneously and to well defined sites, 2) the pKa of each binding site can be calculated directly from electrostatic theory.

A difficulty in using proton binding techniques is determining the ensemble of states populated at any solution pH and quantitating their structures and stabilities.

SOLUTION

This novel technology utilizes the COREX algorithm to generate an ensemble of partially folded states based on the crystallographic structure of a protein. The technology provides pKa values by capturing the cooperativity of proton binding, the pH dependence of stability, the role of specific titratable residues in the pH dependence of stability, and the contribution of electrostatic interactions to the overall energetics of a protein.

POTENTIAL IMPACT

The technology is the first to address the role of partially folded states on the pH dependence of stability of proteins and how the electrostatic contribution to stability is tightly linked to structural dynamics.

Predictive modeling can be used instead of expensive and time-consuming crystallographic techniques to advance protein therapeutic investigation.

PATENT DETAILS

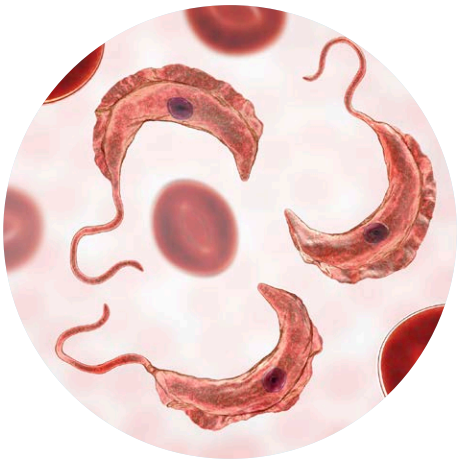
Trypanosoma cruzi Treatment

PATENT TITLE

Compositions and Methods for Detecting Microbial Infections

PATENT # US 9,250,239

INVENTORS | Nisha J. Garg



PROBLEM

American trypanosomiasis or Chagas disease is caused by an Trypanosoma cruzi infection and is the prime cause of death in young adults in endemic areas of the American continent resulting in 50,000+ deaths, 1 million new cases, and loss of 2.75 million disability-adjusted years per year.

Dogs are the most frequent blood meal source for the domestic triatomines. Triatomines are several times more likely to take their blood meal from dogs than from humans. Studies conclude a) dogs are important host blood sources for domiciliary triatomines, b) the risk of T. cruzi infection in humans is increased by the presence of infected dogs, and c) strategies that can limit T. cruzi infection in the reservoir host would be effective in interrupting the parasite transmission to the vector, and consequently, to the human host.

The mathematical models based on epidemiological data suggest that vector control would be the most effective strategy against T. cruzi transmission. However, sustained vector control, followed by constant surveillance, requires large-scale insecticide spraying every year that is not cost-effective and affordable for developing countries. Concerns also remain that insecticide use in the long-term may not be efficacious in blocking T. cruzi transmission, owing to the development of drug resistance by triatomines. The same epidemiological models indicate that dog vaccination would be the second most efficient approach.

SOLUTION

This novel technology provides vaccine, a diagnosis composition, and a treatment for control of T. cruzi infection and disease development in humans and dogs.

POTENTIAL IMPACT

In addition to providing a cutting-edge detection and treatment option, the technology can be used to screen large scale workforce to prevent potential contamination of the donor blood banks. The technology can also be effective in reducing the amount of harmful insecticide used to eradicate the Triatomines vector.

PATENT DETAILS

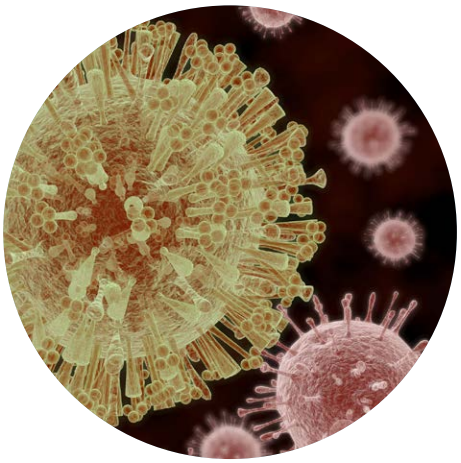
Zika Virus Detection Assay

PATENT TITLE

Method and Kit for Detection of anti-Zika Virus Antibodies

PATENT # US 10,317,413

INVENTORS | Susan Wong, Pei-Yong Shi



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, however, the diagnostic window for detection of viral components is narrow. Therefore, host immune response-based assays play an important role in diagnosis, among which ELISA and PRNT are the two most common.

Serologic diagnosis of ZIKV infection relies mainly upon ELISA which is confounded with the flaw of cross-reactivity among different flaviviruses and the cross-reactive nature of anti-flaviviral antibodies conventionally used in such diagnostic tests.

ELISA results typically require neutralization tests like PRNT 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

A novel method has been developed for detecting the presence of an anti-Zika virus (ZIKV) antibody in a sample. This technology uses microspheres conjugated to a peptide from a group including ZIKV NS1, ZIKV NS5, and ZIKV envelope proteins. The sample is incubated with the microspheres to permit binding of anti-ZIKV antibodies. A second anti-ZIKV antibody detecting-reagent is introduced to permit binding of the anti-ZIKV antibody detecting reagent to the microspheres. A wash step removes unbound antibodies followed by detecting the presence of anti-ZIKV antibody detecting-reagent molecules in the second incubated suspension.

POTENTIAL IMPACT

This novel technology overcomes the limitations of current testing protocols. This technology will better diagnose ZIKV and help understand the epidemiological spread of the virus and support vaccine candidate testing. This detection technology can be configured for other viruses.

PATENT DETAILS

DiH
EDITION

Intellectual Property Showcase:
Diagnostics

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

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